U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMITTEE ON HERITABLE DISORDERS

AND GENETIC DISEASES IN NEWBORNS AND CHILDREN

Monday,

January 14, 2008

Grand Ballroom Salon E

Marriott Bethesda North Hotel and

Montgomery County Conference Center

5701 Marinelli Road

North Bethesda, Maryland

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C O N T E N T S

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P R O C E E D I N G S (9:40 a.m.)

DR. HOWELL: Ladies and gentlemen, good morning. Let me call to order the 12th meeting of this committee. It's the first meeting of the new year, and it's also the first meeting that's not been held in the District of Columbia. So we hope that things will go well out here in the boonies in Maryland.

Look at your agenda. We've got very busy activities over the next two days and so forth, a lot of important presentations. We will introduce later, in a bit more formal fashion, five new members who have just had their ethics briefing this morning, and I trust that they are feeling extremely ethical at this point. Their biographical sketches are in the agenda and so forth, and obviously these are all people of great accomplishment, and I will introduce them fairly briefly in a few minutes.

We have a variety of very informative sessions I think lined up. We have presentations from four different newborn screening programs and systems. We'll hear from Region 4 about their efforts on long-term follow-up. We will hear about PEDIATRIX and their work with Nebraska. We will hear from the New England Newborn Screening Program and the Northwest and Pacific programs. This will provide a variety of different approaches and supporting infrastructures for the newborn screening programs with the different partnerships and so forth, and I think you will be particularly interested in the infrastructure created for the long-term follow-up.

We will also have a legislative update from Mr. Emil Wigode of the March of Dimes. As you know, we obviously, in addition to having lots of primaries that we are all inundated with at this point, there has been a substantial amount of activity in the legislative arena on Capitol Hill. That's always very exciting.

We will also have some recent information from the newborn screening program of the Federal Personalized Healthcare Workgroup, and that will be presented by our colleague, Dr. Steve Downs. Then we will break up later today, as is our custom for the three subcommittees, and then we will hear about their reports tomorrow.

Tomorrow we will begin with the reports from the subcommittees, and we will also have Jim Evans present activities on the Secretary's Advisory Committee on Genetics, Health and Society Task Force on Gene Patents and Licensing Procedures. It's obviously beneficial to hear about the activities of that committee, where there is considerable interest in the same activities that we are dealing with. We will spend a good deal of time on our nomination and evaluation process for candidate conditions for newborn screening panels, and those discussions will be under the leadership of Drs. Perrin and Green, who are dedicated to this process.

I might point out that we would very much appreciate it if everyone would review the nomination packages that have been cleared through HRSA before the discussion tomorrow. The members of the committee have summaries of those nomination procedures.

We are going to then have a presentation by Dr. Marie Mann, who will present the HRSA review process and so forth. In the afternoon, we will have our important public comments session, and there are some very interesting things which have already been signed up there. I think you will find that particularly informative tomorrow.

We will end the meeting with committee business and draft the agenda for our May 2008 meeting. One of the things that I will add to that discussion tomorrow is the issue of authorship and committee and workgroup reports. Let me just give you a brief vignette of that. One of the things that we've been very interested in accomplishing is having all the products of this committee be summarized in an effective way and published in refereed journals, because that way the products of this committee will be accessible for other people's use and so forth, and it's very important that we really have some policy about how the authorships are worked in that, so that that will be an established thing.

If you look at your agenda, the first thing we are supposed to do this morning is to approve the minutes of the 2007 meeting and the minutes of the November 2007 conference call meeting, which I think went very well. I'm going to ask your indulgence to postpone that until tomorrow. Denise Dougherty, who is a member of the committee, had some comments about those minutes and would like to make them personally. Unfortunately, Denise has had a death in the family out in the Midwest and could not be here today, but she will be back tomorrow. So she would like to make comments about those, and then we can review them at that time if that's good with you.

At the last meeting, as you know, we acknowledged several departing members and provided elegant certificates signed by the Secretary, and it's now my pleasure to introduce five new committee members who are tremendously qualified and admired professionals with a variety of expertise which I think will be extremely suited for this committee. I will go through those folks alphabetically, nearly alphabetically, but close to being alphabetically. The hyphenated name ended up at the end for reasons I'm not completely sure of.

But anyway, be that as it may, the first is Dr. Rebecca Buckley, who is sitting directly in front of me. Becky is an expert in pediatrics, allergy and immunology, and is the James Buren Sidbury Professor of Pediatrics at Duke University Medical School. Her credentials are summarized more extensively, but she is a recognized international expert in immune deficiency diseases and the treatment of these conditions, and has been a leader in this area for many years. Recognizing her distinguished contributions has been her recent election to membership in the Institute of Medicine, and we are delighted to have Becky here with her expertise as we move forward in considering immune deficiencies.

Dr. Ned Calonge is the chief medical officer in the Colorado Department of Public Health and Environment. He is also the chief medical officer of the Colorado Department of Public Health and Environment as an epidemiologist, and his expertise as a leader in one of the major state programs will be extremely beneficial. We welcome you very much to the committee.

Tracy Trotter, who is seated to my left, right here near Duane, is a general pediatrician with expertise in children with special health needs. Tracy is based in San Ramon Valley, California. It's hard to call him a general pediatrician because he's been involved in so much activity at the national level, in policy development, and he worked very closely with the American College of Medical Genetics under the HRSA contract that generated the document that has been the source of so much discussion in this committee and elsewhere. Tracy, we welcome your presence very much.

Dr. Gerry Vockley, seated again almost directly in front of me, is a distinguished geneticist recognized for his basic research and treatment in the area of inborn errors of metabolism. Gerry is at the University of Pittsburgh, the chief of medical genetics at Children's Hospital at that institution. He also is a recent past president of the Society for Inborn Errors of Metabolism. Gerry, we look forward very much to having your expertise on this committee.

Finally, Dr. Ohene-Frempong is a pediatric hematologist with a special interest and expertise in sickle cell disease. He is a member of the staff of the Children's Hospital in Philadelphia, where he is associate director of the sickle cell center there. And we welcome you, since obviously your expertise is in an area of great interest to this committee. Thank you very much.

That is the list of the distinguished new members of this panel as we move forward.

(Applause.)

DR. HOWELL: The only other thing as far as membership, at the last committee I got a certificate of appreciation, almost like some of the people who said that messages of your death are premature. But anyway, the Secretary has reappointed me for another four years to the chair of this committee.

(Applause.)

DR. HOWELL: And I appreciate that. I think this committee is really moving into high gear. It is doing some really important stuff, and it's my privilege to work with you.

In view of the fact that we're not going to deal with the minutes, I would like to have your indulgence to skip the break since we just got seated and move into Susan Berry's presentation. Susan is going to be talking about -- Susan Berry, I might point out, was on the agenda of the meeting earlier which we canceled, and we apologize for that. Dr. Berry is currently co-leader of the Long-term Follow-up and Outcomes Committee for Region 4 of the Genetics Collaborative and is a principal investigator of the Region 4 Collaborative Priority Project 2 for HRSA initiation for this presentation. Dr. Berry is Professor of Pediatrics and Genetics and Cell Biology and Development at the University of Minnesota, and we welcome Susan very much to talk about the long-term follow-up in newborn screening of inborn errors of metabolism system.

Susan?

DR. BERRY: Thank you for the opportunity to share some information about this. I am just going to escape from that and start this up, and then we'll roll.

I hope you all like our lovely logo for Region 4, which has been one of the most fun things I had to do professionally in a long, long time. I am actually speaking on behalf of our Priority 2 Project Workgroup, a really interesting and dynamic group I think that's made a lot of progress.

So I'm going to tell you a little bit about our progress in developing, if you will, a mechanism for actually trying to follow kids beyond anecdotally. So let's see how that goes.

The first thing that I wanted to acknowledge is our Region 4 collaborators. It seems sort of self-evident that you wouldn't necessarily need something like this, but I just have to tell you how much has gone into everyone working together in our region, both metabolic clinicians and our state health department newborn specialists, who have formed a really interactive and helpful team in creating new ideas about how to do better long-term follow-up, and we couldn't do it without working together. So between the clinicians and the state newborn health departments, we are just really moving right along.

I put in this other piece. Hopefully, as things go along, if people want to participate in this, there will be opportunities. It's relatively straightforward to do so.

I'm totally speaking to the converted here, but I always think about this when I think about the project that we're doing. We have issues of justice. We need to be fair to everybody. We want to improve outcomes and save lives, but newborn screening is only as effective as the care it ultimately prompts. All the work that many of the people around this table and in this room are doing is about that.

You need to have close collaboration between the screening team, the short-term follow-up team, and long-term care if you really want the screening to do what it was supposed to do, which is to make things better for kids.

Data sharing is going to be essential at many levels, and once again you have to talk to each other. You have to collaborate. So why was this useful in Region 4? Well, we had a lot of babies born there, and we had a commitment to cooperative interaction between the metabolic clinicians in the region and the state departments of health. At the time this all started, we were also unique, although this has changed with time. All states were screening with tandem mass spectroscopy. Everybody knows that selected disorders are common enough to develop protocol, but only a few share, only if you talk together, only if you work with each other. I may have five or six kids a year with MCADD, and that's not

going to do anybody any good. I'll take good care of those individual children, but without us working together we will never have the numbers to get anything meaningful. In our region, that becomes a doable task.

So you guys know all about how this works. How do practitioners decide to treat inborn errors of metabolism? You can only treat things if you have them all there together and you find out how your mentor treated. There are some texts and manuals and guides. I know Mike is working really, really hard to develop, for example, consensus statements on treatment. What has everyone learned from experience or what do our listservs say? Well, the truth is that we haven't had any organized strategy. There is no evidence-based care for this, so we thought it would be very important that that happen. The currency for evidence-based medicine ultimately is controlled trials, but to date there are almost no controlled trials in inborn errors of metabolism because they are rare diseases and they affect primarily children. That may be over-simplification, but the bottom line is that it doesn't exist.

So how do you make that happen? Well, Bob Steiner in 2005 wrote a nice piece for the American Journal of Medical Genetics where he talked about the need for collaboration between centers where you needed both federal and state support to encourage this. You needed to teach the principles of evidence-based medicine in clinical genetics training. We've always been so anecdotal, and we can't do that anymore.

He spoke highly of improving the precision of terminology so you can have people find information, and you need to publish. Can you do this? Well, obviously you can. Childhood cancers are rare diseases, but they have national cooperation, and almost all kids with cancer get treated in research protocols. So there is no reason why the metabolic disease community can't do the same thing.

So what are the challenges? Obviously, the diseases are rare and they affect children. We've already mentioned that. There is quite a spectrum of clinical severity. For me, this next point is the hardest one, which is that it's hard to justify testing accepted treatments which seem to work but for which we have little evidence base. You don't want to throw the baby out with the bath water for doing a good job in treating something. That's great. But if we don't have the evidence for it, it's a little hard to really justify that in some ways. We have really little existing data about the long-term outcomes for these children. It just isn't there. The other thing is that all these things cost money.

I had no idea when I started in this that this was going to turn out this way. We had no idea where we were going to go, but we decided, well, what the heck. So our region undertook this initial project in the first three years of the cooperative activity. Our charge was to develop and implement action plans to address long-term newborn screening follow-up and evaluation. Our original plan was to create standardized diagnostic and medical management protocols and to evaluate the clinical outcomes. But one of the problems was to evaluate the clinical outcomes by identifying elements for outcomes. Well, we were just not sure where this was going to go, but we realized something important relatively early on, and that was that we had to have a way to track this information. If we didn't have a way to capture the information, we were going to go nowhere. So we created as our initial project a registry for medium-chain acyl-CoA dehydrogenase deficiency, MCADD.

We realized that initiating a treatment protocol is a great concept. That's where we wanted to go, but it was going to be really hard to pull off, particularly on a short-term basis. The second thing was -- and I put this in quotes because I was advised by my friends in the heartland region that they were absolutely correct. We can't call this "natural" history. We've already interfered with natural history. There ain't nothing natural about catching a kid prospectively, thank God, because we don't like the natural history outcome. We think it's a bad thing. We want good things to happen. So I am putting "natural" in quotes because it's really more the clinical history, but we don't know what that is. We don't know what the assessment of outcomes will be, and we don't know how we will change that when we apply new protocols.

There are lots of clinicians, there are lots of successful strategies, and who is to say which one is the best? No one. We don't have any way to do that. So what we had to do was to gather uniform data and assess those clinical practice differences, and that might be one way to learn which treatment strategies are most effective. Who is to say that your way is better than my way? But if we collect the same information and my way turns out better, maybe mine was smarter, or yours. It's probably mine.

(Laughter.)

DR. BERRY: Okay. So what happened? Well, we said this is a great idea. How are we going to do it? We realized that it wasn't going to be enough to do just one disorder. We were going to try to gather information on more. So the point is a large-scale follow-up record for exactly the kind of research we ultimately wanted to do. You had to have a way to capture the data. So we started with our one disorder, MCAD deficiency, and we developed a demographic database and disease-specific data elements. We wanted to define which issues were most important in the short and the long-term follow-up for that particular disorder, and we wanted to agree about how to add additional disorders. We had to have a rational way to continue capturing information so that it wouldn't be such a big bite. Start with one, add others, and include the information.

So we decided to start with this condition registry as a research platform. We were going to plan interventions that can be assessed with the data that we captured in our information system. In our initial project it seemed likely, although this is something we want to make sure everybody on the team is working on together, to again examine natural history and short-term outcomes. As soon as you have 50 new babies, you can immediately talk about risks and issues and concerns that might take place in the newborn period, which I think has evolved even as we speak about what the risks, for example, for MCAD deficiency are in the newborn period. Certainly my thinking has evolved.

Now, the thing that's most important in this situation is that at the time, this is a prospective consented participation. Patients who are enrolled in the database sign a prospective consent, and one of the things that they can elect to do, and so far all but one of the people we have enrolled in our own center, for example, have agreed that they will allow contact, continuing contact, and this is really important because that will allow us to engage them as participants in future research trials. This is the exciting part, because now we have a cohort of patients who we are following, on whom we are collecting data, and then we can standardize conditions for evaluation and can undertake a specific project.

So just to tell you a little bit about how we end up deciding on the data elements, because there is no way to start this except to start, and what we decide to do is not necessarily what somebody else in another region or another group might decide to do, but we tried as much as we could to develop some consensus about what information would be included. So we did a review of the literature and existing plans for treatments in our region, and we were so grateful to our friends in the Mountain States Collaborative because they had set up a whole bunch of disease treatment protocols that their physicians have a consensus group to do, and we incorporated the information from those treatment protocols into our data gathering.

We identified all the elements in our region that we agreed were essential and that everybody should do the same, and then we also identified a series of elements that were sort of anecdotal, and then we could ultimately, if we chose to, be subject to randomization in the formal sense. Everybody in our region contributed treatment protocols so those elements of difference could be characterized. The Mountain States gave their information so that we could also build in other large clinical groups' consensus ideas. So we hope that we captured to some degree the questions that people want to ask about any given disorder.

There were some really critical agreements that we had to have. We had to have an easy entry, and we had to set it up so that we had enrollment data so that once somebody was enrolled, they had a whole series of interval histories that we could take. We had to have it Web-based so that everybody

could get to it easily. We didn't want to have to import the data, ultimately. We wanted it all to be there. We needed to have checklists so that people could use them with facility, and there are those who haven't gone to a fully electronic medical record. They could have a paper copy. There are a lot of people who are happy to have a paper copy. We are happy to have a paper copy.

We wanted local control of the private health information that would be generated, yet we needed to be able to share that in a way. So it had to be in the context of a medical record-like activity. We had to have everybody have the right kind of access. We had to have local enrolling centers have access to their data, and ultimately one of the things we need to do, and we think this is one of the reasons why this is a particularly valuable project is it allows departments of health to have access under their public health mandate and they can use this to do follow-up if they choose.

We wanted to have everybody share in the glory that came from all of this, and we wanted to have everybody participate. Everybody in our clinical group was going to be in our advisor group planning for access to the database for research activities. We think this is really important, so we have sort of a scientific workgroup as well.

Again I think our initial projects are going to be descriptions of natural history and short-term outcomes. We needed a relational database with core elements linking to disease-specific elements and tying those to interval elements. If possible, we also wanted to be able to have individual centers also have care plans that would be evolving from some of the things we were following, and particularly for some centers who are really aggressive about this, we wanted to have great developmental evaluations. So we have a whole survey just for neuropsych and psychometric evaluation.

We wanted to do this fast, and so we didn't feel like we could build our own database. It's expensive and difficult and there are smart people who can do that, but we weren't prepared to do that. So we turned to a commercial product, and we've chosen as our instrument DocSite, which is a commercial product. It's a relational database platform, essentially. So because it's linked to medical records, its HIPAA compliant. There is a relative ease of entry at their point of service. It has reporting functions. It's easy to add elements into and to amend those elements for data management and monitoring, and it's relatively easy to export the data for analysis.

This is a slide that the folks at DocSite gave me. Their idea is to be able to connect things together, and since that was congruent with what our goal was, I was glad that seemed to be the priority they had. This is directly from them. They obviously are interested in public health and quality assurance measures. This is what this particular database is good for. That's what we are trying to do, too.

So one of the things that you can do with DocSite -- this is also their slide -- is to be able to have some flexibility in data collection, and it's dynamic for the project needs. You can adapt it and change it with relative facility. That means it's probably good for both us in the clinical care arena and our partners in public health. We are not going to be able to do this without that collaborative interaction.

This is a screen shot of what the demographic information is that comes up. It looks like a standard medical record. For MCADD, for example, we had enrollment and interval update as separate conditions. They are really not. They are really one condition, obviously. But it allows us to separate interval updates from the initial enrollment so that you can continue to enter data continuously on an individual child on a long-term basis.

This is a screen shot of what a visit planner looks like. It has the last data that was entered. It has the dates of the last entry, and it allows us to create on a long-term basis follow-up information. This paper planner can be printed so that somebody can take it with them to the visit and record information. For some people this also can serve as a medical record item that would make it easier for the practitioner who is doing it not to have to write an additional note. It's a small benefit to the people who are working on it.

The data entry is pretty straightforward. It's drop-down menus and click boxes. So when you have the information in front of you and you know what's going on, you can enter and enroll somebody in 10 or 15 minutes max. You can do an interval visit in less time than that. So it's really quick to enter, and that's really important because it's so much work to keep up with stuff like this. So as we've become more familiar with the process, it really is pretty straightforward to both enroll and to continue the data elements follow-up for those individuals.

One of the things that's kind of nice is that you can actually filter out reports for exporting the data. You can set it up as XML, you can set it up as Excel, or you can set up PDFs. So you can have report functions that may be valuable not only for our research activity but may be helpful to departments of health reports as well.

I don't know if we have Internet or not. It looks like we did. At the end I'll go back to it if we have it. I'm going to keep going. I'm going to go through the rest of this and then I'll come back and show it to you if it looks like it's working out.

So our MCADD registry actually evolved from just a single disease to what we hope ultimately will track most of the disorders, certainly the primary disorders, and also the secondary disorders that are going to be identified. That means all the new things you add -- it will be fun to add new things, new elements to our database as they come up. We selected a host that uses that Web-based EMR technology so that it links to medical records. The whole point would be ultimately we would like to tie these to electronic medical records so that this data would serve as part of the record of the child both on a clinical as well as a research basis.

We have engaged the majority of the treating centers in our Region 4 area. We have actually added metabolic leads in some of the larger states because some of our states are big enough that one person needs help and support. We have IRB approval that is already in place in Minnesota, Illinois, Wisconsin, and Ohio. We've begun registry entry for MCAD deficiency for both new and interval. We added the elements for MSUD. The rationale for how we add disorders is we thought we would just add one per group. So we picked an MSUD because someone had a specific interest in it. So now we have the elements ready to go for MSUD. Surprisingly, about 85 percent of the elements we have for MSUD are exactly the same elements that we had for MCAD deficiency because it had to do with the general health and well-being of the child. There are disease-specific elements such as leucine levels and some things like that that we added for MSUD, but surprisingly, the things you want to follow on any given kid are the same from disorder to disorder. So we're going to have a relatively straightforward time adding new elements because the bulk of it is the same. There is not as much to discuss.

So we worked really, really hard to make MCADD perfect, as perfect as one can make things like that. You can't. But it was surprising to us when we got ready to add MSUD how much they had in common as far as what you wanted to follow.

The next thing we did was to define elements for long-chain fatty acid oxidation disorders to extend the category to see if that paralleled, and surprisingly it was nearly mapped, except that obviously we are capturing the newborn screening data, so obviously the things you are going to capture are different from disorder to disorder.

Here was the big bite, and everybody was so brave in our group. I was so proud of everyone for taking on both C3 and C5 hydroxy disorders so that we could start our work with organic acidemias. We decided to include biotinidase in there because it was intellectually related, but it is of course a different class of disorders. That was our third MS/MS category, organic acidemia. So now we have elements for things from which we can build a matrix to add elements.

We are enrolling all our clinic subjects as they give permission. So we are not waiting to see their database. We are enrolling them, and as soon as we have data entry points for any disorder, we can

start adding people to the registry. We are entering new disorder data as the elements are added to the database. So far we have defined the elements for 19 disorders of the primary and secondary panel. The Center so far enrolled 89 subjects, 31 with MCADD, 5 with MSUD, 17 with organic acidemias, 17 with long-chain fatty acid oxidation disorders, and a handful of others because we figured what the heck, we'll just sign everybody up when they come to clinic. So that is basically since June or so, when we started. We have enrolled 89 subjects, entered data. All the MCADDs are starting to enter data. So a third of the patients have had data entry, and more to come.

So what next? Well, obviously, one of the things is defining the strategy and research. We have, I think, worked to attain generally uniform follow-up and reporting, but now we have to have consensus on what questions to ask. We have to add our next disorders. One of the things we've been talking with a lot of folks about is the possibility of doing a specific intervention project using the MCADD information. The project we have kind of tossed out is the idea of testing the outcomes when you use low dose, just barely keeping people's carnitine levels normal, and high dose. Does giving high-dose carnitine protect kids with MCAD deficiency? I don't think we honestly know the answer to that, and so that might be one project that could take place. We have the way to follow it. We have the way to monitor that because we capture things like how many hospital visits do they have, how many emergency room visits, how many days do people spend in the hospital, that kind of information, and we have developmental data.

We had our fall meeting and we had a request for a project, and we talked about a project for the effects on families. One of our committee members is the parent of a child with MCADD who also happens professionally to be a social epidemiologist. So he is very interested in working with families to develop projects for follow-up with the effects on families. Obviously, we want to look at assessment of early MCADD complications, something that clearly has emerged as a prominent part of the management of MCAD deficiency.

We want to work toward integration of our data. It would be nice if we could import the data directly from the newborn screen into the database and vice versa, if the people at departments of health could export the data for their long-term follow-up mandates. We also want to integrate this with emergency services, so we have initiated a project with a Web-based emergency plan activity so that our kids with rare metabolic diseases can have Web-based emergency plans. I'm just going to show you the screen shot for that. One of the things that this would allow is it allows families to directly give access to their emergency plans, or in an emergency room a doctor can break the glass. It turns out you don't want to say "break the glass" with certain cultures. It's inappropriate. It makes people upset. So provide emergency access to the Web-based emergency plan. We would like to have the information system talk, if you will, back and forth to the emergency plan. So we are hopeful that that will take place.

Before I show you the live, if I can show it to you live, I want to acknowledge the interactive collaboration of all the members of our committee. I want to thank Cynthia Cameron for her leadership and insight into how to make a region work together when people might not necessarily want to talk together, and surprisingly people do like it. We have learned to like doing it. I want to acknowledge Sally Hiner, who has been our project coordinator who has been really, really helpful. I want to thank Carolyn Anderson, my partner, who has been working with me directly on leading this project and who is recovering from her second hip replacement in a year. So I hope Carolyn is getting better. My nurse coordinator in our clinic who has been our newborn screening coordinator for Minnesota, I don't think we could have brought the energy to this project that we did without our state collaborative activity. So, Piero, thank you for all the things that we've done together in the State of Minnesota.

Our project epidemiologist and all the members of the committee, you see the list of our state leads as well. Everybody has contributed their intellectual time and energy to this, and it's been a lot of fun.

Let me see if we can do this. I will try it. If it works, then that's good. If it doesn't, I'm happy to show this to somebody at any other time. No, it's not going to work. Anybody who wants to see it, come

see me and I'll show you how you get in, what it looks like, and how easy it is to move around and get data, because we have a great demo site and I am really happy with how it is moving along.

If people have questions they want to ask, I'll be happy to provide any information. Go ahead.

PARTICIPANT: Did you buy the password?

DR. BERRY: No, we didn't buy the password, so I don't think we are going to go in. It's really okay. Anybody who wants to see it, I can show it to them. It's really no problem.

DR. HOWELL: Becky?

DR. BUCKLEY: Hi. I have a question. I am Rebecca Buckley. How did you handle the consent form development? With so many different centers, did you use Western?

DR. BERRY: No, no. I wrote the consent form. Kristi and I wrote it together, and then what we did was give people a disk with all of our forms, with our submission materials, with any conflicts that we raised with our own IRB, and we made ourselves available to provide additional information, and really it's been surprisingly good because of the way we've got it set up, with local access only for PHI to a large extent. It fits into expedited categories. So it has really moved along. Our biggest barrier is that individual IRB's charge to walk through the door. Some of our centers haven't been able to afford that because we didn't budget for it. We didn't know we needed to.

DR. BUCKLEY: So not all of your centers have the consent form, then.

DR. BERRY: I'm sorry?

DR. BUCKLEY: Do all the centers have your consent form?

DR. BERRY: Yes. Oh, yes. Anybody who wants it can have it. I don't care. So we have actually put it up on our website.

DR. BUCKLEY: So you don't have to get any local approval? Is that what you are saying?

DR. BERRY: We do have to get local approval. Each center has to do it, and that's a big task. We tried very hard to set it up so it would be the minimum amount of work. We didn't want to set it up so it would have to go through full committees everywhere. So it's appropriate for expedited approval.

DR. BUCKLEY: When you consent someone to become a part of this, have you had any people who turned you down?

DR. BERRY: We had one patient turn us down, and that's fine. They can choose to be involved. What we have to be really, really careful about is that the way we built it, we built consent to recontact into our HIPAA form, and we have to make sure that when you are doing that discussion, the consent discussion, you make sure that they read the HIPAA form, because people have a tendency to go on, and there is a check box on there, and if they don't check it, you can't recontact them. You can gather the data, but you can't enroll them in other trials. So we are really trying very hard to make sure people know to do that.

DR. BUCKLEY: My last question is who has access to all the information?

DR. BERRY: I do as the project leader. The epidemiologist on the project has access, and that's it. Those are the only two people who have access to all the data. Each center has access to their own data completely.

DR. BUCKLEY: So there are scientific data that you can mine, and who has access to that?

DR. BERRY: Our epidemiologist has access to that.

DR. BUCKLEY: Thank you.

DR. CALONGE: How are you going to resource this long term so the maintenance funding -- I assume it was funded for --

DR. BERRY: It was funded for five years. You know, I don't know that we know the answer to that completely. It would be a shame to have it disappear after five years, but that's one of the risks one takes when you start something like this. It's not particularly expensive. I mean, the data will still be sitting there because we pay for licenses.

DR. CALONGE: That's the other question I had. Will you be able to provide other people in other states with a feeling for what the maintenance costs might be if we signed on other regions?

DR. BERRY: So if the company that has the server keeps going, then basically what you pay is a license fee every year. If you don't, then you export the data and have it sit in a database. You might not be able to add to it, but at least it's still there, because it's not hard to export the data. So we figured what the heck, set it up, let it slide, and see how it goes. I know that's not the smartest or the most forward thinking or maybe the easiest way to do it, but we just had to start. The data is exportable to move and map someplace else if you choose to do so, and we are fully cognizant of the idea that there may be other plans for what happens nationally on a larger scale. What we're really hoping to do is encourage appropriate mapping of our data, and most of it is standard data, lab results, demographics. That kind of stuff is going to map to other places. The hardest part is the little capricious, unusual things, to have it map onto other databases. So we are working with Mike and others to try and maximize the possibility that if there is a meta-database for the world or something like that that emerges, that our data will map onto that. But we didn't want to wait for that to happen, so we just took off.

DR. HOWELL: We have a comment from Sharon, and then from Tracy. Tracy first.

DR. TROTTER: The emergency plan, do primary care physicians have Web-based access to that plan?

DR. BERRY: Yes. That's the best part of that emergency plan. The family, the metabolic specialist and the primary care practitioner have access to that plan. There is an icon-driven note on there so you know whether it was a medical practitioner or the family that adds the data. But all three can, and we encouraged all three to do so.

DR. TROTTER: So when we have an interaction with the patient, it can then be entered immediately into a database?

DR. BERRY: Information that needs to go for the emergency and the primary practitioner wishes to add to it, yes, absolutely. That was one of the attractive parts of that particular sub-project, that it was something that the metabolic specialist, the family, and the primary care provider could share together in developing these emergency plans. So we really liked that aspect of it. We are really excited about how that's going.

MS. TERRY: Susan, I have a lot of concern about the way that we characterize evidence in rare diseases, and a couple of times you said evidence equals controlled trials.

DR. BERRY: That's one part of developing evidence, but actually just having the information will be evidence as well. Absolutely.

MS. TERRY: Okay, because AHRQ has certainly given us a number of ways, especially with rare diseases, for us to look evidence, and I wanted to be clear about that.

DR. BERRY: I think without the platform to gather the data, it would be hard to say you have evidence. But there are a lot of different ways to mine that. You can certainly use it if you choose to do a controlled trial. You can certainly use the platform to gather the data from it. But more importantly, just the clinical history of what happens is itself evidence of outcome. So I completely agree. It allows you to do both things.

MS. TERRY: Okay, and just one other question. So right now, just your epidemiologist has access to the data. Will you be looking at the kinds of systems we are seeing being set up around other big data gathering, like GAIN and other projects, to allow other investigators to have access to that data?

DR. BERRY: Our plan for allowing others to have access to the data would be to have our advisory group -- we're going to have a process by which people can submit a request for essentially access to the data, the information, and as a group we will evaluate the scientific nature of those points. You don't need the names of people. You just need the data, and the data we can give access to, but we want to do that in a collaborative and cooperative fashion.

So, yes. Of course, we want access today. We just don't want people to access the PHI.

MS. TERRY: Right.

DR. BERRY: That's the limitation, the private part.

MS. TERRY: I'm serving on the GAIN Steering Committee and we've worked a lot on how to access data like this and what should be the qualifications. So you might want to look at that policy.

DR. BERRY: That would be great. Anything we can do to strengthen our ability to do that in a fair and equitable fashion is great, because we see this as a public resource. We want people to think about projects that they can gain information from by accessing this, and it's not just our region. If people have an idea and they think that this would be helpful to them, if they think that our region's data could help them, we want people to access it.

DR. HOWELL: Chris has a question.

DR. KUS: You talked about an expanded neurodevelopmental section of this. Are there agreed protocols about tools that are used? How is that developed?

DR. BERRY: Well, we know that there are a lot of different people's favorite tools. So what we did was we incorporated essentially the results from a whole bunch of standard tools, and that's a separate survey. If your group does one standard and ours does another, and we know they're not necessarily comparable, by golly, we will have developmental data. So we have a lot of stuff. Each disorder has an enrollment survey and an interval survey, and then the neuropsych survey is common to them all. You can assign that to every child if you want to, if you choose to do so.

DR. HOWELL: Ned, did you have a question or comment?

DR. CALONGE: No, thanks.

DR. HOWELL: We have two brief comments. Oh, you have a comment? Go ahead.

DR. OHENE-FREMPONG: Just a quick question. When they consent to enroll in this, is it sort of an open-ended consent from the family and also with the understanding that they may become either eligible or at least approached about future research?

DR. BERRY: One of the elements that we capture in the database itself is permission to contact. So if a person says yes, enroll me and keep my data but no, don't contact me, we have that discoverable. It can be sorted for that. Open-ended? Well, it's a little hard to know how to do this with a registry because once you are in, it's a little hard to take you out. If somebody doesn't want to continue participation, all you do is stop gathering the data on them, but we're not going to take the data back out on the individual. That's cited in the consent form. I know one of the issues is what are we going to do when somebody who has been enrolled turns 18. Our plans are to reconsent children when they become adults.

DR. HOWELL: Coleen had a question.

DR. BOYLE: Two questions. They are interrelated. First of all, it's a wonderful presentation and a very exciting project.

DR. BERRY: Thank you.

DR. BOYLE: My question has to do with sort of the long-term follow-up and tracking and your assurance that you are capturing all of the medical events for the child. I was unclear about how that works. Then again, the second part of the question is that that is obviously a public health function. You said the public health community can have access to the information, but how are you collaborating, cooperating in terms of that assurance of long-term follow-up?

DR. BERRY: So what are we capturing? We did our best stab at this, and we tried to figure out what surrogates we could have. So what we captured is, at each visit you ask the family how many emergency room visits did you have? Were those related to your inborn error of metabolism? If somebody goes in because they got a cut on their hand, that's obviously not related, but we capture that, and we capture whether it was related. We also count the number of hospital days that they have in the interval. Now, these are not perfect surrogates, and it's not the only information you would ever want, but it's a start at being able to look at the impact of what happens in the lives of kids.

In terms of access, the plan would be that because it's set up in such a way that you can grant permission to a user for access to certain sets of data, we can certainly allow a department of health access to all the data from their own state's activities for long-term follow-up. In terms of a larger-scale public health interest, obviously it's in our mutual interest to publish this information and share it. But again, if people have projects specific to this or information that we want to capture, it's not that hard to add or change the elements. We don't want to change them very much because it means you have to propagate them through all the sites, because each site has its own stuff, and you can amend things at each site. So we've got some general agreement about adding elements if mutually the group, the advisory group, thinks it's helpful. So if there are better surrogates than just capturing days in the ER, and we want to add that, then we can do it.

DR. HOWELL: We have some questions from Alan, and then Nancy.

DR. HINMAN: Alan Hinman. This is a very exciting project.

I have two questions. One, have you considered adding hemoglobinopathies or hearing screening to your registry? Because you will find, I'm sure, that 85 percent of the data elements are the same for them also.

DR. BERRY: The thing that's kind of a beauty in this is that you can add pretty much anything you want to sit down and write the elements for. So in our own state, for example, they are talking about seeing if we can't expand the database for us to do that. It's a possibility. Really, it's pretty facile to do so. I mean, this is not the only way to do it, but when you've done the work we've done to start it, it's not that hard to add another disorder.

DR. HINMAN: And the second question is one of the possibilities of the system, and it may be part of it that I didn't hear or that you didn't mention, would be to provide educational materials to the primary care physician, for example. Is it set up to do that?

DR. BERRY: This particular aspect of the project, the information system itself, isn't. But one of the things we can easily add to the emergency plan, and it's totally straightforward to do that, is to add links to the ACT sheets, links to OMIM, whatever you want, so that anybody who goes in, the primary practitioner, the emergency room, the family, can have access to that. It's not that hard to do that. So yes, those are important educational tools for all of us.

DR. GREEN: Hi. Nancy Green from Columbia. This is really remarkable, and I congratulate you for getting so much done. It's enviable.

I have two questions that build on your successes. One is sort of a data question, because I think, as you demonstrated and mentioned as best you could, the data system sort of is everything. So the question is once you start doing prospective trials, however they are designed, will your data system accommodate that or do you envision the use of a different research database?

DR. BERRY: Our whole intent in setting this up was so that it could. Now, whether the elements we've chosen will be perfect for every trial, I honestly don't know, because we can't anticipate every trial. But suppose you wanted to try a medicine trial of some sort. We could accommodate that by adding an element saying is this person on this trial and then add information. It's not that hard to do. It's some work, but it's not hard to add additional elements.

DR. GREEN: Okay. The other question is do you have some system set up for banking samples, clinical samples?

DR. BERRY: For doing what?

DR. GREEN: For banking samples for those who are entered into the registry?

DR. BERRY: We have not done that. I suppose it could be done. We are capturing data if it's there about genotype because we think that will be an important analysis point, but we haven't banked clinical samples. No.

DR. HOWELL: And our final comment is from Dr. Arnold here. Georgeanne?

DR. ARNOLD: Thank you. Georgeanne Arnold, University of Rochester. I also am impressed with this. My question is how are you going to keep it updated? Do you have a person to send to each center to go through all of their 200 medical records to count the number of hospital days?

DR. BERRY: I think that's a challenge, and that's probably the most important thing. No, what we are asking people to do, ironically, although it's electronically based, we're asking people to fill out the visit

planners and hold onto them so that if we have problems with the data, we can go back and capture it. So they are just dropping it into file folders. We talked a long time about whether to have double data entry, for example, whether to have people enter it and then confirm it, and realistically we didn't do that. It's not perfect, but it's the best we're going to do for right now. We're going to see how it goes.

DR. ARNOLD: I guess I would say as this goes forward that's a hole that needs to be filled.

DR. BERRY: It's an additional point of refinement that probably deserves some discussion, but we thought we would see how it goes with people's initial passes on it and see how we do. We are going to be looking for inconsistencies in the data to see if there are problems where we can go back and pick up on individual points.

DR. ARNOLD: Okay. Thank you.

DR. HOWELL: Thank you very much, Susan. We always appreciate your good work, and in addition to your own hard work, we always see evidence of expertise in newborn screening you inherited in your maternal DNA, which is always an important factor for this committee.

I should also mention before we take our break that I believe this is the last meeting for Professor Joseph Telfair, who has been serving as a liaison.

DR. TELFAIR: I'm going to misquote you, but the prematurity is misplaced at the moment. I think I was told that I have to wait until there is someone actually to replace me before I go. I don't say that in a negative sense. I say it in a very positive sense. Trust me. Technically, this is it, but until there is someone to replace me, you will see me.

DR. HOWELL: We appreciate very much your service, and whenever the time comes for you to rotate off the other advisory committee and they find someone who can do nearly as well as you, we will look forward to your continued service, Joe. You've done a very good job and we appreciate it.

I think at this point in time we will take a break for about 15 minutes and return and continue with these excellent reports we've been hearing.

(Recess.)

DR. HOWELL: The next presentation is from Mr. Bill Slimak. Where is Bill?

DR. LLOYD-PURYEAR: Right there.

DR. HOWELL: Oh, okay. Wonderful. I'm glad to see you here, Bill.

He will be presenting the efforts of the partnership between private industry and the state public health agency. PEDIATRIX Screening provides laboratory services to the state of Nebraska, and Bill is vice president of operations at PEDIATRIX. I also might point out that Julie Miller, who is the newborn screening coordinator for the Nebraska program, is also in the audience and might be available for questions.

Bill, can we hear your presentation, please?

MR. SLIMAK: Good morning. What I'm going to do is step back a little bit. I come here representing the operations perspective of newborn screening. We take for granted sometimes the operational side of newborn screening. In order for us to optimize some of these great strategies we've seen on long-term follow-up, you've got to have a good basis for screening the actual screening and

short-term follow-up. What I'm going to talk to you about is a partnership, and that word is sometimes overused, but this is a true partnership between the State of Nebraska and PEDIATRIX Screening. What we do in this partnership is exploit core competencies. PEDIATRIX Screening comes with some core competencies in operations and logistics, and then under the leadership of Julie Miller, the state health department has expertise in taking the results we bring forward and actually implementing that notification with the primary care physician and ensuring that those results are acted on in an efficacious manner.

So mine is more of an operations approach. I will use terms and will explain them briefly that are mainly operational terms, will talk about things called LEAN, will talk about things called Six Sigma. These are normally strategies you will see in operations mode, but they have great application to what we do in newborn screening. So some of this will be dry because it talks mainly about metrics-driven continuous improvement. Operations staff get all excited about numbers and continuous improvement. To others outside the operations arena, some may view this as very dry and straightforward. But the point to be made is a lot of times we may take for granted what my operational colleagues can do. I can tell you that with the expansion, there have been many challenges, both logistically and operationally. What I'd like to share with you today is an approach that has been very successful in our partnership with Nebraska and PEDIATRIX Screening.

Newborn screening is achieved using several different models. Obviously, one of the models I want to talk about is where the state contracts out its screening. Again, I want to encourage -- because most of these data I will bring forward were extracted either from advisory committee meetings at Nebraska or a very important document which I would ask everyone to look at, and that's the annual report, the 2006 annual report for the Nebraska program. This is what it looks like. It's almost like a primer to continuous metrics-driven improvement. I think the power of this program is that we have a lot of feedback, quality assurance mechanisms throughout the entire process, and that feedback mechanism and metrics that are provided in that feedback mechanism drive for continuous improvement, and some of the metrics I will show you will show you how -- and we've been doing the testing for Nebraska since 2003. This is our fifth year of testing for Nebraska, and most of those graphs will view that five-year period and look at the improvements that have been driven. Again, they were driven systemically and driven not only by what PEDIATRIX does but what the state organization does. Again, I will keep alluding to the leadership of Julie Miller and how she has driven this quality assurance program.

Again, the concept is optimizing the lab using various business models. The business models I'm going to talk about are strategies we use in operations. Very simply stated, LEAN is using non-value-added activities. An example of a non-value-added activity is an acceptable specimen. You go through the whole process of collecting the specimen. It gets sent into the lab, and what do you have to do? You have to ask for another specimen. So a metric to concentrate on that kind of activity, repeats. A specimen drawn less than 24 hours will cause a repeat. So you will see that throughout this entire program. We've got metrics in place to drive continuous improvement for these activities. Again, many of the business models improve efficiency, reduce costs, and insure quality. These are all quality-driven metrics.

Again, what we want to make sure of is that even though we created this very operational strategy, we have not lost sight of the fact that we are testing babies and affect the lives of babies and their families. If you go into our lab, we test babies, not dots. To a person, anyone who knew us, Ed Naylor, that was his philosophy, and that philosophy remains in the laboratory. If you ask our techs, they test babies and affect the lives of that baby and the family and not just dots.

Again, special thanks to Julie Miller and her crew. Again, without her leadership, this program would not be as successful as it is.

What I'd like to do is take you through the journey of a specimen. Again, this is operationally driven from an operational perspective, and everything we do here is to look at how we can improve result and how we can improve the timeliness of that result. Most of the metrics you will see driven here are driven from collection to results, and then we have some information on short-term outcomes.

This is kind of an overview of the Nebraska program. The specimens are collected in Nebraska. They are shipped to Pennsylvania. Someone may say, well, God, if you're going to ship them halfway across the country, that's going to take time. In general, that takes about 16 hours. We use UPS as our primary courier. We get shipments from UPS six days a week. There are no deliveries of specimens on Sunday. That's an overnight. So they are picked up late afternoon and delivered to the laboratory by 9 a.m. in the morning. So if you take into account the weekends, the turnaround time on transportation is about 1.1 days.

As you look through this chart, each one of these points has a metric in place, and again those metrics will drive continuous improvement. Here is one of the metrics we look at. This is age at time of specimen to collection. You may say, okay, you collect all this data. What do you do with it? All this data quarterly, the State of Nebraska reports back to every hospital this metric. Here is an example. The state lab, or we have a state metric, and then we have a metric for each hospital. So the hospitals know how they compare on all the metrics to the state.

There is a thing in human behavior called the Hawthorn effect. What the Hawthorn effect is is if you start measuring something and you do nothing more than measure it and express those measurements to the user, you get improved service, and that's exactly what we do. We don't do this in a punitive manner. We say here is what you do, here is what the state does, and usually that will generate a phone call saying, look, why am I so much worse than the rest of the laboratories in the state? That will create a continuous improvement. Again, all of these metrics are shared with the hospitals.

Here are some unsatisfactory specimens. Again, we tracked this one very, very hard, because usually most newborn screening units have a lot of changeover in staff, and when the staff changes over, you all of a sudden will see a blip in unsatisfactory specimens. So we feed that back, make sure that there's training involved, and again it's a constant feedback of metrics.

Here are some metrics we look at as far as you can read these and you can see that all of them are going in the right direction. Here is one on turnaround times. Probably the one that I think is most telling is if you look at the one down in the lower right-hand corner. We think this is a metric that's very telling about the system. It's average turnaround time, birth to results. You can see that we've driven that down to about 5.2 days. That takes into account every aspect of the collection, the testing, and the resolving of those specimens. If you look at that, the 5.2 days is almost to a theoretical number, because if you assume that the specimen is collected between 24 and 48 hours, the shipping into the lab, the testing in the lab, you see that we've driven that down to a point of being pretty close to what you theoretically can reduce it to.

The important thing here is that each one of these increments of moving down that continuous improvement does not, in fact, involve little changes, because you can do little changes and you see little changes in what you do. It actually involves changing the way we have operated, changing the way we have scheduled checks, changing the way we have looked at how we result, changing systems. So the approach is always look at it systemically, because if you just try to make little changes, what you will get is little changes. So we pulled back to 40,000 feet. We are constantly relooking at the systems and then doing cause and effect with these metrics.

Again, here are some metrics you will see where we have Nebraska mean averages versus what they got in 2006. You have to be cautious about comparing these results to the national rate, because the national rate has a lot of averages. But the reality is that all of these are tracked, because remember what I told you about LEAN. A false positive is the best example of non-value-added activity. So we try to keep our false positive rates very low. We try to keep our repeats very low. All of these are non-value-added activities, because if you think about a false positive, the same very limited resources that look at a true positive are also looking at a false positive. So the false positive rates become a very important metric that you need to look at.

Again, this is an overview of what we discovered in the 2006 program in Nebraska. Again, here is something on short-term follow-up. Nebraska actually has goals, and they compare themselves to goals on short-term follow-up. The strength in this program is the constant review and feedback of metrics. Again, this is an operational perspective. Continuous improvement can be driven in a very, very deliberate and logical way. When you drive continuous improvement, you drive cost efficiency and you drive effectiveness of a program. Each one of these has a goal and outcome of what the program looks to do as that goal.

We also look at overall average results and we publish these, because for the physicians who are actually talking to the parents, the physicians who are actually dealing with the situation, this is a good benchmark. They can see where they are compared to what the mean is for each of the results. Each of these also talked to the tightness of the program over the years. You will see a little bit of fluctuation, but to an analytical or clinical chemist, these are relatively tight over that five-year period.

Again, it talks about presumptive positives and how we look at that metric. We are constantly looking at these metrics, constantly reviewing them, and not looking at them as if they existed forever because the worst thing that you can deal with -- and there is a little bone in my ear that just vibrates when they say it, that we've been doing it this way forever. No one ever goes back and challenges why they either did that or what they did. The other thing is when we look at Six Sigma -- and Six Sigma very simply is error proofing -- and we drive to root cause analysis, one of the outcomes of a root cause analysis is we check or monitor the efficacy of a corrective action. That's something that we don't often do. If you drive the root cause analysis, you tend not to put band-aids on it. If you don't drive to root cause analysis, you tend to put band-aids on. You never check the efficacy of that band-aid, and five years later it falls into the category of we've always been doing it that way. If anyone says that to you in your laboratory, you should have a flag that's waved, that all of a sudden you better be looking at that because that's the wrong approach.

In summary, I think that this has been an amazingly good partnership with my colleagues at Nebraska. We have started out optimizing the expertise that we have at the laboratory and optimizing what is done on short-term outcomes and with the results at the Nebraska Department of Health.

Again, I want to stress the success of this program. We are a supporting role here. The stars are Julie and her group. The lab is in the supporting role, and we think we do that very well. Thank you.

DR. HOWELL: Bill, thank you very much.

I wonder if Julie Miller would like to make any comments. Julie, are you here? Would you like to make any comments before we have questions and so forth from the panel?

MS. MILLER: The one comment would be that I think the public/private relationship works in this case largely because of the contractual relationship and that we've been able to specify a lot of the expectations within the contractual arrangement. But it's been good cooperation in terms of the quality assurance aspects for our program, and we kind of just have it built into our systems systemically to always be looking at quality aspects. When we do think we are finding a problem, we are able to talk with PEDIATRIX and they do the Six Sigma aspect and do analyze what it might be, and we do get answers and we do get corrections. So I think it has been a successful relationship.

DR. HOWELL: Thank you very much.

I wonder if there are questions of Bill or Julie at this point. Piero?

DR. RINALDO: Bill, a couple of questions. The first one is do you have the specimens come directly to you, or are they first collected in a centralized way?

MR. SLIMAK: Piero, we have a system in place where the courier service that we have, the envelopes are all preprinted. All the hospital does is take the specimens, put them in the envelope, and they come directly to us.

About the logistics, the minute that UPS picks up that specimen, I've got it. By that I mean I can track it. So I can track the shipment. We know when it's received. We can track it through the entire system, and those are some of the assurances that we give the state back.

DR. RINALDO: So how many birthing places are there?

MR. SLIMAK: I believe there are 62. Julie?

MS. MILLER: I think we are at 64 right now. It fluctuates throughout the year.

DR. RINALDO: The other question is I completely agree with you that metrics and measuring them are essential. You said that the false-positive rate is a very important one. So can you tell me what it was if you break it down by tandem mass spec?

MR. SLIMAK: I don't want to misspeak there. If you look at this report, it speaks to it from Nebraska. As far as overall tandem mass, it's something less than 0.1 percent. I think if you take other than tandem mass, and these are general numbers, it's something less than 0.5 percent.

DR. RINALDO: Is that report available?

MR. SLIMAK: Yes. It's available, is it not, Julie?

MS. MILLER: It's actually available on the Nebraska newborn screening website.

DR. RINALDO: Thank you.

DR. HOWELL: Kwaku?

DR. OHENE-FREMPONG: My question relates to hemoglobinopathies. I imagine that you run into hemoglobinopathies.

MR. SLIMAK: Yes. They are in here. The reason we didn't put them up there is because there are so many different categories. It would become very busy to look at them. But yes, hemoglobinopathies are in here. They are culled out by the different types.

DR. HOWELL: Ned?

DR. CALONGE: So your benchmarks for false positives come off of national rates? What is the process for dialing those down and making sure you're eliminating the right positives? Do you understand what I mean?

MR. SLIMAK: The question is always how many have you missed, if that's your question.

DR. CALONGE: No. Well, that's part of the question. Among the positives, there are true positives and false positives. You identify your rate as being higher than the national average. So the assumption, which I think is reasonable, is that there are false positives in there. So what is the process for dialing those down and making sure you don't have false negatives?

MR. SLIMAK: That is, again, a feedback mechanism. We look at outcomes. Outcomes are obviously the rule. We are constantly looking at our testing algorithms. We will come up with what we think are enhancements to the algorithm. We will then take them to the advisory committees. We will present our data to the advisory committees, and in general they will accept that, and we will modify it. But all the state programs we deal with have an advisory committee where we are constantly feeding our data back to them. We give them that data and it's really here's what we have, here is what we think we can do to modify the algorithm, and then they act on it.

DR. HOWELL: Bennett?

DR. LAVENSTEIN: I just have a question. (Inaudible) improved as a business model how the costs have been allocated. What has been your experience in terms of costs?

MR. SLIMAK: My experience with cost is when you start a continuous improvement program, you have low-hanging fruit and you get a lot of change and the immediate savings are very quick. Without exaggeration, low-hanging fruit can be as much as 10 or 15 percent of the cost. Then with a good established program on an annual basis, you can usually drive about a 5 percent reduction in cost. It works. I mean, again, for a lot of people, operational things like this are kind of taken for granted, but good solid quality assurance and continuous improvement programs really do drive cost savings. They're not separate. In the early days we used to talk about quality and cost, and under LEAN and Six Sigma, they are inseparable.

DR. HOWELL: Tim, do you have a question?

DR. GELESKE: (Inaudible.)

MR. SLIMAK: Yes, sir.

DR. GELESKE: Is that the time that the primary care physician receives the result?

MR. SLIMAK: Yes, sir. All of our results are available via the Internet, the encrypted Internet. Abnormal results are called out either directly to the department or with one of our genetic counselors. We have genetic counselors and technical staff that are available 24/7. So, yes, that's when those are called out.

DR. HOWELL: Mike Skeels is on the phone. Mike, do you have any questions of Bill?

(No response.)

DR. HOWELL: He either can't hear or he doesn't have a question. So in view of that, we will move on.

I have two questions. As far as long-term follow-up, do you have any responsibility or play any role in that area?

MR. SLIMAK: Only from the point that we are continuously feeding data. If there is any repeat testing, we do that. Nebraska uses our data system, so we peripherally are involved in long-term follow-up.

DR. HOWELL: And since this is a contract with the state government, I assume that the cost per patient is public information. Is that correct?

MR. SLIMAK: That is correct.

DR. HOWELL: And what do you charge per person for these tests?

MR. SLIMAK: It's two-tiered. Julie, would you want to quote that?

MS. MILLER: The charges are $35.75 from the laboratory to the hospital per infant screened. Ten dollars of that $35.75 gets returned to the state, which we use to help pay for metabolic formula and foods. $25.75 stays with the laboratory for their costs.

DR. HOWELL: So you get $25.75 for the entire panel that you do. Is that correct?

MR. SLIMAK: Yes, sir.

DR. HOWELL: And does that include the UPS? I hate to be detailed, but people are always interested.

MR. SLIMAK: That is door to door.

DR. HOWELL: Okay. You must have a good UPS rate. I pay about $25 to send an envelope.

Brad had a comment, and this is an exciting and interesting thing, but we had better move on after Brad's wisdom.

DR. THERRELL: I just want to clarify one thing. You were very good in giving Julie a lot of credit, but maybe you should give her even more credit because I believe that the report and all those tables are generated by the Nebraska Department of Health, and those are their tables and you feed data under your contract.

MR. SLIMAK: Yes, sir.

DR. THERRELL: I just wanted to clarify that. This isn't a report that comes from you. It's a report that comes from the state.

DR. HOWELL: Thanks very much, Bill. We better zip along. You will be here hopefully for the whole meeting to answer questions and comments.

Our next presenter is Dr. Roger Eaton, who is director of the New England Newborn Screening Program. Roger is Associate Professor of Pediatrics at Massachusetts, and he is the project leader for Priority Focus 1, quality control multi-center validation and algorithms to improve communications for newborn positive screening results to the medical home of the HRSA region, New England regional genetics and newborn screening collaborative grants.

Kristi Zonno of the Rhode Island Newborn Screening Program is also here in the audience and can answer any questions that Roger cannot.

Roger, you're on.

DR. EATON: Thank you. Let me see if I can find this. Thank you for the opportunity to speak today. I thought it would be interesting to the group to begin by orienting you with some examples from the real world. So here is an example of a sample that was collected on day of life 2, received by us on day of life 4. The next day our metabolic specialist, Dr. Neela Sahai, notified the physician, who was a covering physician -- the family's physician was on vacation -- of a very markedly out-of-range ASA and

communicated by phone and by fax with clear written instructions that the next step would be to refer to a metabolic specialist.

So here is where we get the short-term follow-up. The lab did its job, a good analytical analysis, communicated the results effectively to the pediatrician. The short-term follow-up was that Dr. Sahai then called two days later to assure that that connection actually took place. The physician said, well, you know, I did see the baby. The baby was doing well. I know you told us to send the baby to a metabolic specialist, but I just took another repeat filter paper and I'm going to send that in to you and see how that goes before I send the baby for an evaluation.

The problem is that day of life 7 was a Friday, and that in fact wasn't what we had in mind. So on Friday evening when Dr. Sahai and I had a conversation, it was agreed that she should call back and try to persuade the doctor for metabolic referral. Maybe we were lucky that this was Friday evening and we had a different covering doctor for the vacationing doctor who agreed to follow our suggestion. The baby was admitted that day at midnight, and upon admission the baby had markedly elevated ammonia. By the time we got that repeat filter paper, the baby almost certainly would have had a metabolic crisis sometime over the weekend. So it's an example of the importance at least of short-term follow-up.

Case two is trying to look at what's the role of long-term follow-up. I'm not going to be talking about our long-term follow-up project with the region specifically. That's been done by Dr. Comeau to the subcommittee previously. But this is a screen capture of our short-term follow-up database in the metabolic section. I know you can't actually see from there, but we collect diagnostic information. There are tabs that are shown here, if you can see them, plasma acylcarnitines, urinary glycines, things like that.

This is the capture screen for a longer-term follow-up. Each of these tabs across the top, if you can focus in on them, talk about information captured from age 1 year, 1 to 3 years, 3 to 7 years, up to 25 years. There are different data elements that we are capturing for those time frames.

The importance of this is that it is that kind of information that helps us take a longer picture and give that feedback to the quality of care in newborn screening. So after our first 37 cases of MCADD, if I drop down to the bottom of this, we realized that although 35 out of 37 initially did well, which means the contact was made effectively, and referral was made effectively, the baby was connected to a metabolic specialist's care, if you go right down to the bottom, two of those babies subsequently died, one at 11 months and one at 33 months. That's not what we were hoping for. That wasn't our expectation. However, because we knew that information and because of our follow-up databases, we knew where these babies were supposed to be and where they were, we issued a PCP alert to all of the physicians who were caring for MCADD babies and basically wanted them to be aware of that particular experience. We are encouraging them to continue monitoring early signs of illness and immediate medical attention to prevent severe hypoglycemia. That's been expanded more recently to 47 MCADD cases, and that publication is in press.

If I were to reduce the goal of newborn screening into a single sentence, it would be to make use of the blood specimen collected in the first few days of life to prevent or minimize the morbidity and mortality of newborn disorders. It is actually important to know what the goal of a newborn screening program is because although mostly, I think, we think of newborn screening as being a laboratory exercise, and it is important to have an excellent laboratory analysis as part of newborn screening, that is actually one of a number of activities that has to be in place in a comprehensive newborn screening program. It may not matter particularly what the model is to address all these pieces, but I think everybody in the field would agree, whether it's any state in the country or any place in the world, to really look at newborn screening in a comprehensive manner, all these various activities that are outlined in this cartoon have to be covered.

Now I will move to the models in New England. Our model with Rhode Island is built on our model with Massachusetts, so I'm going to start with that. The Massachusetts Department of Health has an interagency service agreement with the University of Massachusetts Medical School. As is true of all medical schools, our medical school has clinical, academic, and research arms. Maybe not so particular, and this may be because it's a public medical school, there is a very specific service arm of the medical school that has a name. It's called Commonwealth Medicine, and it has its own sub-mission, which is written here, to apply knowledge to improve health outcomes for those serviced by public health and human service programs. So if you think about that, that's a perfect home for a newborn screening program, and in our particular case I think it works well for our model. Again, there are a number of models that could meet the needs of a comprehensive newborn screening program, and I think this is one of them.

I've expanded that Commonwealth Medicine piece here to list just some of the programs that fall under that Commonwealth Medicine. In fact, the newborn screening program is one of those programs. All of our staff, in fact, are University of Massachusetts Medical School staff. The senior staff are on the faculty of the medical school.

Also, I've added to this diagram standing specialty workgroups. So for these workgroups, we pull in specialists that are outside the medical school in Massachusetts and the region. For example, we have a metabolic workgroup, a separate CF workgroup, a separate hemoglobin workgroup. We have workgroups for disorders that we're not even screening for yet that are under research and development.

These are the forms where we discuss our day to day experiences. We get feedback from them for improvements. We get advice and recommendations for our fact sheets. We have more than 90 analytic-specific fact sheets, depending on how the lab results come out. So these help feedback to make sure that we have input from the specialty community as we move forward.

So in this environment, I think we have a very good environment for not only the service delivery arm, but also it's a good environment for technical research and development, for studying clinical outcomes and for clinical research, and for publications.

Now, if we move to Rhode Island, Rhode Island layers on top of this. So the Rhode Island Department of Health has a contract with the University of Massachusetts Medical School to provide newborn screening for Rhode Island. Unlike in Massachusetts, where every aspect of this cartoon is covered by the New England Newborn Screening Program in Massachusetts, when we contract with another state, we really just need to decide together through the terms of the contract who does what and have very clear written protocols and responsibility. Since we already do the whole piece from A to Z, it does make for a good environment to make sure that nothing slips through the cracks.

If I went through this whole slide, I'm afraid it would take more than my allotted time. So we will try to focus on the follow-up activities. I will say for example, just to give an example, in Massachusetts it's our responsibility to connect between the Massachusetts electronic birth certificate information and the specimens received to be sure, in fact, that we get every specimen. In Rhode Island, we worked with Rhode Island to produce for them the particular data elements that were required for their KidsNet. You may be familiar with KidsNet. It's a very well respected integration model nationally. Our newborn screening information gets uploaded into KidsNet. It's then Rhode Island's responsibility to do that connection and follow-up and make sure they are not missing a specimen.

Notification I'm going to talk about a little bit later, and I'll do that now. In fact, this slide talks a little bit about the relationship for notification and immediate follow-up. In Massachusetts, the UMASS-New England Newborn Screening Program -- this is talking about notifications requiring referral. There are some differences when there are less urgent notifications. So in Massachusetts, we are in an environment, for example, where there are three metabolic clinics in Boston itself. So we don't know when we first get an out-of-range result where it would be most appropriate for that baby to be

referred. So our first contact goes to the pediatrician. We discuss the out-of-range result, what the next steps might be, and determine what specialist that physician's and the patient's insurance might cover. Then we proactively also notify the specialist. The pediatrician will see the patient and refer the patient to the specialist.

The orange arm here is our follow-up arm where we would make sure that that actually happened, and that reflects back to the first case example that I showed earlier. In Rhode Island, our primary role is to contact the Rhode Island Department of Health, and then they take over using their algorithm for what the contact is. In most cases for examples requiring urgent referral, they contact their contract specialist directly, and the specialist makes a referral to the pediatrician. There are exceptions to this, but that's the simple model for now.

The Rhode Island Department of Health then does their follow up to be sure that that referral took place. The dotted line just indicates that we understand with each other, we have a protocol so that if our lab gets results either during the holiday, during weekend, during an evening, when the Rhode Island Department of Health staff may not be available, that we have all of their contact algorithms and we go ahead and make that contact ourselves, and we notify them of the contact so that they can do the follow-up later on.

For most cases, that's very clear, it works out very well. The case study I chose for our partnership with Rhode Island isn't as dramatic as the first example I gave, but I think it illustrates that because we do A to Z in Massachusetts and we were closely with Rhode Island, it allows us to also work out of the box a little bit when an example comes up that doesn't quite fit the algorithm. So in this case the Rhode Island baby had an out-of-range CF screening. The New England Newborn Screening Program notified Rhode Island DOH according to algorithm. The Rhode Island DOH contacted the pediatrician. In this case, that's the CF algorithm. He recommended a sweat test and genetic counseling. The baby got a sweat test. This was early on in their CF implementation in Rhode Island. The test was QNS. The family preferred to get the sweat test redone in Boston rather than go back to the same center that had a QNS test. In fact, the baby did get referred to a Boston clinic.

The Boston CF clinic is more used to dealing with us, so they proactively contacted us according to the (inaudible) algorithms. It was very simple for us to keep them in the loop. We knew what the long-term mission was and to communicate those long-term follow-ups to the Rhode Island Department of Health.

Again, Dr. Anne Comeau is the project leader for Priority Focus 2, which is analogous to the Priority Focus 2 that was already discussed earlier. Our approaches are similar, I think somewhat different. I think one of the things that we evolved differently is that we built our long-term follow-up on our experience of short-term follow-up within the newborn screening program. So within our system the long-term database grows out of the newborn screening database. It does help us in having all of the numerators. We actually start a case into the long-term follow-up, which is really just an extension of the short-term follow-up. Upon the initial contact, we don't give it a diagnosis at that time. We would give it a candidate disorder and status report and flip that over to confirmed if and when the baby gets a confirmed diagnosis. That does help us to be able to compare babies with out-of-range initial results that didn't become disorders from those that are, and it does help take an analysis of what might be the indicators of a false positive test.

I wanted to mention a little bit about education. I've listed on here a number of different sources for anybody receiving a newborn screening result of what that result might mean. There are some very good pieces out there that are nationally and publicly available. This committee participated in some of these, the ACMG fact sheets, the parent fact sheets from the STAR-G program, HRSA-developed parent brochures.

Another piece that I like to mention always as a source of information is the laboratory that actually performed the test. I think that it is not possible to have all the information available from some generic sources that could be downloaded from the web that are not more laboratory specific. So, for example, on that piece, in our example the laboratory that performed the test would be our program. We have on staff more certified clinical geneticists and biochemical geneticists, endocrinologists, pediatricians, et cetera. So we are able to apply an experience-based laboratory analysis in our academic environment as well as our service environment and provide 90 result-focused fact sheets. Just to take one example for propionylcarnitine elevations, we would look at a lot of different kinds of results or comparison of the various markers that taken together indicate a low, medium, or high probability of a true disorder, as well as indications of a likelihood of which particular C3-associated disorder that is. We will give advice as to urgency, next steps, and provide fact sheets appropriate to the specific analysis.

In a nutshell, I think that captures what our models are in the newborn screening program in Massachusetts, and I'd be happy to take any questions.

DR. HOWELL: Roger, thank you very much.

I wonder if Kristi Zonno from Rhode Island would like to make any comments before we move to have a few questions.

MS. ZONNO: Good morning. I have a few things I can share if there are no specific questions just about our collaboration. We have had this ongoing collaboration with the New England newborn screening program, which is, of course, based upon our contractual agreements, but there are many benefits that the state gets. One of them is the cost benefit in a very small state with a small number of births. So for us to have our own lab to do mass spec screening and all this analysis, it doesn't make sense for us. So that's one very important factor.

Another thing when we started our expanded screening in July of 2006, we relied significantly on the expertise and experience of the New England newborn screening program since they had so much experience with expanded screening, and that really helped us to set up our system in Rhode Island. It also allows us participation in the regional long-term follow-up grant. It facilitates the coordination between other states' newborn screening programs, the other states that use the New England newborn screening program laboratory. They are also small states with limited resources. So we are able to really have a facilitated collaboration for many things from them.

DR. HOWELL: Thank you very much. I think it's a very important example of a small state taking advantage of a neighboring state to do this.

We need to move along relatively briskly, but I wonder if there are a few questions of Roger at this point. Let me ask you one question. As you were talking about the fact that the state health departments are generally closed on Saturday and Sunday, do we have any data about the bad effect that comes from that? Obviously, state health departments ordinarily are the site where these results go, and I can imagine that there must be examples of data that's acquired on Friday night or something and maybe not get acted on until Monday. Do we have data on that?

DR. EATON: I don't know if maybe Brad has some data on that. He says no. In our situation, we aren't only open Monday through Friday. We do analysis on Saturday because we also receive specimens on Saturday. We do analysis on Sunday which are retests and confirmations of specimens received on Saturday. With all of our states we have an understanding that if something -- we understand what the goals are, and the goal is to interface a baby with effective care. So with each of our contracts, it's understood that if there is any issue about connecting with the public health lab that is outside of our program, we will go ahead and do what we do in Massachusetts in their state. We have the contact algorithms.

This might be, because of weekends and holidays -- another example was an ice storm in Maine when they just couldn't get in. The important thing, again, is the outcome. It's to get the job done, and we are very comfortable doing that because we do all those pieces in Massachusetts.

DR. TELFAIR: Thank you. That was an excellent presentation. I learned a lot from it. One thing that I just want to ask about is if you can speak briefly about the relationship you have with the community providers, as well as some consumers in the follow-up activities specifically. In your example, I thought you were going to go a little bit further in your discussion on that, but you stopped in terms of just talking to the providers and the tertiary care centers. I was wondering if you would talk a little bit about the community providers' relationship you have also with the follow-up activity specifically.

DR. EATON: I just want to be sure I understand your question. Specifically, community providers --

DR. TELFAIR: Yes, providers in the community, primary care, the PCPs in the community. What is the relationship you have with them? I understand it a little bit from your example, but in general what is your relationship in terms of involvement with the follow-up activity?

DR. EATON: If I understand your question correctly, we make use of our specialty workgroups primarily, like for example to discuss what data elements ought to be collected for our follow-up information. That basically comes from the specialty workgroups. I did give an example of feedback to the primaries on the MCADD test so that we communicated that alert back to the primaries. Other than that, the input from the primaries would be more on the level of the newborn screening advisory committee in each of the states, which would have representatives from pediatricians on different levels. I'm not sure if I answered your questions.

DR. TELFAIR: Yes, okay. (Inaudible.) What I am understanding is that you get work mostly in an advisory capacity with a lot of providers, apart from the direct contact related to a test, a follow-up to a test that is done. But I was wondering about assurances related to that actual follow-up itself in terms of treatment, in terms of the other services that they may need.

DR. EATON: Maybe I'm understanding your question. In the data information that we collect, short and long-term, a lot of the short-term information would come from the primary pediatricians, that would come from the specialties. Again, I think our primary contact to collect -- again, I'm trying to get your question exactly, but as far as where we get the information, the initial contact goes to the primary pediatrician, and our educational materials go to the primary pediatrician. For collecting the long-term information, first up is generally the specialty centers. It is more efficient to go there instead of having connections with hundreds of different pediatricians.

One piece that this helps me focus on is because our system grows out of the newborn screening program, we also have built in here some tickler files. For example, we work with our specialty workgroups and find out from them how often you think you ought to be seeing a baby with MCADD or a child with MCADD. If they say we should be seeing this baby at least once a year, our long-term database is visit-focused. So if we see that there are no reported visits, then we will go back to the specialist to find out what happened with that. They may or may not know what happened to the family, so one of the advantages that we have, I think, is having the system centered in the newborn screening database, because we then do have the private PCP. So we would contact the PCP to find out are you still seeing this patient as the next level, and maybe that PCP will know that actually this baby isn't being seen there, it's being seen over there. So when a baby transfers from one center to another, I think that helps us having it integrated with the common system. We would go back to the pediatrician to find out.

DR. HOWELL: Joseph, if you have any more questions, maybe you can discuss that later because we are substantially behind. But we will have one final question from Kwaku, and then we will end. Thanks very much.

DR. OHENE-FREMPONG: I will be quick. The Nebraska example that we heard with the PEDIATRIX, the samples were mailed directly to the lab. In my mind, that suggests that if some sample did not reach the lab, the state may not be aware of it. In the Rhode Island program that you have, do the samples go to a state office that collates them and records it before it comes to you?

DR. EATON: No. The samples go directly from the site of birth to hour lab. In fact, in the past they used to go centrally, and that just really introduces unnecessary delay. As Bill talked about, there are ways of tracking packages that were picked up by UPS to be sure they get there. We also glossed over in one of the cartoon examples that one thing that our program does is that we monitor, that we send out a package from every site at least once a day. If we don't receive one in Massachusetts, we proactively ask the site to see if they shipped one. In Rhode Island, we contact Rhode Island and they do the same kind of thing. So that's on the front end. On the back end, we are both doing comparisons between the (inaudible) to get information and specimens received. That is a little more delayed because you can't contact them right away. It has to be about a week and a half to two weeks to be sure the sample got here. But that closes the loop on samples that may have gotten lost in the system. But it is better to go direct, actually.

DR. HOWELL: Roger, thank you very much for that excellent presentation. I appreciate that a great deal.

The fourth unique newborn screening system that provides outreach laboratory services is the partnership with the Pacific area. Dr. Mike Skeels, who is a member of this committee and the committee on public health laboratories, was called away to be the interim state health official. Since this is a new opportunity, at the last minute shall we say, with a lot of new duties, he is unable to be with us today, but he is on the telephone. Dr. Skeels is director of the Oregon State Public Health Laboratory and he presides over a five-laboratory section for newborn screening, virology, immunology, microbiology, and laboratory operations, as well as compliance and quality assurance.

Sylvia Au is here from the Hawaii Department of Health in the audience and can also help with any questions that come.

So with luck, we will hear from Mike via the telephone.

DR. SKEELS: Hello. Can you hear me all right?

DR. HOWELL: I can. It's good. Maybe we can turn the microphone on and put it close to the phone. That will be good. We will even hear better.

DR. SKEELS: Do you have my slides up yet?

DR. HOWELL: Well, they are coming. We have the first slide up of a bunch of very handsome people standing in front of a laboratory.

DR. SKEELS: That's a picture from my vacation. That's a mistake.

(Laughter.)

DR. HOWELL: Yes, right. Well, everybody does have on bathing suits.

DR. SKEELS: Thank you for accommodating my schedule. As you just said, Ron, I have an interim assignment. I have to be in Oregon all afternoon today and most of tomorrow. So I'm sorry I can't be with all of you. I have enjoyed the last couple of talks even though I couldn't see the slides. The interplay between folks was very interesting, so thank you.

What you see on the first slide is just a little group shot after our most recent regional newborn screening program meeting. It's a reminder to me that our program is really about the people who run the program and participate in it. There are people from several different states who were there to serve the babies.

Could I have the next slide, please?

This should be a picture of the Oregon State Public Health Laboratory. Is that what you have up? Okay. What I'm going to do as I go through these, since I find that clicking my mouse here really has no effect whatsoever on the East Coast, I'm going to just stay click when I want you to click to the next slide or the next animation. I regret that I didn't remove the animation from the slides before I sent the PowerPoint to you, but we are going to have some at some point, so I will try to avoid confusion.

We just moved into the new state public health laboratory yesterday, and I'm sitting in my new office, and the building that you see here is where we are. This is also the focal point for the Northwest Regional Newborn Screening Program in terms of where the testing is done and where we provide our consultation services and so forth.

Next slide, please.

This should be a slide that shows the states within the Northwest regional newborn screening program, and you can see that there are six now. As was mentioned earlier, Hawaii is one of those, and Sylvia Au, I believe, is in the audience there today, and I hope, Sylvia, that when the time comes, you will either embellish or add to what I said or answer questions if I am unable to do so, because I think the perspective of the states in the program is very, very important.

We have contracts between the Oregon public health division, which is to say our state health department, and the other state health departments in the region. Then each of the states operate what we hope is as autonomous and state-centered a program as possible so that we enable and encourage and support. But it is very much a state-centered program in the way we try to operate it.

Could I have the next slide, please?

You can see that we also have some military bases for which we provide newborn screening services. The largest of these is Madigan Army Hospital in the Tacoma area, but we also have some others in the state of Washington. We have one in South Korea, we have one on a little base in Southeastern California.

Next slide, please.

You can also see that we provide services to some birthing facilities in places like Guam and Saipan and Kwajalein out in the Pacific. In addition, we have three Navajo Nation service units. You should be looking at that slide. These have recently come on board in our program. These babies are born in Arizona. A few are born in New Mexico, which is part of our regional program anyway from the state level, but we are now doing more Navajo babies. So that will give you some idea about the scope and size of our program.

Let's go to our next slide.

The first click should give you a pop-up box that talks about the population in six states. It's about 11.5 million people, which is almost 4 percent of the U.S. population. Then number of births -- next click, please -- is about 193,000, which is just a little over 4.5 percent of births.

Next click.

The number of specimens we received in 2007 is about 336,000. So if you compare that to births, you can see that some of our states do more than one sample on a routine basis. Oregon is one of them, and of course we are the biggest state in the region.

Next click.

The land area of these six states is about a million square miles, which is 30 percent of the U.S., and this is thanks to Alaska, which is about 60 percent of the million square miles.

(Laughter.)

DR. SKEELS: Not only do we have the huge state of Alaska, but we also have a great big ocean out there. I am bringing this up just to say that although we have a small percentage of the births in the United States, we have special problems when it comes to transportation and distance and timeliness and so forth. So if you are a baby born in Barrow, Alaska, you are a long way from Albuquerque. If you look at the size of the geography that we're dealing with here, it does create some special challenges.

Then the last click on this slide is just a little box to say we have eight time zones. Not just the miles but the time zones themselves are a challenge when it comes to communicating with people and making sure that follow-up and tracking get done very effectively.

Okay, let's have the next slide.

Now, this should be a March of Dimes photo that I purloined from the web. Thank you very much, March of Dimes. This slide is just to remind me to say maybe the most important thing I'm going to say this morning, and that is that our regional program is a partnership between our health departments in the various states, the birth facilities, the practitioners and the families. We happen to be providing the laboratory services and a lot of other things, but none of this would work without any one of the important pieces.

Let's have the next slide.

The first bullet, if you'll click that, this is a description, sort of an overview of the continuum of services that we provide. I think I heard Roger saying this as well. I mean, this isn't just a lab test. This is a public health service program that happens to have a huge laboratory component, but we run it as seamlessly as possible and on a population basis.

I'll start with parent and practitioner education. We perform lab screening and confirmatory testing, some of which involves sending out to confirmatory labs.

Next click.

There is short-term follow-up and tracking, which is going to be the main thrust of the rest of what I am going to say in a minute. We also provide medical consultation and referral.

Next click.

The next click says population-based public health model, which I already mentioned. The last click should say cost-effective pooling of resources. So these bullets sort of summarize our program and our approach. The idea has been through time that many of these large, sparsely populated Western

states have low birth rates and a paucity of specialty medical care services. So this regional program started in the 1970s and it has continued to grow.

The next slide just shows the English and Spanish language versions of our brochure, and this is just to remind me to say that we do the best job we can of parent education, although we're starting to believe that it really needs to be done in the prenatal period rather than the perinatal period so that someone will read these things. But each of these brochures is customized for the states. Each state can make its own brochure, deliver its message the way that it wants to. What you see here happens to be the one we use in Oregon. It's a generic brochure that's available, but each state can choose to customize the way they want it. Likewise, the practitioner's manual.

Next slide, please.

As has already been said, practitioner education is a very key component of what we do. As Roger also mentioned, I think, our practitioner education includes online access to this manual and everything in it, but also extensive fact sheets about all of the disorders. So these are all on the public portion of our website.

Next slide, please.

What you should be looking at is a slide that says each regional state newborn screening program should have its own independent identity. We think one of the reasons that our regional program has been so successful is that from the point of view of the practitioners and the parents and families in a given state in our program, it looks to them like it's their own state program because it is. It's a program that they run, and we are there to provide whatever level of support they need, and that includes a vast difference in follow-up and tracking depending on which state we happen to be serving. I'll say more about that in just a moment.

The next click.

We provide the lab testing, medical consultation to the extent that it's needed, and in fact it is needed in several of our states, and other services to support the states and their efforts.

The next click.

This is really important. The states in our program vary widely in their capacity to provide a number of different things, including the program administration itself, the management, education, and follow-up. Different states have different abilities to do these things, and we encourage them to be as strong and self-sufficient as possible, but we recognize that states differ in their resources and in their legislative environment and in their political environment.

Let's have the next slide, but don't be taken aback by this slide, all right? This is a series of three impossible to read, icky slides, but they make the point, and this is really the thrust of what you asked me to talk about, this makes the point that we have a specific array of long-term follow-up activities. If you look at what we provide to the different states, it's different depending upon what they can and cannot do.

So if you just look on the west side of this slide you will see, for example, mailing normal results is something we do for every state and the military bases. For some states we fax results; for others we don't. If you go on down you'll see that we get to the point of significant abnormal findings. Whether we mail them or fax them is (inaudible) for most states, but then things change. You will find that some of the states pick it up from there and do more than others do.

Can we have the next slide?

Again, it's a busy slide but the point of the slide is not so much the content as the fact that it shows that there is a difference in the way we manage depending upon the needs of each state. So the follow-up activities are highly tailored to the states themselves. Obviously, you have a copy of this. If anybody wants a hard copy so they can pore over this and study it more, you are certainly welcome to do that.

The next slide should be the third of these (inaudible) services provided slides. You will see again that we do a lot of things right down to the detail of making sure that every baby gets followed, that no baby falls through the cracks, and that specific information that is needed to do testing is obtained if it's missing, that every baby that needs confirmatory testing gets it, and that every baby that is found to have a disorder gets referred for medical consultation.

We also provide screening practice profiles, as I heard a previous speaker described. I think that was Bill. These are birth center by birth center specific. They show what screening errors have occurred, how that particular birthing center is doing compared with others in the state, and so on and so forth. Judi Tuerck was the first person to pioneer this idea a long time ago, and she's still with our program, and we've been able to refine it so that it's very helpful, I think, especially to the people who are coordinating and running the newborn screening programs in their states.

I should also mention that it helps us target our practitioner education in those birth facilities that are maybe having trouble.

Then the last slide I have is just a picture of our medical consultants. This is just a reminder to say that one of the strongest things that we have to offer to the other states in our regional program is the talents of the metabolic, endocrine, hematological and other consultants. I don't have our CF consultants, Mike Wall, on here because I don't have a good picture of him yet, but these folks are there to work with the practitioners in very distant areas, as I said, in eight time zones and many thousands of miles, to assist them in the care of babies that are found to have disorders.

Judi Tuerck has been an integral part of developing and implementing our practitioner education for a really, really long time, and I want to acknowledge her contributions as well.

In an effort to try to get you back on time, I'm going to stop there and just say that I'll try to answer questions if you have any, and I would also again welcome Sylvia to add anything that she wants to say. I was having trouble a minute ago hearing the questions that were being asked from the floor, so you may have to repeat those for me if you would like me to answer them. I would also like to say I am just a lab director. I am not a real newborn screening program manager, so it's possible I won't know the answer, but I know who would know. Thank you very much.

DR. HOWELL: Thank you very much, Mike, for that excellent presentation.

Sylvia has found her way to the microphone. Would you like to make a few comments, Sylvia?

MS. AU: Well, Rod, I think your number one question is money. So I will tell you in Hawaii currently our cost for the screening is $47, which hasn't been changed for the last three years. We have some regs to change it to $55, and that includes the collection kit, education materials, initial screen, any repeat screens, confirmatory testing, all the consultants that Mike talked about. We subsidize our own genetic specialists in Hawaii. The entire follow-up state staff is funded through that fee, so the program is totally sustainable and doesn't use a penny of state money. We also do a lot of quality assurance things with the practice profiles. We also do a lot of surveys with our providers, and we do things like focus groups with families and things like that.

We also subsidize our hemoglobinopathy clinic, and recently we decided that we have enough money to actually do the alphathal DNA testing for the families because we're having trouble getting that

covered for mom and dad. Because we have 30 to 35 screen positives for alphathal a month, we figured that would be a good use of money.

Our samples are FedExed over to Oregon, so they go overnight. I have to say that during the first year of our FedEx contract, our newborn screening coordinator really held them to that one minute guarantee and made back about half the money that we were supposed to pay them.

(Laughter.)

MS. AU: They did not deliver within one minute. She kept track of that, too.

We also pay Oregon to do our data entry for us. We get a download every morning. It also includes our Neometrics software system for follow-up. The fee also covers any uninsured people that cannot afford screening, and also the home birth families. We have a very good relationship with our midwives. So they are able to go into any lab and we will cover the screening for them. We do have some families that mail in the money, but we don't care where you have your baby. We just want to screen.

The great part about working with Oregon is that there are great people there. We have tons of consultants. The time difference has not made any difference at all. We get our results within less than a week. We get our mailers. They phone us all the time. We are in contact with them.

The other really great thing is that we work really closely with all the other states that contract with Oregon, and we've been able to do some really great things together. We share resources. We share educational materials. We share information. So I think that that has been a really, really big plus for a state that is (inaudible) and only has 19,000 births. A little over 10 years ago we were only screening for two disorders and we were the last in the country, and to be at the point that we are now is just really exciting and in large part due to Oregon and all the services they provide us.

DR. HOWELL: Thank you very much.

Are there questions of Sylvia and Mike? This was a wonderful presentation. It's amazing to deal with such extremely divergent populations as far as space is concerned. Obviously, we are much less close time-wise to Europe than you are to Hawaii. So that's very interesting. But you get your samples just as quickly as if they were going from somewhere to somewhere else in the same state.

Ned, you had a question?

DR. CALONGE: Actually, I had a couple of comments that should follow along with all of the presentations. One is that I think the states that are doing newborn screening programs pretty much face all the same elements issues that we've heard described across all the different programs. What was useful was hearing how different programs, regional or state programs addressed those. I would think it would be useful to the community of states, especially those that are anticipating bringing expanded screening up, that some will be able to catalog how the different states have done this and give kind of a menu or a toolbox for public health officials and other programs for trying to decide how to do this, either through contracts or other arrangements.

So I think that's what's been useful to me, because Colorado faced all of these same issues. We addressed them in slightly different ways. We contracted with Wyoming for their services. A lot of the same issues have come up, and the cost variation is very useful.

Another comment was just to comment on the timeliness, which I know everyone is commenting on. In response to timeliness, we had to expand to adding Saturday analysis. I think all states try to

figure out what to do with the weekend. But I want to make sure that people understand that there are many sources of slow up that states will have to analyze. One of the things we found is that hospitals would batch their samples because it was cheaper than sending them off, and that would build in over the weekend an unacceptable delay.

So looking at PEDIATRIX, their work and thinking about quality improvement exercises that minimize that turnaround time to results is something that all of us should be looking at. And again, it would be useful to have toolbox ideas on how to implement those.

DR. HOWELL: Thank you very much, Ned. I think there might be an opportunity for HRSA through somebody's cooperative efforts to catalog some of these things and publish them. I think that might be useful.

Mike, thank you very much, and Sylvia, for those presentations.

We have one other brief presentation before lunch, and I'd like to ask Emil Wigode, who is the director of federal affairs, the Office of Government Affairs for the March of Dimes -- he has been good enough to come today and bring us up to date on the tremendous amount of activity downtown.

Emil?

MR. WIGODE: Thank you very much, Dr. Howell. I know I am on borrowed time, so I will try to be brief here.

Newborn screening is a March of Dimes priority at both the federal and state levels, so we appreciate the opportunity to give the committee an update on what's happening mainly at the federal level. But I did want to just briefly say that last year 18 March of Dimes chapters, along with other organizations that are represented in this room, secured expansions in the states, and we now have 16 states, plus the District of Columbia, that are screening for the core panel of 29 disorders that this committee has recommended. In 2008, March of Dimes state chapters that are in the states that are not at 29 yet, it will be part of their priorities to get those states up and expanded to the full 29.

On the federal level I just wanted to give a quick wrap-up of what happened at the end of last session, talk a little bit about what is expected to happen this year, and then give an overview of the Newborn Screening Saves Lives Act.

At the federal update that the American Academy of Pediatrics gave to this committee last time, there was discussion of the State Children's Health Insurance Program reauthorization. So I just wanted to let you know that that bill, after a few unsuccessful attempts to override a presidential veto, the program was extended by Congress until March of 2009, but it did not make any policy changes to the program. So they provided sufficient funding to allow states to continue to cover the approximately 6 million children that are currently covered. But the reauthorization bill would have allowed an additional 3 to 4 million children to be covered, but that was not included in the final bill.

On the appropriations and funding side, again the Labor/Health and Human Services appropriations bill, which includes most of the public health agency funding, was in November. The president vetoed a version of that bill that included some good increases for many of the agencies -- HRSA and NIH and CDC and a lot of the activities. That bill did include an increase for HRSA's heritable disorders program within the MCH block grant and increases in a lot of different areas. But that bill was vetoed.

In the final wrap-up at the end of the session, they passed an omnibus bill that included funding for 11 of the 12 appropriations bills that are supposed to move separately. In that negotiation they cut

almost $6 billion from the Labor/Health and Human Services bill, and the result of that was, for the most part, either level funding or small increases or small decreases across the public health agencies. The heritable disorders program was level-funded in that bill.

So moving to 2008, the House of Representatives reconvenes tomorrow and the Senate comes back next week. We have the President's State of the Union coming up on January 28, and then he releases his final budget proposal on February 4, and that kind of gets the whole funding process started. So I think overall it's going to be a very difficult political year. We have a narrow margin in the Senate, a presidential election going on, so it's not expected that any real major pieces of legislation, especially in the health care arena, will be moving this year.

But we do have I think the opportunity to move some smaller, non-controversial bills such as the Newborn Screening Saves Lives Act. This is a bill that the March of Dimes, along with a coalition of between 12 and 15 other groups, have been advocating since 2003, and it actually passed the U.S. Senate on December 13 unanimously, and it has now been referred to the House Energy and Commerce Committee. The House version of the bill has 68 co-sponsors, so we have some good support on the House side.

Overall the bill reauthorizes many of the newborn screening activities that were authorized originally in 2000 in the Children's Health Act, but it does expand into new areas, and so I thought I would just spend a minute kind of highlighting a few of the areas that this bill would expand.

It authorizes a series of grant programs designed to -- one grant program would provide states with assistance to increase the amount of screens that they're doing, and with that the state would have to -- in order to receive that funding, the state would have to move to the recommended panel that this advisory committee makes. So it would be an incentive for states to move to what are now the 29 core conditions. There are also grant programs authorized for educating and training health care professionals, educating parents, and also establishing a coordinated system for follow-up care for newborns. Again, this is just an authorization bill, so there isn't any funding attached to this bill. That's going to be a separate process that we will be working on to fund some of these grant programs.

It does reauthorize this advisory committee for five years. It has a provision in the bill that would require the Secretary to respond to advisory committee recommendations within 180 days. The Secretary could either accept or reject your recommendations, but there would need to be a response by the Secretary.

It also adds FDA as a full member of the committee, and also adds experts in infectious disease and ethics to the advisory committee.

Just a couple of the other provisions in the bill. It does authorize an information clearinghouse that would be an Internet clearinghouse where different educational pieces, family support, any sort of resources like that related to newborn screening would be on there, but authorizes the quality assurance that CDC is currently doing related to laboratories, and finally it asks CDC, in consultation with HRSA, to develop a national contingency plan for newborn screening in disaster events.

Just one other area. It also does have a provision related to NIH's research on newborn screening. It's called the Hunter Kelly Newborn Screening Research Program, and it really just authorizes and would allow NIH to expand on some of the activities that they're currently conducting related to newborn screening.

So we'd welcome any committee members' interest and help in getting this bill across the finish line in the House. We have a full summary of the bill that I'd be happy to give the committee for your reference afterwards.

The only other piece of legislation that we have mentioned in previous committee meetings is the genetic non-discrimination bill, and I would defer to Sharon to give a detailed update. I think it would be safe to say that nothing has changed. It has passed the House and is currently awaiting Senate action, but it has been delayed in the Senate. So that's kind of where that's at.

I will be happy to answer any questions.

DR. HOWELL: Emil, thank you very much.

DR. LAVENSTEIN: Emil, Bennett Lavenstein. On March 3 or March 4 of this year, the American Academy of Neurology has their "Neurology on the Hill" day, and there will be approximately 100 adult neurologists, a few child neurologists, coming to lobby or to advocate, and interestingly the American Academy of Neurology is taking universal newborn screening as one of their topics. So there will be approximately three topics that people will be programmed to speak on to their representatives or to their senators about, and obviously the focus will be on the House. So we tracked this thing from the time Senators DeWine and Dodd introduced the bill originally. It sort of sailed through the Senate. It met a major barrier in the House. But I think having a hundred people on the Hill touching base with representatives throughout the United States will be very helpful, and we are going to brief those people on these very topics. So if I could get a copy of your remarks, that would be super.

MR. WIGODE: Absolutely. Thank you.

DR. HOWELL: Thank you very much.

Are there other comments?

(No response.)

DR. HOWELL: Thank you very much.

We have just a couple of things before we depart for lunch. Michele has a list of housekeeping items.

DR. LLOYD-PURYEAR: In case you haven't found the restrooms yet, they are located to the left of Salon E in the foyer area.

DR. HOWELL: If you haven't located them, you are in trouble.

(Laughter.)

DR. LLOYD-PURYEAR: Breakfast and lunch for committee members, speakers and organizational representatives, will be held in the Meritage Restaurant, the hotel's restaurant on the main level. You should have tickets.

The subcommittee meetings are being held from 1:30 to 5:00 p.m. on the lower level of the hotel. Just follow the signs. Laboratory Standards is Brookside A, Education and Training is Brookside B, Follow-Up and Treatment is Linden Oak, and the logistics staff here can help direct the attendees.

This is a reminder that the meetings are open to the public, and also we have -- I don't know if you've said this -- three new committee chairs. Dr. Gerry Vockley is the chair of the Laboratory Standards and Procedures Subcommittee, and we have two co-chairs of the Education and Training Subcommittee, Ms. Jana Monaco and Dr. Tracy Trotter.

If presenters have changed their presentations, please save a copy of your presentation on this desktop with a name.

There is dinner tonight for committee members and speakers at 6:30. Again, it's in the Meritage Restaurant here in the hotel. The restaurant has asked you all to bring cash instead of credit cards.

For anybody who is local, we have free hotel parking passes, and just pick them up from the registration desk outside here. That's it for members of the committee.

DR. HOWELL: Let's go to lunch. Why don't we do the following? Let's return at 1:15, and that will allow you just a bit of time, and we'll be back with Steve Downs.

(Whereupon, at 12:25 p.m., the meeting was recessed for lunch, to reconvene at 1:15 p.m.)

AFTERNOON SESSION (1:21 p.m.)

DR. HOWELL: Ladies and gentlemen, I think if we could take our seats, we could just zip along here.

We are going to have a very informative presentation about the Personalized Healthcare Workgroup update on the Subgroup on Newborn Screening. We are actually going to have two people present here.

Greg, I think you're going to go first. Is that correct?

Dr. Greg Downing is the project director of the Personalized Healthcare Initiative at the Office of the Secretary. Greg has spoken before briefly about that. Then we're going to hear from Steve Downs, who is the co-chair of the Subgroup on Newborn Screening.

Can we begin whenever you're ready, gentlemen?

DR. DOWNING: Great. Thank you, Rod. It's a pleasure to be back. I'm here on behalf of Secretary Leavitt's Personalized Healthcare Initiative, which is one of his top nine priorities for his administration. One segment of that has been the Personalized Healthcare Workgroup, which is a component of his advisory committee, the American Health Information Community, that is setting the stage for an integration of electronic health information for health care delivery purposes. A number of the members of this committee are new relative to the prior discussion. So I just wanted to give a very brief overview what this workgroup's activities are about. Quite a number of the members of this group, as well as others in the audience, have been participating in this, and I want to acknowledge the work of the co-chairs on the Subgroup on Newborn Screening that we will be hearing more about today from Peter van Dyck from HRSA and Steve Downs from Indiana University.

The Personalized Healthcare Workgroup is one of seven active workgroup committees within the American Health Information Community, and Steve will describe some of the functional aspects of this. Our broad charge is to make recommendations to the community for a process that facilitates a broad and community-based approach to establishing a common pathway for the integration of common data standards to facilitate an incorporation and interoperability and clinical utility of genetic and genomic information and analytical tools and electronic health records to support clinical decision-making for the clinician and the consumer.

The specific charge and activities that we have been engaged in for the last 15 months include making recommendations to consider for establishment of standards for reporting and incorporation common medical genetic and genomic tests and family history data into electronic health records and

provide incentives for the adoption across the country, including federal government agencies. So this works collectively across not just the department but the veteran's health administration, DOD, the health care delivery system, and many others. A partnership with the private sector facilitates integration of data standards through the adoption in electronic health records systems. This is coming to your community, if it isn't there now, and we believe that one of the important parts of newborn screening capabilities rests in the future on being able to utilize electronic health information exchange to get critical information on a demand time basis to the clinicians and the care deciders.

The Personalized Healthcare vision and priority areas is a consumer centric approach to this in which clinicians customize diagnosis, treatment, and management plans to suit individual needs based on biology and health care aspects, and to that extent the newborn screening components come into this because of the genetic aspects of this. Four perspectives were identified as important to this vision, including the consumer or the surrogate of the consumer in this particular case, clinicians, researchers, health plans, and payers for health care. The priority areas that were established by AHIC included genetic and genomic tests, family health history, confidentiality, privacy and security issues, and clinical decision support.

In July of this past year, AHIC received an accepted recommendation for genetic and genomic tests. These will be common polymorphisms associated with specific diseases, and their coding and incorporation into electronic health records. A number of activities undergoing standards development for family health history are also underway.

The clinical decision support areas are something where there is a great deal of activity going on within this community, and we are looking at ways to facilitate the integration of what are now Web-based tools or print materials into electronic health records for facilitating medical decision practices.

I will turn now to one of the co-chairs for the subgroup who has presented earlier here some of the concepts we are working on. Steve Downs, one of the co-chairs of that subgroup, will be taking over the discussion from here.

DR. DOWNS: Thank you, Greg.

It's a pleasure to be here again in kind of a different role than previously. I am relatively new to the AHIC process, so I'm going to present a little bit about what I've learned about what's going on. During the March 2007 vision meeting and priority setting session, newborn screening was raised in the important category of genetic and genomic testing. Some people in his room were helpful in bringing this to the attention of the group, I think. Informational discussions occurred throughout the summer of 2007 with HRSA, ACMG, NICHD, and NLM on this topic. It was first introduced for detailed discussion in August to the PHC group, which I will mention a little bit more later. A presentation by Michael Watson and Marie Mann was given then, and resource development consisted of a staff field visit to the Maryland state laboratory in October of 2007, and the newborn subgroup was formed in October of 2007 and charged with developing actionable recommendations around harmonization of standards for electronic health information reporting and exchange of state mandated newborn metabolic, genetic, genomic and hearing screening results. That's where I kind of entered into the picture.

I was asked to co-chair, along with Peter van Dyck, this group, and I am grateful for Peter's help, as well as Greg's and many others in negotiating this. I just want to make sure everyone understands that the players here at the national level are the Office of the National Coordinator for Health Information Technology, ONC, at one time ONCHIT, but I think the decision was made that ONC was a better acronym.

The American Health Information Community, or AHIC, is the advisory group that formed the Personalized Healthcare Workgroup. What Peter and I are chairing is a subgroup from that workgroup. So we are not quite within spitting distance of the Secretary.

The AHIC has the following role. It's advisory role to the Secretary of Health and Human Services with the charge to accelerate the development and adoption of health information technology, and to establish uniform standards with the goal of promoting interoperability between health information systems.

The Newborn Screening Subgroup has a very specific task within all of this. One is to make the case for a newborn screening use case. I will describe what I mean by use case in a moment or two, but basically to make the case that AHIC should take this up as one of the areas in which to develop these standards; also to suggest a brief or high-level use case or use cases in this arena; and finally to consider some of the implementation issues that come into play when one envisions actually implementing a system in these use cases.

I'm showing this largely just to impress you. This is the long list of people involved on the subgroup. If you are good at distance reading, you can glance through the list, but it's fairly sizable, and I am grateful to all the people who have put forward a great deal of work, and this is only page 1. Here is page 2. But a lot of people have been involved. Many of those people are in this room, and this is where the real work of the intelligence of the masses comes into play.

I had mentioned the term "use cases," and I think it is worth defining that for those of you who don't know it. A use case, loosely it's a formalism. It's not really highly formalized, but it's a software development strategy to aid in the design of information systems, and it has certain defined components that I'm going to go through briefly just so you understand what this task looks like.

Any particular use case defines a goal for a particular use for which the information system is going to be put. It refers to the system, which is treated as a black box. That is, there is nothing about a use case that says how a particular program will be written or how a particular piece of software will be put together. It's just as a black box, what is it supposed to do. The actors are the people or the other information systems or other objects that need to interact with that information system, and they are primary or secondary depending on whether the system is acting on them or they are acting on the system.

There are preconditions or triggers, and that describes in detail the situation in which an information system should come into play and what should trigger it to act. Then there is a general description of the course of events, what should happen in this particular use case when the actors interact with the system. Finally, there are post conditions, what will be the state of the information system and the actors when they are done.

This is kind of a loose description of what goes into a use case. There may be more or less depending on the particular needs. But this is the level at which the AHIC proposes to develop a description of what health information systems in support of newborn screening should look like. These use cases are intended to be given or made available to software developers who can use it as a guide to develop software systems that will meet the specifications of the use case.

So in the instance of newborn screening, components of the use case or goals for the use cases that we are envisioning, after discussions with our subgroup, include the process of recording data collected with the blood spot, to record bedside hearing screening results, to transmit birth site data to public health and to newborn screening labs, to record blood spot test results, to transmit newborn screening results including quantitative values from laboratory tests, and to transmit those to the medical home, to families, to public health, to registries. In other words, to create the ability to deliver appropriate information to any of those sites.

In addition, the group envisions looking at providing decision support to providers. That can be in the form of guidelines. That is a pull technology in which a provider may reach out to pull in information such as the ACMG Act sheets as appropriate to a particular case, or reminders. Push technology is

where, for example, we might want to remind a provider to check newborn screening results on a young child.

Other uses are to track positive screens, to assure diagnostic confirmation and clinical follow-up, to track confirmed cases, to assure long-term follow-up across time, which can include the life span of an affected child, and distance, which could include crossing state lines, making data available with appropriate precautions for quality improvement and for research, and that could include research around testing or treatment or quality improvement.

The development of use cases begins with descriptions of newborn screening information flow. Pretty much everyone in the room knows what the information flow looks like in newborn screening. I'm going to show you three screens full of stuff like this, not to show you all of it but to give you a sense of what's out there, starting with the baby. You can see in the yellow box that parental information needs to be provided, informed consent in some cases needs to be provided, a slip needs to be filled out completely to accompany a dried blood spot. Performance of hearing screening has to happen. The results of that need to be added to the slip that is filled out. That needs to be sent by lab courier to the state lab, and so forth and so on.

This is the overview of the information flow that was developed as a first step in beginning to look at the report that is going to go forward from the Personalized Healthcare Workgroup. The results of that and a number of discussions that I will overview in a minute has been a newborn screening draft recommendation that focuses in three main areas that recapitulate the charge of the group: the development of a newborn screening use case; issues around confidentiality, privacy, and security issues related to newborn screening; and reporting of newborn screening results to public health and to public health repositories.

The Newborn Screening Subgroup activities to date have included three meetings that were held in October and December. Issues considered included the need for standards, for test information, including the LOINC codes, diagnostic codes such as SNOMED, Medcin, ICD; raw data from laboratory instruments and how those are going to feed into the data standards above; tracking of qualitative testing and subjective observation and quantitative numeric values representing analytic values, percentiles and/or ratios accompanied by expected ranges; and interpretive reports to patients, clinicians, and registries; confidentiality, privacy and security concerns; research use of screening data; examination of other registries such as the hearing screen registries and immunization registries; and linking of test results to clinical decision support tools.

Issues were prioritized for recommendation development, and a recommendation draft has been created. We also fielded a newborn screening survey with state lab programs through the National Newborn Screening and Genetics Resources Center, and we're currently finalizing the draft recommendations and developing newborn screening high-level use case.

There have been some challenges. There are a lot of trade-offs that go into this, and I am not sure where all of this is going to land in the end, but right now we are working toward a comprehensive description of opportunities for health information technology to improve newborn screening, all the way from nuts to decision support and focusing on quick wins such as defining messaging and vocabulary standards for transmitting data, which can be done in short order and is a necessary prerequisite to the more elaborate potential for health information technology.

So, next steps. As I mentioned, the draft report to the Personalized Healthcare Workgroup is now under review by members of our subgroup and is scheduled to be presented at the Personalized Healthcare meeting in January, on January 30. At that point it will go under consideration by the Personalized Healthcare Workgroup and then the AHIC to consider for development of full use cases. This is the time line for that. On January 16, in two days, we have our next meeting of the subgroup to finalize the draft recommendations, and that will be forwarded on to the PHC Workgroup on

January 30, as I mentioned. Sometime between those two dates we hope to forward a copy of that recommendation to this group, looking for your input but also looking for your guidance as we respond, because on January 30 this goes up for vetting and is an opportunity for public comment, and to have the expertise of this committee in responding to public comments would be valuable.

On February 6 the staff will present the draft recommendations to the AHIC Population Health and Clinical Care Connections Workgroup, and on February 26, once consensus has been reached, the PHC workgroup co-chairs will advance the recommendations onto the AHIC for final consideration.

Ongoing, assuming we proceed with these use cases, the subgroup will continue to work on high-level use cases for newborn screening, describing the information flow for both newborn blood spot screening and early hearing detection, and we will be working on a newborn screening matrix of standards development process, that is a matrix between the data requirements to carry out these use cases and the existence of current standards and looking for where the holes are and where those things will have to be developed.

That's the activities of the group in a nutshell, and I'll open it up for questions at this point.

DR. HOWELL: Thank you, Greg and Steve.

Are there questions about the project? I know that the document that has been circulated has had a lot of activity as far as comments.

I think Ned has a question or comment.

DR. CALONGE: I just wonder, from the standpoint of the groups you work with, if there is concern about emphasis and direction for health information technology strategies going beyond this administration to whatever the next administration looks at.

DR. DOWNS: Well, I may not be the best person to respond to that because I'm not really much of a political wonk, but I can tell you that I do observe that to some extent as a medical informatician, and I haven't seen any lack of support for this sort of activity on either side of the aisle.

DR. HOWELL: Any other questions or comments?

(No response.)

DR. HOWELL: If not, thanks.

Michele?

DR. LLOYD-PURYEAR: I have a question. Did you want formal comments from this committee?

DR. DOWNING: I think informal in terms of getting to the January 30 meeting.

DR. LLOYD-PURYEAR: Getting to it or after it?

DR. DOWNING: Getting to it informally but in the process of leading up to -- and I don't know what your timelines would be to do this, but to have any official action or adoption or any issues coming as a recommendation for committee action from here would be helpful I think in terms of continuing to support these development activities. I don't know if you have a procedure for doing that, but I think it would be worthwhile hearing from you.

DR. LLOYD-PURYEAR: We do if we have a formal conference call. I just need to know.

DR. DOWNING: I'm certainly not intending to disrupt your activities are schedule, but I think any time between now and when the use case prototypes start to come out, which will be probably a month after the AHIC's action at the end of February, there is probably two to three months lead time in here, and there will be plenty of time once the recommendations when presented to AHIC are accepted and move forward for the use case, there will be many subsequent opportunities to weigh in on them as they go forward. But I think for the committee's activities here and their interest overall on health information, it would be worthwhile having some official action from the committee.

DR. HOWELL: Thank you very much.

Seeing no further comments or questions from the committee, we will move on with the rest of our afternoon. Michele mentioned earlier that as we move forward, we have three newly appointed subcommittee leaders. Jana Monaco and Tracy Trotter will co-chair the Education and Training Subcommittee, and Gerry Vockley will chair the Subcommittee on Laboratory Standards and Procedures. Coleen will continue her excellent work on the Long-Term Follow-Up Subcommittee. The Laboratory Standards Subcommittee will be in Brookside A, Education and Training in Brookside B, Follow-Up and Treatment in Linden Oak.

At the end of the day, that's that. So we'll see you back here in this room promptly at 8:30 in the morning, where we will zip along. Thank you very much.

(Whereupon, at 1:47 p.m., the meeting was recessed, to reconvene at 8:30 a.m. on Tuesday, January 15, 2008.)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMITTEE ON HERITABLE DISORDERS

AND GENETIC DISEASES IN NEWBORNS AND CHILDREN

Tuesday,

January 15, 2008

Grand Ballroom Salon E

Marriott Bethesda North Hotel and

Montgomery County Conference Center

5701 Marinelli Road

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C O N T E N T S

P R O C E E D I N G S (8:36 a.m.)

DR. HOWELL: Let me welcome you to the second day of our meeting, and we're delighted to see you on this very chilly Bethesda morning here today.

The first item of business today is that, as you recall, yesterday we postponed the review and approval of the minutes because Denise had some specific comments, and we would like to hear her comments before we finalize those. And I think Michele also has some modest changes that have been submitted. So the first item to be considered are the minutes for the September 2007 meeting.

Did you have comments about that, Denise?

DR. DOUGHERTY: Yes. On page 33, under "components of long-term follow-up care," the second bullet under that about five lines down, rather than "Dr. Dougherty disagreed," I'd like it to say, "Dr. Dougherty suggested that families' preferences may not always be have a physician be the center."

DR. HOWELL: That is to put your thoughtful comments in a more positive light.

DR. DOUGHERTY: Yes, thank you.

DR. HOWELL: So there's not a change in the text, but I think Denise is getting ready to run for office. It's that time of the year.

And, Sharon, you had some comments?

MS. TERRY: Yes. On page 42, the top of the page, "Natasha Bonhomme presented" not on the Genetic Alliance's other two newborn screening projects, but on the other two newborn screening projects, and then they're listed underneath. So we just don't want to make it look like these are Genetic Alliance projects as well.

DR. HOWELL: Okay. That sounds like a note of clarification.

Now, did you have comments from these minutes, Michele?

DR. LLOYD-PURYEAR: Just to change "Luminex B" to "Luminex beads," and that will be done. So the changes will be made as suggested.

DR. HOWELL: Are there additional suggestions for changes in the September meeting?

(No response.)

DR. HOWELL: Can I then have a motion to approve the minutes as modified?

PARTICIPANT: So moved.

DR. HOWELL: Second?

PARTICIPANT: Second.

DR. HOWELL: Those favoring? We need to formally do this since they become part of the official record and posted in perpetuity.

(Show of hands.)

DR. HOWELL: Thank you very much.

We then had a November the 7th conference call, which I think most people felt was very productive. I wonder if there are comments about the minutes for that meeting. Are there any suggestions for change?

(No response.)

DR. HOWELL: If not, can we have a motion to approve the minutes that are, again, in your book from that session?

PARTICIPANT: So moved.

DR. HOWELL: Is there a second?

PARTICIPANT: Second.

DR. HOWELL: All favoring?

(Show of hands.)

DR. HOWELL: Any opposition?

(No response.)

DR. HOWELL: Unanimously approved with no modification. Thank you very much.

We will now move to the reports of the various subcommittees. Apparently the subcommittees yesterday had very productive discussions, et cetera. Our first presenter is the Laboratory Standards and Procedures Subcommittee, and that's headed by Dr. Vockley who appears to be imminently ready to start.

DR. VOCKLEY: All right. Laboratory Standards and Procedures Subcommittee.

Members present you can see listed. Missing was Mike Skeels.

I'll just point out that Ned and I were new members, and I will admit that we spent probably the first hour to hour and a half of the meeting sort of trying to figure out what we were doing as a new chair. It was interesting.

Anyway, we started off with looking at some old business and Harry Hannon reported back on a study that the committee had begun now probably about 15 months ago on a routine second screen study. This focused on congenital hypothyroidism and adrenal hyperplasia and was to examine the need for a second screen to improve the sensitivity and specificity of the pick-up.

It has both retrospective and prospective components. It was to work through the state screening labs and be coordinated by Harry at the CDC. The goal was to enroll 12 states and to have about 25 percent of the births in the U.S. represented.

It has met with some difficulty, mostly with trying to figure out who can or should approve the study and a lot of back and forth between the CDC IRB, Harry, and the state IRBs. The bottom line is that currently only three states have actually approved the protocol. All three granted waivers for the retrospective portion of the study, but one of the states actually wants them to go through a full application for the prospective portion of the study. So Harry is continuing to work on this and will, hopefully, be able to give us some additional follow-up in the future.

Some additional difficulties that he has identified as part of this. One of the issues with IRBs in some of the states has been who is qualified to be a PI of the study. There were different consent processes, of course, for each state and each IRB, and as I mentioned, there really was no consensus on the level of risk by each of the individual IRBs.

Mike Watson, I think appropriately, suggested that the research subcommittee or workgroup, I guess it is, of this committee might be able to help expedite some of those things. As I've also just joined that workgroup, hopefully we'll be able to make a little bit of progress in trying to expedite some of these kinds of issues, and I'll look forward to working with that group in the future.

Steps that the full committee can consider is somehow or other advocating for a national approval process for newborn screening studies or screening studies in general. That's, obviously, a bigger piece than the Laboratory Subcommittee, but I throw it out there for consideration.

We also talked a little bit about the potential for adding a second screen -- evaluation of using a second screen in the tandem mass spec part of newborn screening. Because we didn't want to derail the current process for the other two conditions, it was felt that if that were to happen, it should be a separate study. But, in fact, what we may be able to do is to leverage some of the information that is being collected on a collaborative basis by now 41 states through Piero Rinaldo's effort. And we're going to have a presentation by Piero who, of course, is a member of the subcommittee, to the group perhaps the next time to look further into how we might either better stage a study or if, in fact, we have the information that we already need based on that.

The subcommittee took a look at whether or not there needed to be more input of the subcommittee into the technologic aspects of adding disorders to the newborn screening panel. This was something that was reviewed about a couple of years ago by the subcommittee. We talked about it, again, more just to decide whether it needed to be revisited. The subcommittee felt that the process has been appropriately and adequately incorporated into the Evidence-Based Review Group and that there is a member of the subcommittee on that group and that we really didn't need to revisit that any further.

As we spoke a little bit about the tandem mass spec issue regarding that last point, we also felt that we should look to the example of collecting and improving, refining national standards for or making available standards nationally for newborn screening results and for other disorders or for other technologies. The subcommittee, if it concentrated on highlighting needs through discussion and reports and testimony at the subcommittee meeting, reporting those back to the committee, could push that progress forward without the need for probably any sort of full protocols or trials sponsored by the subcommittee, that simply raising these issues by the full committee will focus attention on them and, hopefully, spur cooperation on testing standards. So again, as I feel my way through organizing this committee, by the next time we meet for the full committee meeting, hopefully we'll have some specific angles on things that we really need to spend some more time.

There was a discussion on reexamination of the newborn screening panel, disorders added to the newborn screening panel. Currently the assumption -- and I don't know if it's more than that at the level of

the full committee -- is that subtractions from that panel will occur through a process that is very similar to that of addition so that that will largely be a mechanism, probably through the Evidence-Based Review Group, but that the Technology Subcommittee could and should focus on modification of testing mechanisms for disorders that are currently in the panel, recognizing that it's the disease that's part of the screening panel and not the testing technique so that if a testing technique for a disease that has been considered appropriate for the panel through additional experience is subsequently viewed as not necessarily being robust enough, that the subcommittee can focus attention on that technologic deficit and spur improvement because we would still like to be able to keep the disorder in the panel.

We had a presentation again from Dr. Rinaldo on tyrosinemia type 1 as an example of this. There is a very nice study from Grant Mitchell that we hope will see the light of day soon and be able to present to the subcommittee in a formal way that clearly shows that the disease is treatable and should remain in the panel as a result of that. However, standard MS/MS experience, again reviewed by Dr. Rinaldo, was again very convincing that tyrosine levels really don't correlate well enough to the disease to be reliable. So another technology is needed.

He presented their group's work on succinylacetone which was reliable first as a second-tier test and then could be incorporated into a first-tier test. The subcommittee will plan on inviting a broader discussion of this for the next meeting and come back to the full committee with specific recommendations for altering the technology for identifying tyrosinemia hopefully by the next meeting.

This is the final piece. We then had a discussion about the role of molecular techniques in screening with the recognition that there are a growing number of genetic disorders that are amenable to molecular screening. This falls into a couple of categories, first of all, as follow-up to the current newborn screening panel. The inborn errors, MCADD, and galactosemia are good examples of how that's being incorporated in the field today. CF and hemoglobinopathies are also good examples of that. However, it is also going to be clearly the primary method of choice for some disorders as we move forward. Good examples that came readily to mind are hearing defects and some of the immunologic disorders that are receiving increasing focus. So the subcommittee really felt that this was an area that we needed to place some more focus on in the future and we'll do so.

I included a note to myself that while this committee has focused a lot on newborn screening, screening can actually occur in other periods of life. So we need to maintain that as a concept that the group continues to throw around. When is it appropriate to start thinking about screening for some of these other disorders?

With that, I will be happy to take questions or, Rod, do we do this afterwards?

DR. HOWELL: Thanks very much, Gerry. I had the privilege of being at that meeting, and it was very informative. I'll elaborate briefly on the tyrosinemia discussion, which was I thought terrifically informative, because tyrosinemia is a very serious condition and the data are overwhelming that it's eminently treatable. Piero's study where you're looking at values that have actually been obtained and looking at the cutoff values that are being used by the states would clearly indicate that the current tyrosine screening technology doesn't identify the patients properly. So you need to switch tests. And I thought that was an extremely informative type observation that comes from experience in screening and looking very carefully at what you're doing. Again, I think it will be exciting to see what comes out of that further discussion.

There was never any question about the importance of the condition and keeping it on the panel, however, but it was clear that the technology needed to shift to be more robust.

Alan?

DR. FLEISCHMAN: I just wanted to make a comment about the potential for collaborative research going forward. First, I think it's important to read some of the distinctions between public health surveillance and human subjects research that have been published by the CDC and have been opined on by the Office of Human Research Protection. Sometimes what some IRBs at the state level or in institutions consider research, there would be others that would not.

The second, I think, is an important collaborative piece of work that Office of Human Research Protection with the Association of American Medical Colleges and the NIH is doing on alternative models for IRB approvals, that is to say, so-called central IRBs or collaborative processes, which are, in fact, supported by the regulations if people wish to defer. Within the regulations at 45 C.F.R. 46.114, for those who are research ethics groupies, there is a part called "cooperative research" which allows any IRB to defer to a central or other IRB to allow for collaborative work and to shorten the process of IRB approvals. Now, it does take some commitment on the part of an IRB to trust another one, but it makes sense in this kind of work to support that kind of effort.

It's unlikely that Congress is going to opine about newborn screening in my opinion, opine about newborn screening research on its own in terms of changing regulatory structures to allow it, but all these other activities allow for it in a streamlined way. And we might ask our chair to request of another Secretary's advisory committee, the Secretary's Advisory Committee on Human Research Protection, to assist in thinking about how to streamline this kind of very important collaborative work and see if they might come up with some thoughts about how to create that kind of national collaboration.

DR. HOWELL: I will comment briefly. Some of the research programs that have recently been begun by the NIH that involve states have had tremendous issues with getting underway because of the way that various states deal with IRB issues. So I think that as we move forward and do a lot of research in newborn screening, I think solving this and making this more efficient is just absolutely essential.

I wonder. Harry, are you here? Could you comment briefly about what was the issue? Would states not defer to a higher power, shall we say, or to another power? Not higher by any means.

(Laughter.)

DR. HANNON: States will defer to a higher power, but they could not come to a decision which higher power they would defer to. It depends on your religious link.

Our issue with the IRB somewhat has to do with how we design this study. The study was designed, for some reasons that I will not discuss, that it all be collected at APHL in terms of the data coming in. CDC was involved in designing the protocols from both the laboratory and the medical aspect in terms of collecting the data. None of the data actually comes to CDC. So it became impossible for me to get an IRB either through Birth Defects with the medical link of it or from the laboratory. We got responses from the first CDC IRB that at least the retrospective study should be no problem and just get waived and that the prospective study might be researched but it could be waived also.

Then when I couldn't get an IRB number, which the states were requesting to refer back to the CDC IRB, I went to Stuart Shapira in Birth Defects to try to get it on the medical piece, and we came back from a very comprehensive IRB group who got together and discussed it, which included the IRB person from my center, and said both should be considered as research. And APHL has no mechanism to get IRB. So we got in this dilemma that we couldn't get a central IRB approved for the states to use to defer back to.

And then we have the states who have got approval. In one case, they approved one as a waive because it was anonymous, and the other one they would not approve because it was research and it had to be considered differently. And in one state, both were waived. So, I mean, there is high inconsistency among the states in terms of the IRB.

But we couldn't get a central IRB that could be considered by the state IRBs to defer back to just because of how we started out with the study. If we had decided that the data was coming to CDC and that we would have a strong role in managing that data, we could have gone through to the CDC IRB process and had a central IRB to defer back to. So part of that is the spinning of a learning process that took approximately a year to get to where we are now.

Presently the head CDC IRB person in Birth Defects, Scott Campbell, has volunteered to interact with the states to help them get their IRB. So now we're going on a one-on-one contact with the states and their IRB issues to try to get each of them approved through the state IRBs. So your information would have been helpful a year ago.

DR. HOWELL: The second specimen study is an important study, and I think it's fair to say that, because of these issues, it's not gone forward. So I think it's essential.

We will take Alan's advice and get someone here.

Michele has a comment.

DR. LLOYD-PURYEAR: And we've also been in conversations with the Secretary's Advisory Committee on Genetics, Health, and Society who also are interested in this issue, multi-centered, multi-site research and issues around IRB. And they also pointed to the need to include the Office of Human Research Protection.

DR. HOWELL: We'll be in contact with that group and schedule actually someone to come and present.

Coleen has a comment.

DR. BOYLE: I just wanted to make the group aware of another possible mechanism to use in thinking through issues that perhaps have public health emergency perspective and that is the Epidemic Intelligence Service Epi-Aid mechanism. It may have been that we could have used this type of mechanism for this study. What that allows us to do is to act quickly, responsibly, work with state health departments. It allows for expedited IRB. It allows us to waive OMB, and it's a very, very useful mechanism. CDC does all of its emergency response work through that mechanism. So we just might want to think through in the future perhaps using that in this context. I think it would actually be an excellent use of it.

DR. HOWELL: It's clear we need to have this as an agenda item with some outside experts to come in and help us move ahead because this committee should be able to make a significant contribution there.

Joseph, were you or Sharon having some comments?

DR. TELFAIR: Yes, just a comment, a piggyback on Michele's comment. One, Hunt Willard led the group within the Secretary's Advisory Committee on Genetics, Health, and Society on the long-term study follow-up, and on the website, there is the report that covers a section of the issue that Michele just referred to. The report itself is downloadable to review. But Hunt Willard is the person from that committee who, if you needed to speak to someone about those issues, chaired that committee.

DR. HOWELL: Yes?

PARTICIPANT: Yes, thanks. I have one comment about that subcommittee meeting, and I'd like Piero's response.

It seems to me like it might not be a good idea to have in the minutes of that subcommittee meeting that the second-tier succinylacetone is actually a reliable method for screening for tyrosinemia 1. I think it did eliminate the false positives. There wasn't any demonstration of detecting tyrosinemia 1, and I think the ranges of known tyrosinemia 1 cases were below the suggested cutoff for a second-tier. The primary is actually the direction that I think would be most effective.

But I would like Piero's comment. We'll go by whatever he suggests on that.

DR. RINALDO: Well, the data shows that the second-tier test of the tyrosine level of 150 micromolar will pick up 75 to 80 percent of cases. So it's certainly better than the alternative. Now, is it perfect? No. Is it an improvement? I believe it's still an option if, for whatever reason, people don't want to expand their primary screening. So I think it's a good way that will have, again, a likelihood of detecting cases, basically 7, 8 out of 10. So it's a subjective call at that point.

DR. HOWELL: But would not be as reliable as a primary screen using succinylacetone. Is that correct?

Any further comments for Gerry and his committee? It was a very lively committee. There was a lot of discussion. Kwaku?

DR. OHENE-FREMPONG: One quick question about the molecular screening. Besides Pennsylvania, is the committee aware of any other state that uses molecular screening as any part of the hemoglobinopathies screening?

DR. HOWELL: Michele is saying California.

Brad?

DR. THERRELL: Texas also. Texas. Washington State is a second-tier. Right? New York is a second-tier and California is a second-tier.

DR. HOWELL: Thanks very much.

Perhaps we better go ahead with the Education and Training Subcommittee. We benefit from having two new fearless leaders of that committee, Ms. Monaco and Dr. Trotter. Apparently Tracy is going to be speaking for the group.

DR. TROTTER: I lost the flip.

First of all, thank you all for joining us yesterday. We had a room full of knowledgeable, enthusiastic, and passionate folks, and if there are any of you who are quiet and shy by nature and would like to come to the next meeting, please join us. That would be good.

We had a lot of new people, including myself, and probably a third of the room, I think, was the first time they had been to this subcommittee meeting. So we also spent the first couple of hours trying to find out where we had been and where we should be going based on that. And out of the kindness of my heart, I will not have any slides about those two hours. So we'll move ahead to the couple of items that we did come to action, thought about.

First was a concept that had been in front of the subcommittee for some time, which is in some way having a national newborn screening repository to provide a user-friendly access to education materials in multiple languages. It had been noted by a number of people that these translations had been done by various states, regions, individuals and were often not available to other states, regions,

and individuals on a timely basis and that there was a lot of duplication of effort that seemingly could be avoided because these are difficult technical problems from a translation standpoint, as many of you know, and it seemed if somebody had done a diligent job that we could pull that together in some fashion, not necessarily a physical place but a web-based place. So using many of the organizations who are represented here and who have been in this business for a long time, this should be a doable program in some fashion, and that will take some steps.

The first step was a recommendation to this committee that there be a specific section of the national newborn screening website that contains newborn screening educational material in multiple languages and information that's accessible to all of our five target audiences that are listed there below. This sort of becomes step one.

Hopefully, we will then have a workgroup from our subcommittee. We've had more than a few volunteers to help us look at maybe some more specific thoughts about translation guidelines, literacy guidelines, things that might represent a threshold that would be helpful to Brad's group -- and they've always vetted very well what goes through or is linked through their website anyway -- to make this a little more formal in the future.

We then talked about future directions and how do we provide the education and training that is in theory what our subcommittee is supposed to be directing for these five groups. Obviously, you can't do everything for everyone, and how might we focus on that. There was a clinical report in Pediatrics written by a number of people who are at this table and in this room who were on the authoring committee which published this week I believe. From the abstract, on this slide you'll see are a few pithy phrases that with the advances in newborn screening, the new challenges to the primary care physicians -- this was written for pediatricians but certainly applies to anyone providing primary care at any level -- from both an educational and management perspective, these challenges are going to be increasingly great, and we in practice require access to this information. And the recommendation is that there's collaboration with local, state, and national partners. And I think we probably fit that role pretty well.

It is, we felt, an opportune time timing-wise for this group to partner with the existing other professional groups who, hopefully, will be similarly motivated, but of course, for them it's a small piece of their plate and for us it is what we do. Our job is to make it a bigger part of theirs. One of our thoughts was -- and we're now awaiting proposals both from our subcommittee and I'm requesting proposals from this group as a whole on where you think we should be going to focus this. One thought was that if one looks at the role of the primary care physician in newborn screening and the different roles that they play and target those, that you end up targeting most of the rest of the audience that we are required or mandated to approach.

The response to the initial out-of-range result, which of course is now becoming something that all of us in practice deal with, which for the first 20 years of my practice I think I dealt with once -- now that we have expanded range of testing, all of us are getting out-of-range results. Three out of four of them are false out-of-range results, which is a whole new can of worms that we deal with. The geneticists get to deal with the real one, and then we have to deal with those other parents for the next eight years.

And coordinate the complete evaluation. In some states it is literally up to the primary care person to get that done. In others, it's taken over more readily by someone else.

Most importantly is to continue to provide the medical home and coordinate the ongoing care, which we haven't talked about a lot in this committee but is going to become more and more important that we understand, as we get into the long-term follow-up.

And the trickle-down effect, if you will, of all of this is that we will end up educating the families and educating the health care workers that we work with in nurseries and birthing centers, et cetera. So if the

primary care physician is more well educated, they can become the person who trains the next stage in sort of a "train the trainer" type approach.

Overall, this increased pervasiveness of genetics in the world of practicing medicine, which most everybody in this room, of course, has understood for a long time, but most of us in practice and most of my colleagues are just now being hit by it, is going to require a lot of education and a lot of training. A recent poll quoted in a recent paper said that 4 percent of practicing primary care pediatricians felt confident reading the results of a molecular genetic test. Four percent is not quite the number we're looking for.

So I think there are a lot of ways we can impact genetic literacy at the primary care level and that that impact would, hopefully, then most likely hit every other group that we're looking at.

Those are sort of a broad brush of a thought or a focus, and we're now looking for more specific, more focused type ideas from both our subcommittee and from the committee as a whole. Thank you.

DR. HOWELL: Thank you very much, Tracy.

Are there questions or comments from other members of the committee to Tracy? Jana?

DR. TELFAIR: Joseph. I just want to make a comment. Thank you for the report.

I just want to bring into the minutes, if I can, that the Secretary's Advisory Committee on Genetics, Health, and Society has started a similar group to this one, and I would suggest that maybe an opportunity to have a cross discussion with that committee chair, Barbara Burns McGrath, would be beneficial to exactly the things that you're bringing up now. That group is getting started, but it's been a long-term discussion within the committee itself for quite a while and recently that group has gotten started. So I just want to make a suggestion, if the opportunity occurs, to do that.

DR. TROTTER: Thank you.

DR. HOWELL: What's the official title of the group, Joseph? The reason I'm having trouble communicating is you can only have two microphones on at once.

DR. TELFAIR: Thank you, sir. It's not a problem.

The Task Force on Education is the official name of it, the Task Force on Education for the Secretary's Advisory Committee on Genetics, Health, and Society. That's the official name.

DR. HOWELL: Tracy, as you folks move forward for the next session, what are going to be your very high priority items to move ahead and have actions on?

DR. TROTTER: The first is to sort of help get this repository in place. I think that between now and our next meeting, we should be able to come back with a concrete movement on having that going.

Second is we're going to attempt to review at least and come up with guidelines for translation and literacy requirements that would be appropriate criteria and can be used by this group.

More importantly I think is to sort of launch our approach to filling this educational gap that we talked about.

DR. HOWELL: What about any formal ideas about working with the Academy of Family Practice or Pediatrics about specific educational efforts in this area?

DR. TROTTER: Yes. We, obviously, have representatives on our committee who attended our meeting. So we hope to be able to take back to each of those groups, hopefully, opportunities to provide workshops at the annual meetings, to be available for CME type of introductions to this process of medical genetics. That's been a bit of a struggle in the past, but this is an opportune time where they're going to be looking for more of that information.

DR. HOWELL: Would it be worthwhile to have a request from this committee to the academy to do a workshop or something, or would that not be helpful?

DR. TROTTER: I think that would be helpful, yes.

DR. HOWELL: Would the group think it would make sense to ask the academy to focus on planning and working on a workshop that would focus on these issues? Becky, I see you shaking your head. Do you think that would be worthwhile?

DR. BUCKLEY: Yesterday I suggested that pediatricians be genetic counselors at the first level, and I got royally negated on that response because apparently there's some data saying that -- maybe one of the people who were there could comment -- a certain percentage of pediatricians have no knowledge of genetics. But I know that in order to pass your pediatric boards, you have to have some fundamental genetics education and knowledge. So I know this is something that, if the Academy of Pediatrics got behind it, could really be helpful in trying to bring up to date the education for genetics and genetic counseling.

DR. HOWELL: Michele is suggesting that the subcommittee develop a formal recommendation to the AAP that could be endorsed by this committee, in other words, sent forth from this committee so that it's a little more clear about what we would like the academy to do.

DR. TROTTER: Yes. We would like to develop that for the AAP, AAFP, and ACOG. We think all three of those would benefit from targeted sort of CME meetings.

DR. HOWELL: Michele is suggesting perhaps you could do this during the break today with her, and then we could come back and get that going soon, rather than many months from now.

DR. TROTTER: That doesn't sound like a break.

(Laughter.)

DR. TROTTER: Yes, I'd be happy to.

DR. HOWELL: We're going to have 15 minutes. I mean, you can't use all of that drinking coffee. So why don't you all meet with Michele.

Becky, I think the concern that was expressed to you yesterday is I think that the average practicing physician has essentially no information on genetics. The younger folks have increasing amounts, but I think it's going to be very important that the primary care physician be the first contact for genetic information, and I think it will be the duty to try to see if we can fix that.

Coleen has been very patient down here.

DR. BOYLE: I just wanted to comment about the issue of the repository, the website for education materials. I guess when I start thinking of it, waiting my turn to speak, it's a very complex issue. Obviously, there are lots of materials out there, and whether to establish links to those materials, whether putting the materials under the website of the advisory committee sanctions those materials. I mean, I don't know. There are just a lot of thoughts there. I assume you've had a very robust discussion about this issue already.

DR. TROTTER: That was the first two hours.

I'm not sure we've solved all of those questions. I think the idea is to start out by seeing if we can pull information that's out there together and then maybe see where we are.

DR. HOWELL: Chris and then Piero.

DR. KUS: Just to follow up on Dr. Buckley's comment, one of the things I think in doing this is trying to be clear in having discussions with the academy and with family practice about what's the expected role for pediatricians and then train to that because I think the comment was you mentioned that they are going to be genetic counselors. If you're a pediatrician, you're going to say, whoa, that's not what my job is. But I think it's important to be clear about what's the expectation, given today's world of primary care.

DR. TROTTER: Well, and copies of the publication that I quoted in here are in the back, but maybe not everybody looked at that. If you look at it, it is very clear, at least for the pediatricians, that this is your role, and I think there are going to be a lot of my colleagues who are going to look at it and say, holy smokes, I didn't know that, and now how do I do that.

DR. HOWELL: I think it's a necessity. You're going to be there and you're going to get these results back, and there has to be some initial advice that should be properly done.

Piero, you had a comment? Mike has.

DR. WATSON: Just briefly, I think one of the things that we don't publish traditionally is some work that we've done. Back in July we went to the U.S. medical licensing exam. The National Board of Medical Examiners reviewed all of steps one, two, and three of USMLE to identify the proportion of questions that included genetics content either at the basic science level or at the skills development level. And because of the NBME rules of security and not letting people know really what's on the board exams, we don't publish those kinds of things.

But we have a lot of data about what medical students are doing. Frankly, they're doing pretty well in basic science in genetics. There's very, very little in skills development about how to use that knowledge in practice. I think if you look at the entry point of people going into residencies in pediatrics and take that whole spectrum, you'll get a much broader perspective of where to hit educational pieces.

DR. GELESKE: I think the role of the primary care physician, to a large degree and what the paper speaks to, is providing chronic condition management for children with metabolic diseases and special health care needs. There needs to be a working literacy of genetic issues. What I see a lot of our role is is providing that medical home. It's coordinating their care and making sure the kids get the services they need as kind of the central hub for the family. I think pediatricians could use some more education on how to do that properly, but I think they both go hand in hand.

DR. HOWELL: And Brad has been very patient at the microphone.

DR. THERRELL: With respect to the first suggestion about access on the National Newborn Screening and Genetics Resource website, we concur with that and we've actually done some preliminary work already. So at the next meeting of the subcommittee, we'll be able to report back on what some of the issues are whether or not we are able to fulfill whatever the expectations of that committee are.

DR. HOWELL: Any more comments from this committee?

So you're going to meet at the break which will be adequate to have coffee and a report and come up with a recommendation that can be then considered by the committee after that. Thank you very much, Tracy.

Our final subcommittee report is the Follow-Up and Treatment. Dr. Coleen Boyle.

DR. BOYLE: We had a wonderful meeting yesterday, like my two fellow colleagues who led their respective subgroups. I want to thank all the participants for a very lively discussion.

I just want to review for you all the activities for the Follow-Up and Treatment Subcommittee. As I reported back in September, our subcommittee really has been focusing on two issues. It took us a year or two actually to sort of get our direction and our feet on the ground, for those of you who are starting afresh in terms of your leadership for the Lab and the Education Subcommittee.

But as you all know, we've been focusing on the issue of long-term follow-up related to the newborn screening system, given the fact that this aspect of the newborn screening system is probably least well developed. As I reported on last time, we had a stakeholders meeting in April of 2007 where we brought together many of you who are currently in the audience to really look at two issues. The first one was to take a step back and really define what the components of long-term follow-up were, and then the second part of that activity was to look at the primary participants in long-term follow-up and try to enumerate and evaluate their various roles and responsibilities. Actually the statement that just came out by the AAP that all have been referring to does a nice job of highlighting what roles and responsibilities of the primary care provider are in that regard.

The other major issue that the subcommittee has been focusing on is the issue related to coverage for medical foods for children identified through newborn screening. We actually have a workgroup that has been focusing their time and attention on this, and I'm going to highlight the activities that that workgroup has been focusing on. They focus on two issues. One is really trying to characterize the problem, and they're doing that really through the development of a survey tool that will help describe the problem in more detail.

And the second issue that we've actually started to get engaged in in our September meeting was really to look at what are the existing policies, professional policies, as well as state-level mandates regarding reimbursement for medical foods.

So I'm going to go through each of those activities in terms of where our subcommittee is.

I did report to you last time in September that the product from the first part of the long-term follow-up activity, and that was identifying and highlighting what the major components of long-term follow-up are. You saw this slide last time. Dr. Alex Kemper has really taken the lead for our subcommittee in developing a white paper. That white paper was very brief. It's probably about five or six pages long. You've all had an opportunity to vote on it. For those of you in the audience, the white paper was approved by the full committee either in October or November. I can't remember when our conference call was. And at this point we are going to be submitting a white paper to Genetics in Medicine.

Just to review for you, the paper itself highlights what the goal of long-term follow-up is for children and their families. It defines what long-term follow-up is in terms of its major components, which are evidence-based treatment, coordination of care, continuous quality improvement, and new knowledge discovery. Obviously, the principal individuals and groups involved in long-term follow-up really take a major emphasis in each of these components, and that's really the second part of this.

Yesterday, with Alan Hinman's help, we had a very, I think, productive and lively discussion really trying to move the second part of the long-term follow-up white paper along. In our April meeting, we had really come up with a tentative draft of the roles and responsibilities of the four primary participants in long-term follow-up. That's the individuals and their families, the primary care providers, the specialty and subspecialty providers, and the state and local health agencies. Yesterday we reviewed those and refined what we saw as the major roles and responsibilities, and we also prioritized those lists, really trying to highlight what we thought were the principal roles and responsibilities for those participants.

We also identified a number of other groups that we felt were key to the success of long-term follow-up, and this included sectors such as the insurance sector, the education and social service sector, the information and technology sector, the policy makers, both at the state and federal level.

Our thought in terms of, again, trying to move this to a product that's a product of the committee in the months between now and our next meeting, which will be in May, is to do two things. One is to refine and try to, again, develop into a white paper this whole roles and responsibilities for the four major participants, circulate that to those that were in attendance at our subcommittee meeting yesterday, as well as, hopefully, to all of you for comment, perhaps even do a broader dissemination of this to get better feedback into what we have highlighted as the major roles and responsibilities, and then relate that back to the major components of long-term follow-up so this sort of all fits together nicely, and then to develop it into a consensus document that we would bring back to you for consideration like we did with the initial components piece of it. So we anticipate having it for our May meeting. We're hoping we can have all of this done by May so we have a draft for your consideration.

In terms of our other major activity, the medical foods and formulas, I want to highlight the contributions of a number of people who have really moved this issue along, including Jill Shuger, Rani Singh, Mary Kay Kenny, and Jill Fisch who really moved this issue along. Really without their hard work over the last couple of months, this issue would not have moved along as quickly as it has.

What we're focusing on is really to try to understand, as well as to reduce the financial barriers to families in obtaining medical foods and formulas. As I highlighted in my introduction, what we're doing is a number of things. We're working on developing a survey tool and implementing that survey tool to get better information on the need, as well as to use that tool to try to track what we consider appropriate changes to the system over time. We're exploring state legislation and we're trying to understand its impact. And then we're also evaluating existing professional policies on medical food requirements and need for formula and food coverage.

Regarding the first aspect, state-level mandates, Alyssa Johnson, who was formerly with NCSL, reported to us yesterday an inventory that they had conducted. Apparently there are 36 states that have some type of legislative language addressing the issue of coverage for medical foods. Obviously, the language varies from state to state. The implementation of that language varies from state to state. Some of them include just PKU. There are age limits. There are caps involved. So it's very unclear right now how that legislation translates into practice. She was advising that we actually talk with or do a survey of private insurers at the state level to get a better sense of how that state legislation translates into practice. So, again, how we move forward on that whole state-level mandates issue I think is an important one, which I don't think we came to a conclusion yesterday.

Rani Singh gave us an overview of the professional endorsements. AAP, the Committee on Nutrition, had a 1994 statement endorsing private insurance and public insurance coverage for medical

foods, and there are two more recent endorsements by the Society for Inherited Metabolic Disorders, as well as the Genetic Metabolic Dieticians International Society, both endorsing medical food coverage.

As a next step, we are considering doing some type of state-level survey to get a better sense of legislative mandates and then also engaging the insurance industry. Alan Hinman was walking us through how coverage for vaccines became a mandate, and he was suggesting that we need to really engage as a very active participant in our subcommittee the insurance industry. So I think that's something that we're going to need to consider.

In terms of really getting a better understanding of how the legislative aspects translate to both the provider and the parent, I think the survey tool that Mary Kay Kenny has helped us develop is really going to be very helpful in that regard. We reported back to you in September our work in the development of that survey tool. There has since been some additional cognitive testing, a group of parents in New York. We are actually going to do some more testing with parents to really increase the reliability and the validity of this instrument and also make it more culturally sensitive and appropriate. We're really hoping to try to engage some of the regional collaboratives in the implementation of this survey, both in terms of the validation, as well as sort of the implementation, so we get better information on that.

I think that's it.

DR. HOWELL: Thank you very much, Coleen.

I wonder if your group discussed how research would be integrated into the long-term follow-up program as far as the outcomes of the folks screened, the outcomes with regard to treatment, novel treatments, et cetera because that's obviously going to be a key way that we really gain evidence for the future. Did you all discuss that extensively?

DR. BOYLE: We talked about it in terms of the roles and responsibilities of the participants in long-term follow-up and obviously their active engagement in research, as well as their active engagement in terms of the long-term follow-up and monitoring. So clearly new knowledge discovery, which is one of the major components of long-term follow-up, is integral. I actually see that as some of the future steps for our subcommittee once we get through this portion of it, but obviously clearly highlighting the roles and responsibilities for all to be actively engaged in this issue was clearly on the table yesterday. So I don't know if anybody else who was in attendance wants to comment on that.

DR. HOWELL: Any comments?

MS. MILLER: Hi. Julie Miller.

I just wanted to comment that as we were talking about roles and responsibilities, particularly for public health and not necessarily related to the day-to-day implementation of long-term follow-up, but more broadly in terms of public health functions, I think at least some of us, maybe not a majority of us, felt that there is a role and responsibility not just at the state and local public health level but at the federal level because certainly policy development and core public health functions at the federal level do have a large influence at the state and local level relative to this.

DR. HOWELL: One of the goals of this committee, when reports are developed by the committees and so forth, is to really focus on getting them published in refereed journals so that they can be accessible. That, obviously, generates a considerable degree of interest in how authors, et cetera will be determined. In other words, if you have a product of the committee, et cetera and it goes in, and we have made an effort to submit these to Genetics in Medicine so, hopefully, they will be reviewed favorably and get published so that there would be a consistent location of the reports.

But Michele might want to comment briefly about some of the scenarios that have been discussed as far as authorship is concerned because I think the key thing is that we want to be sure that the reports are appropriately labeled as products of the committee, but it's also important to recognize those people who have worked hard on the effort. Michele, do you want to comment?

DR. LLOYD-PURYEAR: I think the first question is if you go back and look at the long-term follow-up report and also the report that addresses the review process of the committee, to make sure that everyone is in agreement with how authors are chosen. The long-term follow-up report is largely that subcommittee. It's not the committee as a whole. Although the report was endorsed by the committee, it's largely the subcommittee, and that's the same with the committee report on the evidence review process. It's a smaller group of the committee. And to make sure, as we go forward, especially as evidence reviews are generated and recommendations are made by the committee -- first, a reminder that the committee's work is already public because of the transcripts and the meeting summary and the committee website. So publishing it a second time that's getting in a journal or some part of that, some aspect of that public meeting that summarizes what happens in this meeting -- getting a journal to agree to publish something that's already sort of been published is an issue.

But I want to make sure that people are thoughtful about and in general agreement with authorship. I think it's hard to anticipate, but looking at those two examples, those two reports that have come out, are they in agreement with how authors were chosen? Because as we go forward, there are more reports that are going to be produced, and I want to make sure that people think the process is fair.

DR. HOWELL: And for those of you who haven't followed that carefully, basically it has listed the committee or the workgroup that did the work, and it says for the committee. That's basically how they've been done, which seems sensible to me, but I think it's important that the committee thinks that's the sensible way to go forward.

DR. TELFAIR: I think it's been more than fair. I've appreciated the discussion that has gone about in terms of decision-making, and also just the way that the group has been conducted. It is a real strong belief that those that actually do the work should be recognized for that, but to be fair to the rest of the group who have contributed. I know I'm not a voting member, but my contribution is that the way that it was gone about, the level of respect that was given to the members, and then how the final decision has been made and leadership was very fair from where I sit. So the way it comes out, I think it's more than a fair process and more than a fair recognition.

DR. HOWELL: I see no burning dissents from that, but it seemed like a sensible thing to, obviously, have the people that did the work be on the thing, but clearly recognize that it's a report from the committee and not an individually generated thing. Okay. Hearing no further comments, the committee will continue to do that.

Sylvia has been very patient waiting here.

MS. AU: I just wanted to make a comment about the medical foods legislation. California in our region is moving towards trying to do some state legislation on medical foods. The other states in our region do have some legislation. Our problem that we found is basically state legislation mandates. Most large group insurers are exempt from needing to cover it because they're under ERISA so they don't have to follow state mandates.

In our state, we have very broad legislation which covers medical foods and formulas regardless of age, up to at least 80 percent of the cost. What we've found is basically insurance companies either make families pay ahead of time and wait months to get reimbursed, which is not really good for families, or they just decline to pay because they're under ERISA and don't really have to pay even though you have a state mandate.

So I think that we're actually moving towards a model where the state has to be the provider of the medical foods and formulas and we actually bill the insurance company because we have a bigger stick and we can do group billing rather than individual families fighting with insurance plans. That's just not working for families. So that's what we're moving towards now in our state.

DR. HOWELL: I thought you were going to say up to age 80, and it turned out it was 80 percent.

(Laughter.)

DR. HOWELL: Anyway, we realize Hawaii is generous.

There probably are a variety of models that hopefully this committee will identify and that can serve as help for certain of the states to move ahead on that.

Yes?

DR. KASLOVSKY: Hi. I'm Bob Kaslovsky. I'm a pediatric pulmonologist in Charleston, West Virginia. So I treat CF patients. One of the big issues with long-term follow-up is you really have to make it long because once these folks hit age 21, most of their coverage for state programs and things is just cut right off, and I think the committee really needs to give long-term consideration because, as we improve screening and as we improve care for these individuals, there are going to be lots of adults with whatever condition it is. So that need has to be taken into account.

DR. TELFAIR: There are a number of transition advocates that sit on the committee, and clearly under every category, we did make it very clear that transition to adult care and issues related to adult care from pediatric into adult care is one of the responsibilities of those in those groupings and categories. So that's going to be there. It's also included in the data gathering and new knowledge information. So when the report comes out, you'll see that that's a major piece of what we're talking about as well.

DR. HOWELL: Obviously, the CF patients are excellent examples of persons screened in the newborn period who are living far into adulthood, needless to say.

Any further comments about the long-term follow-up issue?

(No response.)

DR. HOWELL: Thank you very much, Coleen, for that effort.

Mike Watson is heading a new group on research that we've discussed briefly in the past, and I would like him to make a few comments about the efforts and get the input of the committee.

DR. WATSON: We opted not to meet. It was exceedingly difficult to find a place where a cross-cutting group looking at research could actually meet at a time when many people from the subcommittees are actually part of that workgroup. So we're going to probably develop a mechanism of doing a lot of work off-line, and we've done a fair bit of work off-line already.

We have put a couple of people from this committee on the Research Workgroup as an initial group really. Piero Rinaldo, Alan Fleischman, Barbara Burton, and Gerry Vockley have all agreed to be a member of the Research Workgroup.

The reason I said it was the initial group is that there's a few pretty large pieces of this puzzle waiting to be sorted out. There is the Newborn Screening Translational Research Network that NICHD is

developing, and we want to make sure that whoever gets that particular contract from NIH is part of this particular workgroup. I think we had hoped that that would happen much sooner and would be in place by now and we'd know the answers to all these questions, but we don't. So we're going to be maintaining a piece for that.

We also want to be able to involve ongoing activities. So the regional collaboratives for genetics and newborn screening have a data collection workgroup. It involves a number of the people who you heard yesterday presenting that we want to directly involve in this Research Workgroup. And there are other entities. The NNSGRC, for instance, does a lot of data collection, and as we look across the full spectrum of areas of data collection and research out there, we want to make sure we've got everybody represented.

Now, it's a huge area. It's vast and it cross cuts every one of the subcommittees of this committee. We're developing a mechanism to go to them and I was only able to sit through the Laboratory meeting yesterday, but we had a number of areas identified where clearly the Research Workgroup can have some involvement.

We're organizing now already a meeting that's partially funded by NICHD and partially funded by HRSA through the National Coordinating Center to be able to bring state officials together to really talk about the issues of how do we move from really sovereign state control of data and information to national data collection activities. What are the impediments to aggregating data? And they are as variable as there are the number of states out there. We want to look at the ability to develop a dried blood spot repository that can be used in research and all the data collection that will inform everybody's subcommittees about what's going on.

I guess the main thing that we've done over the last couple of months really is to begin to figure out how to get at what's going on in research, and that's something that I'd welcome your input on.

The Secretary's Advisory Committee on Genetic Testing in, I guess it was around, 2002 put in a request of all federal agencies under the Department of Health and Human Services to inventory all research that was being supported by those agencies related to the analytical and clinical validity of genetic testing. And we've gotten all of that material and all of their reports have been moved to us. They're a bit old and don't represent a lot of what's going on right now.

There was an interesting reaction from all the agencies, which was, oh, my God, how do we do this? There weren't robust systems available at the time to actually do an easy extraction from their own research inventory of what's going on, specific to an area as big as genetics. And we don't want to do something that's nightmarishly onerous to all the agencies to try to extract from them what is being supported specifically. The CRISP system I think is one way we can get at it through NIH, and newborn screening, for instance, is a pretty targeted area where one can go in and find out what is being supported that has any relationship to the newborn screening programs. Genetics is much harder because it's so broad.

So we're interested in getting your input, especially the partners from the federal agencies, about what is an effective way to get information about what your organizations are supporting and funding in the area of genetics research without taking an entire staff person a year to put together and then overlaying on that the fact that newborn screening is a state-based activity, to a large extent, and a number of states do have research programs. So we'd want to be able to not just know what's going on in supporting research at the federal level, but also at the state level where pilot studies are going on and other forms of translational research. So I'm interested in hearing from you about what's a manageable way of trying to get at this kind of information.

DR. HOWELL: Thank you very much, Mike.

Are there questions or comments for Mike about his committee?

I might comment I think most of the people in this room are aware of the fact that the National Institute of Child Health and Human Development has issued documents concerning its intention to fund a newborn screening translational research center that would focus on newborn screening research. Obviously, having the NIH come to the table to support research on screened conditions and so forth should tie in very well with what this committee is doing and permit some really exciting opportunities in research.

DR. DOUGHERTY: I wanted to know if Mike was asking the federal agencies right now. Yes, you're asking us now.

DR. WATSON: (Inaudible.)

DR. DOUGHERTY: Well, on that I would say be specific as to what you mean by genetic research. Don't limit it to grant activities because AHRQ doesn't do that much, but most of what it does is done under contract. And those are more difficult to find, and I don't think they're in the CRISP system, for example.

DR. WATSON: (Inaudible) research and the infrastructure needed to do research, and AHRQ does a lot of work in developing the evidence development systems out there and is significant.

DR. DOUGHERTY: You might want to gather some of us and get some key words and differences.

DR. TELFAIR: I just have a question not too dissimilar from what Denise just asked.

First of all, thank you for what you said because I appreciate the fact that you recognize that it's difficult to participate in two things at the same time.

But I was wondering whether or not you had a statement of purpose or intent or a set of goals and outlines for your particular committee in terms of requesting participation in that because would be really helpful in making some decisions and also providing you with feedback on some of the things that you've just requested.

DR. WATSON: No. We actually collided with a bit of a staffing issue in the development of the workgroup. Michele Puryear is going to be the primary staff person to the workgroup. But we wanted to develop a mechanism of essentially co-chairs with a secondary chair coming from NICHD or NIH, given that so much of the research agenda is within that organization, and the individual who we had identified there went from maternity leave to long-term maternity leave. So we haven't regrouped yet.

We talked today about how we should develop meetings of this group, really better define its mission, given its cross-cutting nature. So, yes, we're planning a conference call sometime in the next four weeks of the core group and expanding it to some of those other organizations that are active in this area, identifying the people they would want to represent them on that workgroup. So we'll give you a lot more at the next meeting.

DR. HOWELL: Yes?

MS. WILLIAMS: Hi. Andrea Williams.

I just wanted to comment that I see a clear balance in including in your subgroup the role of a consumer. So I think it's very important that we don't heavily out-balance ourselves with all of the

professional organizations. So it doesn't matter which consumer, but I think there's a role there. Do you agree?

DR. HOWELL: Thank you very much.

Are there further comments or questions?

We're running ahead of schedule, which is always great on a chilly day. So what we'll do is we'll take our break a little bit early and we'll take a bit longer break so that this group that's headed by Tracy and Jana can have a cup of coffee and so forth. We'll return in a half an hour.

(Recess.)

DR. HOWELL: Ladies and gentlemen, Joseph and company, please take your chairs. And Kwaku and Piero. Where's Gerry? Excellent, super. Everybody is convening quite rapidly after that fairly extensive break.

We're delighted to have a presentation this morning from the Secretary's Advisory Committee on Genetics, Health, and Society given by Jim Evans. Dr. Evans is Professor of Genetics and Medicine at the University of North Carolina, which is just down the street from Duke, in the Department of Medicine and the Divisions of General Medicine, Hematology, and Oncology. He, of course, is a member of the Secretary's Advisory Committee on Genetics, Health, and Society. So, Jim, we're delighted to have your presentation on the assessment of the impact of patents on access to tests in both clinical practice and public health settings, and we appreciate very much your coming.

DR. EVANS: Great. Thank you. I appreciate you asking me.

I want to emphasize that this is really kind of a procedural update. We're in the midst of our study, and we are in the process of collecting data, collecting information. So what I'll really be relating to you today is the process which we're going through, how we're analyzing these issues. I don't have conclusions to give you at this point. Those will be forthcoming, but we have to do things in the proper order.

I do think that this issue has a lot of resonance and a lot of overlap with the issues that you all spend your time thinking about. Especially with newborn screening, we have new technologies. We have emerging genotype/phenotype relationships, and particularly in the issue of patent thickets, there are a lot of issues related to patents that may affect newborn screening and how it's practiced. So I'm delighted to be able to tell you what we're doing.

The committee itself, the task force that's looking into this, has quite a large membership when we look at ad hoc members and agency experts, in addition to the members of SACGHS. We really did spend a lot of time trying to make sure that this committee represented a balanced table of experts and people with stakes in this issue. When it comes to the issues that the Secretary's committee has taken on since it came into existence, I think that this is one of these issues that raises passions and has a lot of folks with vested interests and with high stakes. Therefore, it was especially incumbent on us to have a committee that not only had the proper expertise but also represented those various stakeholders. We have individuals who are laboratorians, who are academics. We have people who have expertise in the law itself, folks from the Office of Technology Transfer, et cetera. So I like to think that we have a well balanced committee and I think that's probably borne out by the spirited nature of our discussions.

We first identified gene patents and licensing as a priority issue in the Secretary's committee in 2004. However, at that point there was a National Academy of Sciences report that was going to be forthcoming and we felt that it would be premature to tackle this issue before that came out. In fact, we

thought it might be entirely possible that we wouldn't need to look at anything if the NAS did our work for us.

In October of 2005, we formed a small group within the committee to review the NAS report, which had come out by that time, and in the spring of 2006, we relayed those conclusions in the NAS report to the full committee and discussed it.

And the general feeling in the committee -- and I think it's a general feeling that's been borne out by most people who have looked at it -- is that it's an excellent report and it definitely fulfilled the mandate that they had. However, the one area that the National Academy report did not weigh heavily on had to do with clinical activity, and since that gets to the heart of what the Secretary's committee is all about, we did feel that perhaps there was a need for some more activity on this front that would especially address access to genetic tests from a clinical standpoint.

The activities to date on the committee since then. In June of '06, we held an informational session. I think that while there's a lot of activity around the patent issues, it's a confusing subject and it's a subject that has a fair amount of detail that was important to try to bring people up to speed on. We decided to move forward with an in-depth study. We did not want to just confine our inquiries and our scrutiny to patents, but obviously we needed to look at licensing practices as well since those go so hand in hand. We established a task force, and we discussed at some length the study scope and the work plan. We presented that study scope, which I'll get to in the next slide, to the full committee in the fall of '06 and that was eventually approved by the full committee and was quite a feat, figuring out the scope.

The scope boiled down in a nutshell as the following. SACGHS felt that it was important to look at both the positive and the negative effects of current gene patenting and licensing practices on patient access to genetic technologies. We wanted to focus on gene patents for health-related tests, that is, diagnostic tests, predictive tests, or other clinical purposes. I'll define these terms more specifically in a moment. We wanted to encompass what we had termed both clinical access and patient access, which are overlapping but still somewhat different concepts, as you'll see. We also felt it was important to look at the effects of these types of policies on translational research.

So what do I mean when I say clinical access and patient access? By clinical access, we mean the health professional's ability to obtain a genetic test for their patient. The reason why this was one of the front and center issues was that much of the activity and much of the concern about patents and licensing stemmed from laboratorians who felt constrained in their ability to offer specific tests to patients.

Ultimately, it can be argued, clinical access in some ways is really a proxy for our major interest which is patient access. What we're really ultimately interested in is the ability of a patient to obtain needed genetic testing and whether patents and licensing practices, as currently formulated in this country, enable that or hinder that or what have you. If we just confined it to patient access, it's a much harder question to address. That's an extremely difficult issue to really get at with hard numbers, and by looking at clinical access as well as somewhat of a proxy for patient access, we felt that we could get a broader and perhaps a more definitive picture.

We also need to look and to consider in our deliberations and in our queries the issues of reimbursement and cost because, of course, ultimately that is one major arbiter of access. I would add specifically we're not focusing on patents that are related to drug or product development. That's primarily because those are two very different beasts. Most of the activity, most of the concerns that people have in the realm of patient access, at least proximally, have to do with diagnostic tests, and we felt that while certainly a legitimate focus for scrutiny, it was outside the scope of our efforts at this point to also look at essentially drug development.

So here's our study plan. Let me take you through this not quite in the order that you see here.

Part one was data gathering and analysis, and I would emphasize, as many of you know from trying to look at this subject and think about this subject, getting hard data on the impacts of patents on patient access to testing proves to be a very difficult problem. One is forced to use a variety of indirect measures, and it's difficult to get definitive data. But be that as it may, we envisioned this process as being constituted of a literature review, of expert consultations with the various stakeholders and various experts in the field. I'll talk more in a minute about case studies. I think this is an extremely important part of our approach to this and I think ultimately perhaps one of the most fruitful areas. And whether additional research that could be done in a timely and cost effective manner would be part of this.

I'm going to skip over for a minute to part three because these are not serial. They are being pursued in parallel. And that's the gathering of international perspectives.

Now, we're very, very aware of the fact that the U.S. patent system is in our Constitution. So we're not naive enough to think that it's an entirely fungible process and one that we can just make blithe recommendations about which can then change the entire scene.

That being said, I think that we can likely learn a lot from how other countries have dealt with similar issues especially, for example, in the realm of licensing. We identified experts engaged in data gathering, had a roundtable, as you'll see, on this international issue, and are in the process of analyzing those perspectives.

The public perspective is a very important part of this. I think that perhaps aside from the issue of genetic discrimination, which was a high profile subject that the Secretary's committee took up a few years ago, I just anecdotally suspect that there are few subjects that raise as many passions among the public as the issue of gene patenting and one sees that by op-ed pieces in the New York Times and the Washington Post, popular novels by popular writers that weigh in on this subject. So this is not a subject that is really that far removed from the interests of the public, and therefore public perspectives are very important to take into account front and center with this issue.

We will be soliciting public comments probably in response to a general draft type of statement and engage in a roundtable and public hearing. We'll then analyze and synthesize these various aspects of the study and come out with a draft report for the Secretary, which will then ultimately be finalized.

Now, I want to talk just a little bit more about the case studies because I think that these are one way of getting some data on what proves to be a really very difficult issue to try to get reliable data about.

The case studies that we are pursuing provide a comprehensive analysis of patenting and licensing format for disease genes and diagnostic tests, and what they try to do is they try to take advantage in many realms of kind of natural experiments that exist.

For example, there are genes for very similar conditions that have been cloned and for which diagnostic tests exist. Some of those are under patent; some of those are not under patent. Therefore, the ability to try to learn general lessons by comparing and contrasting such situations we feel could be a fruitful type of endeavor.

A good example of that, for example, would be the issue of colon cancer genetics and breast cancer genetics. As everyone here knows, the genes that predispose in a high penetrance context to breast cancer and ovarian cancer are under patent with exclusive licensing. On the other hand, a very similar disease in many medical contexts in its incidence and its severity and its treatment and similar from a genetic standpoint is colon cancer. Yet, the genes that predispose to colorectal cancer are not under patent with exclusive licensing. Therefore, we're afforded a situation which, with all of the vagaries of trying to make those somewhat apple and orange comparisons, I think can be instructive.

We're trying to derive general lessons, when we can, from these situations, especially with regard to diagnostic development, commercialization, communication and marketing, adoption by clinical providers and third-party payers, and ultimately consumer utilization or, I would say, patient access.

The case studies that we're focusing on at this point, with help from colleagues at Duke University, are hemochromatosis, congenital hearing loss, cystic fibrosis, breast and colon cancer, Tay-Sachs and Canavan's disease, Alzheimer's, and spinocerebellar ataxia. These were not randomly selected case studies. They all have some rhyme or reason as to why they are being entertained. I just told you about breast and colon.

I think of special interest to you all would, for example, be congenital hearing loss and the SCAs. The reason I say that is that when you think about, for example, congenital hearing loss, you're talking about a fairly general phenotype with significant genetic heterogeneity and the need to look at a number of different loci in order to ultimately figure out what's going on with that patient. The same is true for spinocerebellar ataxia in which you need a panel of a number of genes in order to differentiate phenotypes that are remarkably similar. So, again, these things I think will have some real applicability to the types of things that you do, especially in this realm, for example, of patent thickets.

In March of 2007, so a little less than a year ago, we had a primer on gene patents and licensing practices in the U.S. Jorge Goldstein, Claire Driscoll, and Lin Sun-Hoffman all presented and gave really wonderful primers that helped everybody get up to speed.

This summer we had a roundtable discussion on international practices in gene patents and licensing, and you can see the presenters there.

We also had an appearance by Pauline Newman, Circuit Judge of the U.S. Court of Appeals for the Federal Circuit, who gave us an update on the very active scene with regard to legislation and patent reform that is being carried out at this point.

Now, the study plan you can see here in red. The pieces of the puzzle that we have largely completed. That leaves much of the hard work to do, which is analysis and synthesis, and that's what we will be tackling over the coming months. The final literature review and case studies should be completed this month. We will then use those and try to synthesize those into some coherent whole, as well as try to identify the types of lessons learned and ultimately any recommendations that we can provide the Secretary with that might improve the situation where there are deficits or where there are problems seen.

Again, the public comment aspect of this is very important, given the vested stake the public has in this whole situation, as well as, I would add, kind of the emotional investment that people have in this realm.

We'll then revise that report with all that input and get eventual, I hope, approval by the full membership. And we anticipate the release of the final report in late 2009. With a new Secretary of HHS, et cetera, coming on line between now and then, those things will be open to some revision perhaps with the time line.

But I'd be happy to take questions or comments.

DR. BUCKLEY: I wonder if you would comment on the difference in impact between the patents and the licensing.

The reason for asking the question is that there's a commercial lab in Boston, for example, that does mutation analysis for genes that affect the immune system. Prior to that, there was only one other company that did that, and that was GeneDx outside of Washington. But most of the mutation analysis

has been done in academic institutions by people who are doing research on those conditions. But we understand that this company in Boston is licensing certain of these genes. Now, is that going to preclude other entities from doing testing?

DR. EVANS: Right. I think that your question is a really good one. It gets to the root of the practicalities of how you approach access. My own personal feeling is that licensing practices is where we probably have the most latitude in trying to rectify any problems that do come up. In other words, the patent system itself -- well, it's in our Constitution. Right? Although there's legislative activity around patenting. My own feeling, though, is that licensing will be where we have the most traction and the most ability to impact the access to tests.

I think that if you look at NIH best practices, if you look at what people say, they are generally in favor of fairly broad licensing arrangements, and I think that there's a lot to be said for that position. I think we all worry when exclusive licenses exist. That said, it does all have to be balanced with the very intent of a patent which is, of course, a monopoly for a limited period of time. That's what a patent is. Right? In exchange for openness, in exchange for essentially publishing it.

In a roundabout way, I hope I'm answering your question. I think that much of the practical traction that can be brought to bear on making the patent system work best will hinge on licensing issues, and in general, I think it's hard to argue that at least some degree of broad licensing isn't a good thing.

DR. HOWELL: Any other questions? Dave?

DR. LEDBETTER: Yes. Just another comment about licensing being the important factor, but of course, just like a patent, once the licensing is done, it's very difficult to go back to the company and the institution, often an academic institution, to get them to change it from an exclusive license to a non-exclusive license and allow multiple labs to offer testing. So the process of encouraging non-exclusive licensing needs to be up front at the time of the initial gene discovery.

When the academic investigator who cloned the gene, in partnership with families and family support groups, makes their disclosure to their institution, which goes to their technology transfer office, if the investigator doesn't participate in that process, the technology transfer people will often negotiate an exclusive license to the highest bidder. The investigator must stay involved with that process and encourage the technology transfer office and their institution to consider broader, non-exclusive licensing for the diagnostic field of use for that gene discovery because the financial investment of any genetic testing lab to develop a test is relatively modest compared to the huge investment in drug development where an exclusive license might be a reasonable consideration.

So all of this means that most genes are discovered in academia with NIH funding. Most investigators would like to have the technology for genetic testing available as broadly as possible, but currently most investigators don't participate in the technology transfer process. There needs to be a lot more education on the part of professional societies and family support groups who are involved as collaborators in the research to the investigators that they have an important role because they're then named inventor on the patent although the university owns all of the rights but shares the income and revenue of that invention and royalties with the individual investigators. But they need to be proactively involved in encouraging the broadest access of their discoveries.

DR. EVANS: Yes. I completely agree with that. I think that that's, obviously, somewhat difficult given the constraints of the individual investigators to stay involved. It's hard. You're right. Once you make those arrangements, the cat is kind of out of the bag.

DR. LEDBETTER: I think, again, the family support groups, who now are important collaborators, if they were aware of this entire process and the ability of institutions -- even with NIH funding or funding from any other source, the institutions are free to choose how to commercialize their inventions in an

exclusive or non-exclusive and to separate diagnostic from therapeutic fields of practice for the technology. I think if everybody is more aware and up front has formal or informal contractual arrangements that when a discovery is made, we are committed to non-exclusive licensing strategy as our first priority and only if that can't succeed, which would be rare in diagnostic testing, can you revert to an exclusive.

It's always struck me as an odd situation that the NIH intramural research program has a rule that all discoveries must be disclosed and they seek commercialization, but they must seek commercialization through non-exclusive licensing unless that fails, and then they can revert to an exclusive licensing. So 10 or 15 percent of the entire NIH budget research is committed to that non-exclusive, greatest access licensing strategy, but when the NIH gives money extramurally to an institution under the Bayh-Dole Act, the institution is then free to commercialize without any rules about how they develop the licensing models. But on a volunteer basis, the institution and individuals can influence that.

DR. HOWELL: Interestingly enough, the conditions that this committee deals with largely are very rare, and certainly I'm aware of circumstances where when a gene was patented and there was an effort then to license that particular patent, only one person would come to the table because of the rarity of the disease. So that's another thing that would play into the kind of thing that David was talking about.

Mike had a comment.

DR. WATSON: It's a mix of a comment and a question. One of the things the laboratory subcommittee talked about yesterday was the question of when one begins to integrate genetic testing, not the functional tests, into the algorithm of the screening test itself, you can begin to move into diagnostics by bringing some mutation testing into the newborn screening algorithm itself.

So I'm wondering the extent to which, among your use cases, you had cystic fibrosis and hearing loss, which are quite different in the way the licensing for the CFTR gene, you know, is pretty open and pretty accessible versus Connexion 26, at least the 35 del gene mutation in Connexion 26, which is the most common form of nonsyndromal hearing loss in caucasians at least, and the consideration of whether that goes into public health programs because it is so common or stays in the diagnostic setting. Did your use cases in those two areas that are already part of newborn screening of CF and hearing loss extend to sort of the effect on the public health versus the diagnostic sector?

DR. EVANS: Yes. That's definitely part of the analysis, yes.

DR. JOHNSON: John Johnson from Mountain States. I'll take a patient advocacy view. I'm a physician.

One big player between clinical access and patient access is Medicaid, and although it's not federal, there are some rules that apply to all the states, and one of those is a lab that does the testing must bill for the testing. It used to be, before a few years ago, that you could route a test through your local lab. They could send it out of state to a lab. They could bill Medicaid. No longer true. So what we find is obstacles for Medicaid patients to be able to obtain tests because of only certain labs doing the test. That could be a patent issue or just, as you said, a rarity issue and there are only a few labs that want to do the test. But if they're not a Medicaid provider for your state, your patient has to pay for the test or you have to pay for the test. A huge obstacle in the access equation and you'll have to take that into account somewhere in your research.

DR. EVANS: Yes. That's one of the reasons that we kind of highlighted specifically the reimbursement type issue. To say it's a tremendous drive for patient access is a ridiculous understatement. Some would argue it's the whole ball game. So, yes, that's going to be an important and difficult issue to consider. I think those fortunately, at least theoretically, are amenable to fixes. So that's the good part. Now, getting those fixes actually implemented can prove to be difficult.

DR. HOWELL: Sharon?

MS. TERRY: Jim, I think you're aware of this, but to sort of further David's comment, even when the patient advocacy group and the investigators are interested and aware of the patenting and licensing issues, it's difficult. I'm a patent holder as are now several advocates, and our biggest problem is working with the university where the other inventors work and working with them around the licensing issue so that when, for example, in my case GeneDx through the CETT program is putting out the test, they've asked us to double the cost of the test so that they could split the profits with us. We, of course, have said that that's completely unconscionable because we want the patients to have the greatest access, and we're, in fact, subsidizing the test. They really went to bat for it. We had to get pro bono lawyers to have them stand down. So I think the tech transfer offices, unfortunately, think that there are cash cows in diagnostic testing, and I agree with David there aren't and that that will be a very serious consideration, I'm sure, for your group as you go forward.

DR. EVANS: Yes, I completely agree.

DR. HOWELL: Michele has a question.

DR. LLOYD-PURYEAR: I notice that tandem mass spectrometry, although not a disease, is a testing technology, was not included as one of the case studies. Was that considered at all? Because there is a patent issue with that.

DR. EVANS: Yes. I'm going to speculate here because I don't remember precisely the discussions around that. I think that what we are really trying to focus on is the patenting of nucleic acids and information as opposed to the techniques and technologies. I think that really those, while they overlap, are quite different. So I think it would have been outside our purview to really look at, say, mass spec just as it would to look at capillary sequencing, et cetera. Those are really technology patents that in many ways fit much more nicely into the long history of what patents are all about and don't have some of the novel nuances of gene patenting. I think that would be my off-the-cuff claim to why we didn't include that.

DR. HOWELL: Jim, thank you very much for that very thoughtful presentation.

DR. EVANS: Thank you.

DR. HOWELL: It was very informative and we'll look forward to seeing the progress of your committee and to its report in the fall of 2009. Thank you very much.

DR. EVANS: Well, thank you, and I really also want to thank the staff of SACGHS, especially Yvette Seger, who are incredibly helpful in all this.

DR. HOWELL: We're now going to move along. Actually this will be a continuation of our ongoing discussions about the committee's evidence review, and Jim Perrin will give us an update and review the committee's external Evidence Review Workgroup, and then Dr. Nancy Green will summarize the work of the committee's internal Nomination Workgroup.

I might point out that each of you has received summary nomination packages submitted to the committee by HRSA, and the committee has, at this point in time, received two nominations from HRSA that have been judged ready to go to the committee.

So, Jim, welcome and thank you very much. Although the first name on your sign is correct, this is, indeed, Jim Perrin. I'm talking about the sign sitting on your desk.

DR. PERRIN: Right. Thank you so much.

DR. HOWELL: Dr. Perrin, as I think you know, is Professor of Pediatrics at the Harvard Medical School and Director of the Division of General Pediatrics, also the Center for Child and Adolescent Health Policy at Harvard at the Massachusetts General Hospital for Children.

DR. PERRIN: So I'm going to give an update on our work since the November call of the committee and, for the purpose especially of some members of the public who may not have been able to participate at that time, some review of sort of our plans here. But the reality is that we are very much waiting for the advisory committee to give us the next steps, which is really to make a recommendation for us to carry out a specific review.

I want to just update you a little bit on the team members that we've put together just to remind you that we have sort of two teams. One is our, I'm calling it, local team. It's not entirely local, but these are the people who include both the active day-to-day staff for this project, as well as a series of advisors, most of whom are in the New England area who meet now every other week at least by phone or in person. But they include experience in genetics through Marsha Browning, Anne Comeau, and I apologize, Anne, if you're here. I did not correct the state, your connections here, but officially it's not the Massachusetts Department of Public Health, but rather it is the University of Massachusetts part of it. Nancy Green, who has been the major consultant; Alex Kemper, Lisa Prosser. When we met in November, we did not at that time have a consumer representative, but Denise Queally, who has been very much involved in the PKU Coalition, is now a very active member of the team, and it's been great having Denise discussing with us.

The last four members before Marie are our actual staff working on this project on a day-to-day basis as we move forward.

And then we have an external advisory group which includes four people at the moment, and we've had some advice from the committee and from the HRSA staff about membership for this. And we are likely to expand this as we really get moving ahead, but so far we have this group of people working with us.

I've discussed this before. We are, in general, going to be looking at pretty rare conditions which will lack a lot of the traditional kinds of evidence that goes into an evidence review, and that's where you're going to need to be imaginative and seek the help of this group and your experience as well in figuring out in how we can take fairly limited data and provide them in a way that gives you enough evidence to make some appropriate decisions here, but traditional randomized controlled trials will exist in a few cases but not in a very large number.

There will be limited information on cost and benefits across all potential outcomes, especially some of the newer conditions in the sense of people who are test-positive, as we learn more and more about the spectrum of certain diseases.

We've discussed before our strategies with respect to access to evidence and, indeed, also working with investigators. There will generally be a relatively small number of investigators working on any particular condition. We want to get the very best and most recent evidence that they have and put that into our review, but in a way that maintains some substantial degree of transparency and making sure that we don't find ourselves overly biased by investigators' views.

Nancy is going to talk in a few minutes about the work of the Nomination Review and Prioritization Workgroup. That group, of course, is the one that is referring to the advisory committee, making recommendations to you about which tests to then turn over to us for review.

In some recent activities since our November meeting, we have developed an abstract form. I have not sent that in to the book this time, but we will be delighted to share that with the group as you wish. But this is really based on both our previous work in other evidence reviews, but also our efforts to deal with transparency questions and our efforts to deal with certain kinds of ways of measuring quality of data in the context of the lack of typical quality measures for some of the types of data we will be analyzing.

We have a clear conflict of interest policy. We developed conflict of interest forms that all staff, consultants, and collaboratives will complete. Anyone providing evidence to the Evidence Review Workgroup will respond in these forms. We base them in many ways on the kind of conflict of interest mechanisms that the Institute of Medicine has used for most of its committees, and I would stress that that does not basically say that a person with any conflict of interest cannot participate in our activities, but rather, that we're very clear on what those conflicts are and that we will be able to share those conflicts publicly as we present information back to the advisory committee.

Our key staff have already completed this process. We've had some discussions among the group about potential conflicts, and I think we're as a group okay. Marie has participated in those conversations, and I believe we're comfortable with where we are there.

So as I said, staff, previously described consultants, for the main national consultants, will meet all the same criteria.

Based on our conversation at the November meeting, I think our plan with respect to condition-specific consultants -- we would encourage them to testify to the Evidence Review Workgroup, but they will not be involved in the analyses of data by the Evidence Review Workgroup. We will, in appropriate cases, share summaries of our analyses of the research findings but with the emphasis really being on accuracy, not on interpretation, which really becomes our responsibility rather than those of the investigators.

Investigators too will share with us their conflict of interest. So a person who is unwilling to do that or unable to do that -- we will not be able to use that person's advice in any way or even share their data with us in any fashion. So I think since we met in November, we've done a good deal of work in the conflict of interest areas.

I've gone through this before, the structure of the evidence review outline that we propose to do. I believe you really have approved this in the last meeting, but I thought I would quickly share it with you, again, as much for people who may not have been able to participate in the November session.

The review will start with the rationale for why it was being done at this time, and that, frankly, will build on the work of the Nomination Review Group which will have considered the nominations. And by your discussion at the last meeting in November, that nomination must provide some prospective pilot data regarding population-based assessment.

The spectrum of disease must be well described. We have carefully not exactly defined "well described" here.

There is a screening test that is capable of identifying the condition. I know you had a substantial discussion of this issue at the November meeting.

And the treatment is also well described. Obviously, in many cases there will be some information regarding recent changes in treatment and screening that will have led to the nomination and to our work.

And the objectives, again, of our review are to provide timely and carefully analyzed information to the advisory committee so that you folks can then decide what recommendations you want to make for a specific screening protocol.

Again, I'm going through things now that we have talked about before in general. The questions for review will be the natural history, including variations in the phenotype, the prevalence of the condition, including variations in genotype and phenotype, the impact and severity of the condition, the methods of screening and diagnosis, diagnosis and screening positive individuals, screening test utilities, and then the feasibility and acceptability issues of screening here as well.

We will also look at the benefits of treatment going on beyond the disease itself. Obviously, with the help of Denise and others, we've talked about both efficacy and effectiveness trials that we will look at here in screen-positive individuals and in otherwise diagnosed individuals, people who have been diagnosed clinically without necessarily being screen-positive originally, and that will be true for some of the earlier case reviews that we are likely to come across.

We will examine what is known about the harms and risks of screening, the harms and risk of diagnosis, and harms and risks of treatment. The first two probably really flow together given current evidence.

We will look to the degree available, but I suspect we're not going to find a tremendous amount of extremely helpful information here on the costs of screening, treatment, lay treatment, and the failure to diagnose in the newborn period.

Our methods will be very carefully described in our report to the advisory committee, including the decision model that we put in place for the condition and the development of evidence questions around which we are gathering evidence for the committee. We will describe in detail the search methods used, including the time frame and the search engines used. It's easier than some of the searches we've done recently for other data work.

This is a hard slide and I apologize. I should have broken it into two. Study selection. We will describe for you the inclusion and exclusion criteria. We will be using peer-reviewed published literature not exclusively, by the way. We will use English literature. The gray literature -- we will be limited to pharmaceutical companies' data and to unpublished studies. We will exclude single case reports although, based on the conversation we had last time, we will provide -- we've always, by the way, planned to provide analysis of multiple case reports, and we will provide a bibliography of case reports for the advisory committee as well.

We will also review consensus statements in a particular disease for guides but not for abstraction. The abstraction quality assessment -- we will use standard and somewhat unstandard quality assessment methods, standard ones for traditional randomized controlled trials and the like and for well-described screening efforts, but we will be applying some other ones that we've been working on recently as well.

We may carry out additional analyses of raw data from unpublished sources. That will depend a great deal on what kinds of relationships we develop with the investigators in a particular condition and the degree to which they are willing and able to share data with us. We've actually worked on data sharing agreements. I think they will actually vary from person to person and condition to condition as we develop them.

As we've described in the past, we will develop focus groups of experts to answer some questions for which we think there are no data or essentially no data available. These are basically focus groups where we ask parents or investigators working in this area to give us their best estimates of certain aspects of the condition like, for example, what is really the natural history, what do we expect with

it. Given the variation in the case studies that have been published so far, what really seems to be going on here, and what do you know about the real value of treatments? So these are some of the things that we will likely do with focus groups.

I would be honest in saying we are not planning a large number of focus groups because that will slow down the process and get you folks a review less quickly, but we think there are likely to be in each case interesting problems for which a bit better data would help you make some decisions.

We will talk about, of course, our methods of data synthesis.

Our results for you will follow the order and the content of the main questions, and we will likely provide you some outcomes tables in a couple of areas for each of the questions that we are studying.

So that's basically what our outline of an evidence review will look like. You folks have been very helpful to us as we have refined that over the last several months together. This is essentially what we presented in November with some minor changes based on the November discussion.

So the next steps. Again, we are awaiting eagerly, quite eagerly, initial assignments from the advisory committee to the workgroup. I think we are ready to go very much at this point. We've actually done a little bit of sort of testing all the systems with a couple of candidate conditions, but we've done nothing in depth because we're really waiting for that.

I've provided a time line that we think is reasonable, but we're going to find this out when we really get going. We expect that we will be able to provide you a response basically in about six months' time after getting an assignment from you, and we'll do everything we can to speed that up. But I expect that's a pretty realistic amount of time.

I know we've been asked in the past are you doing to do 2, 3, 4 or 20 at the same time. We would propose to get started with one to get our feet wet, and four to six weeks thereafter, if you have a second candidate, we would be prepared to start a second one in approximately that period of time. We don't want to really go barrelling into two or three all at the same moment.

So I think we're ready to get up and started and do more than one now and get you some results along this time line, and we will, obviously, report to you if we're finding we can go a lot faster or if we're finding major roadblocks and have to go a lot slower.

So let me stop at this point and see if you have questions and comments. I think Nancy is also going to follow with some discussion about where the Nomination Workgroup is.

DR. HOWELL: Jim, thank you very much.

Are there questions or comments for Jim at this time? Let's start with Denise and then Ned.

DR. DOUGHERTY: Thank you, Jim. That's really coming along.

I may have missed it in your slides, but what would you do about reporting back to the committee on the quality of the evidence you've reviewed? Will it kind of be embedded in each section, or do you think that, like some of the evidence reviews that are done, you could have a separate section that talks about the quality of the evidence and the kind of methodological improvements that would be needed?

DR. PERRIN: So the answer is I'm not sure at this point. Our plan really has been to embed that, but to be very explicit about the quality measures we're using for the variety of data that we have available. So, obviously, for RCTs this is pretty simple. Not really simple. That's perhaps an

exaggeration. It's relatively simple compared to the other data that we're likely to have. But where we're dealing with, for example, investigator-provided data, we're going to be having to describe what the quality is there, and where we're doing any kind of analyses of case reports, which is much more difficult, then again we will provide you with the strategies that we've used to judge the quality of the evidence certainly. So, I mean, it may be as we move along, Denise, that we would be wiser to separate that out and put that as a sort of weight of the quality here and we could certainly do that.

DR. DOUGHERTY: Or at least have a summary paragraph at the end. Maybe Ned has something to say about what's the best strategy to convey the quality of the evidence.

DR. PERRIN: We would certainly have that, undoubtedly have that. Yes, absolutely.

DR. HOWELL: And Ned?

DR. CALONGE: I think this is a very good piece of work and I appreciate the work the committee has put in.

I was going to go with a little separate issue. I think the quality issue is -- you have the right idea about how to rate the quality and I think summary statements that are available to us.

What I really wanted to discuss, though, is beyond the production of the systematic evidence review, which I think this group has moved so far ahead on and created good content. The committee needs to think about what our decision-making construct is for taking this information and turning it into a recommendation because we will get some information that says something. I think, Dr. Howell, we'll need to figure out maybe a separate process for what's our framework for saying we're going to recommend this or we may not recommend this.

There are at least three approaches that we could look at. One is the task force which looks at this concept of net benefit of screening. A second is the community guide that CDC runs, which talks about sufficiency of evidence, which is a different construct and looks at the quality and the number of studies in a slightly different way. And then the third is the work done by a group called GRADE, which is kind of an update international approach to taking systematic evidence reviews and turning those into recommendations.

And they all kind of get around this issue of the risk of being wrong or the certainty of being correct. I think what our job will do is to minimize our risk of being wrong and maximize our chances of being correct by having a matrix that we take this information and make a judgment that's in some kind of consistent process.

So it's an additional activity that we should anticipate prior to receiving the first SER. I think it would be prudent to do that.

DR. HOWELL: Do you have some specific recommendations of how the committee approaches its job in this area?

DR. CALONGE: Perhaps what we could do is provide those three different approaches, the task force matrix that it uses, which I think I presented to a smaller group of the committee at one point in time, the matrix that the community guide for Community Prevention Services uses for CDC, and then the GRADE information, and then we could kind of compare and contrast those from a standpoint and then think about the anticipation of what the SER might provide us.

DR. BOYLE: I was just going to make a recommendation that we form a workgroup and that Ned take leadership in terms of helping us move this along.

DR. DOUGHERTY: I just wanted to know. Does EGAPP also have a process for doing this?

DR. CALONGE: EGAPP basically decided to use the Preventive Services guide, the task force's guide, with a few changes to try to make the answers a little bit more simple, the guidance a little bit simpler.

DR. HOWELL: I think establishing a workgroup with Ned running it would be a good idea, and we can probably identify some people to participate on that and we'll do that. Maybe we can have a report at the next meeting about how we do that. That will be prior to getting any recommendations back from this committee. But, obviously, it's going to be important to have a procedure.

Is everybody comfortable with what Jim has told us about the plan? I think this is an extremely important effort because it really will be the first time that there's really been a systematic look at how you assess the evidence in these rare diseases for screening. And we want it to be done right and the best we can do, and it will, obviously, be the gold standard for that. So we want to be sure that everybody is comfortable with the way it's proceeding and that there's not some major issue with that.

Coleen?

DR. BOYLE: I just had one other comment. I appreciate the care and consideration you have given to the conflict of interest issues. Obviously, you're venturing into new territory, particularly the fact that you're considering proprietary information. I know that it will be a particular challenge to think about conflict of interest issues relative to that type of information, that type of data. I don't know if you have given any thoughts to that.

DR. PERRIN: We are certainly open for advice here, Coleen. We've given a lot of thought to it. We've talked to a few people who are expert in the area of this.

We have, I think, benefitted from the experience of the Institute of Medicine in this area because many of their committees do, in fact, have representatives on them who have very clear conflicts and clearly represent a point of view. And that point of view is clearly stated. What's interesting, of course, there is they actually have voting rights despite that point of view. Now, there are certain conflicts that essentially would prevent participation, but in fact, the IOM committees are typically put together to be relatively balanced in their views of issues.

So that's a long response to say that I think our strategy at this point, Coleen, is that where there are proprietary issues involved, our strategies are sort of twofold.

One is we would like to have access to the data so that we can really look at the data as cleanly as possible, but you all know, as well as I do, that there are still ways of sort of giving some but not all of the data. Thus, there are always opportunities there for incomplete information that I don't believe we have any clear ways of assuring that we can get through.

Second, as I said earlier, people who provide us data of that sort -- we will very much look forward to their providing those data to us. We will be responsible for the interpretation of those data. Per our discussion at the last meeting, we will share our analyses of those data, if we carry out some, with those proprietary sources, but only asking them for information on the accuracy of our analyses and not for their opinion of our analyses.

That's how we've approached this. Again, if you folks have further advice, we would be delighted to have it. This is not an easy area.

DR. HOWELL: So is there any other comment about this?

I would hope that you would work very aggressively to make that six months shorter and still, at the same time, do the important work you have to do.

As we review the official relationships of the Evidence Review Committee to this committee, it's required that we ask two members who are appointed members of this committee to serve on the external advisory group as a liaison, not on an every-other-week working group. And I would like to ask Ned and Piero if they'd be willing to be a contact point as they proceed with this. Would you be willing to do that? I think that would provide some very important expertise from the committee so that you'll serve as former members of the committee as the expert advisory group.

Michele has a comment.

DR. LLOYD-PURYEAR: We also had a decision process workgroup already. That's already been established. Some of the members of that workgroup, though, are no longer committee members, but Piero, Coleen, and Denise were on that, along with two other people, Nancy Green and Amy Brower. Oh, three. Peter Coggins. I think that was it.

Would you three that are still committee members be willing to be the core part of that decision workgroup? Then we can add. Okay. I just wanted to make sure. We can add. Since you already have experience because this is one of the issues that came up.

DR. HOWELL: Again, going back to the technicalities, as you know, the nominations come in to HRSA. HRSA does the things that Marie Mann is going to later discuss. And then once they're all ready with all the I's dotted and the references and everything in great detail, they come to this committee, and the committee has received two at this point in time, again, as I mentioned, Pompe disease and SCID.

Nancy Green has been very hard-working in looking at the internal review group. This is a small group from this committee that looks at these and makes recommendations about the fact are they ready to go to the evidence group. And if you have more than one, what would be the order in which they would proceed. Nancy is going to tell us the results of the deliberation of her internal review group.

DR. GREEN: I will. Let me also just say that I was asked, because there's a large number of new committee members, I was asked to review the entire nomination process. So for those of you who have endured this presentation before, my apologies. It will be, I think, terse.

DR. BURTON: Can I ask a question while we're waiting for the computer?

At the last meeting, we were told that we had Crabbe and SCID had just arrived. What happened to that application?

DR. LLOYD-PURYEAR: Marie Mann will go through this, but there were a series of nomination packages that we received, some of which were complete, some of which were not. So those packages have been reviewed by HRSA and two have been passed on to the committee.

DR. GREEN: Barbara, thank you for the distraction.

So, again, much of this you've heard before and the slides have been captured by the minutes of previous meetings. But just overall to review the nomination process, conceptually these tenets were discussed and agreed upon by the committee, I guess now about a year and a half ago, that there would be broad access to the nomination process, that there would be considered review, as I think Jim's presentation just captures very well, that the process would be streamlined, and that it would be transparent, and that there would be consistent criteria throughout the nomination process at each review

step. And then there would be a structured evidence-based review, which I don't have to elaborate on, and that the three main conditions would continue to be the condition, the test, and the treatment.

So in a very simplified version, the paradigm for committee consideration would be, again, the nomination form that the committee members have copies of, and in fact, the nomination form is posted on the HRSA website for this committee. There would be some federal administrative review, which I believe is now HRSA administrative review and, hence, the funneling from incomplete nominations to now the two completed nominations, presentation, of course, to this advisory committee, and interaction with the Evidence Review Group, which I'll talk about in a moment, and then the recommendations to the Secretary from this committee regarding the nominated conditions.

So just to go back from the beginning, the Nomination Workgroup was formed at the chair's request in 2005. The members are listed here: Coleen, Amy, Peter, Denise, Piero, and myself, as well as Marie Mann from staffing from HRSA.

And that workgroup had two tasks. One was to design a nomination process and then to create the form, which many of you are familiar with. This process has been described in a publication in Genetics in Medicine, as Rod described, a report from the committee written by the workgroup. And the nomination form is, as I mentioned, on the HRSA website and that's the URL.

So this is just, thanks to Piero, the actual nomination form. It's a two-page form and is, by necessity, brief.

One of the aspects that has held up some of the nominations, in fact, has been incomplete filling out of this nomination form, as well as a signature for a cover letter and also not only a list of references used for substantiating the statements made on the nomination form, but in fact, copies of those references. So for those of you who are considering nominating conditions, please be thorough in those submissions to prevent delay.

So then in the fall of 2007, having fulfilled the tasks of the first Nomination Workgroup, the group was reconfigured at, again, Dr. Howell's request to be the catchy title of the Nomination Review and Prioritization Workgroup, maybe only shorter than the name of this august committee. The members of this workgroup are many of the same members from the previous nomination group: Amy Brower, Rod Howell, Piero, myself, and Marie again as staff. The tasks being to develop criteria for readiness for referral to the Evidence Review Group and a preliminary review of nominations and a recommended prioritization for evidence-based review for the committee. But just to clarify, this workgroup is tasked with making recommendations to the committee, but in fact, it is the committee's responsibility to make those assignments to the Evidence-Based Review, and I think the intent is to go through that following my presentation.

So then just to elaborate a little bit more on the process. Again, this slide has been showed to the committee before. So once the advisory committee receives a completed nomination, that information, as I mentioned, is referred to this Nomination Review and Prioritization Workgroup which then, as I will do in this presentation, reports our recommendations back to the advisory committee. And then, as I mentioned, the advisory committee will charge the Evidence Review Group with their tasks, their nomination to consider. Then that workgroup, led by Dr. Perrin, will report back directly to the advisory committee and not to the Nomination Workgroup.

Then I've just outlined some possible recommendations for the advisory committee, but this is in no way determined. I think, in fact, the creation of a new workgroup will be very useful for this. But just to remind the committee, it has in fact a variety of potential recommendations it could make following this review process, and those include addition to the current universal panel, as originally described by ACMG, targeted screening, pilot studies, describing critical studies that would be needed. It could abstain

from making recommendations or it could, in fact, recommend against inclusion in newborn screening. All of this is, of course, a dynamic process as new evidence arises.

So I'm speaking for the Nomination Review and Prioritization Group. Our recommendations were made to this committee at the November 14th teleconference, and we made the recommendations around prioritization that Jim actually mentioned already. So I'll go through this quickly.

One, that the nominated conditions are medically serious; that disorders would have priority for which there is prospective pilot data from population-based screening. The spectrum of the disorder is well described to help predict the phenotypic range of those children who would be identified through a population-based screening process.

Three more recommendations include the characteristics of the screening are acceptable, and I don't think we need to get into that in any great detail, but there is an acceptable screening test. If the spectrum of the disease is broad, to be able to identify those most likely to benefit from treatment, especially if the treatment is onerous or in any way risky or if there are other limitations for treatment, such as availability. And then lastly, there are defined treatment protocols and use of FDA-approved drugs, if that's applicable, and again, treatment is available.

So those six recommendations for prioritizing nominated conditions. And as the minutes of that teleconference committee meeting from November reflect, those recommendations were accepted by this committee.

This is the new business then for the committee. As was just mentioned, following administrative review by HRSA, the two completed nominations were forwarded to our workgroup, again, the forms, as well as the submitted references, each for Pompe and for SCID. Our workgroup had a teleconference last week to discuss this and to make recommendations for the committee. I would like to invite other members of the workgroup who are present, specifically Rod and Piero, to make comments as soon as I finish here.

The four of us unanimously voted that both nominations should be moved to evidence-based review, that they both fulfill all of the criteria for evidence-based review. So we had to then decide which one would be first, and as Jim, though, I think mentioned and I would hasten to add, Jim has agree to review two conditions at a time. So it's really sort of which is first and which is second, but presumably not separated by vast oceans of time because, in fact, as many fine committees or groups are, we were split in our vote. Two of us voted that SCID would be first and two of us voted that Pompe would be first. There were many positive attributes about each of those conditions nominated and the data supplied through the nomination process.

Just in broad terms, there was concern -- and again, I invite my fellow workgroup members to comment -- about sort of the maturity of SCID, in terms of undergoing population-based screening on the one hand and some of the analytic outcomes based on a Taiwanese screening program for Pompe. So with that split decision, we referred to this committee for charging the Evidence-Based Review.

We also very much expressed the recommendation that I know HRSA has fulfilled that the committee members would receive all of the nomination forms for the disorders considered by our workgroup, so not necessarily all of the references, but certainly the two-page nomination form I think is appropriate because you all are charged with making decisions based on that form, even as filtered through our workgroup.

So I don't have any further comments. Piero and Rod, perhaps you'd like to make comments at this time.

DR. HOWELL: Thank you, Nancy. That was an excellent report.

I think that the small committee that was convened, with the sole purpose of saying they're ready to go and the order, was very, very clear in feeling that both of these satisfied the requirements of moving forward very, very well. I think you categorized it very well.

Piero, would you like to comment? I'll be quite open. Piero was one of the folks favoring SCID going first and I favored Pompe, and I'll come back and comment about Pompe.

DR. RINALDO: My only comment reflects what I think I've been saying consistently at many meetings of this group. I understand that there is a prospective study in Taiwan, but I think there really should be national prospective studies before a condition should be considered mature for this step. So that's really what was driving my preference for one rather than the other. And I also think there could be an incentive to accelerate implementation of pilot studies somewhere in the U.S. for the other condition, if not already there.

DR. HOWELL: I think that's well put. I think that the population data that are available on Pompe, as Piero pointed out, at this time have been obtained in Taiwan. We had, in the original idea, planned that we would look at international as opposed to U.S. studies, but obviously, U.S. studies really do need to be done. There's no question about that.

But I think that the critical issue, as far as I'm concerned, is that the subcommittee felt strongly that both were ready to go forward. I was encouraged that Jim is now talking about a very short time spread between number one and two. So it's not a discussion about which goes first or second. It's really not terribly critical at this point in time, I think, because of the short space here.

Gerry?

DR. VOCKLEY: I just had a question. We heard about a six-month window for this review once it goes to Jim's committee. Do we have targets for the length of time before an application comes to HRSA for original administrative review until it gets referred to us? I just look at the dates on these two applications and I see that the Pompe one was submitted in May of 2006. Is that right? No, that can't possibly be right.

DR. GREEN: I don't think they were completed.

DR. VOCKLEY: So it was sent back.

The other one, the SCID one, was in September. So that's a nice short time line, but I just don't know if we have any idea of how long the administrative to this group, back to the full committee is going to be.

DR. LLOYD-PURYEAR: Marie is going to go through it. It is actually very rapid because it's a very simple review. But it's really our review and our review is for completeness since we're spending considerable money and time and thought as a committee and as a group of agencies on this review process. This is to make sure those nomination packages are complete and with signed letters and signed conflict of interest forms. So it took some time to get stuff back and forth, but the administrative review is actually very short.

DR. DOUGHERTY: It sounds like there's not really a difference in timing of these two. But I know Jim is spending a lot of time on definitions of things. So I'm just wondering if somebody could explain. You said the two criteria you were looking at were maturity and population-based something. I don't quite understand what those are. So I think just as a principle for our discussions and votes, we need to understand those kinds of things.

DR. GREEN: You're asking the criteria by which this nomination review group undertook a decision?

DR. DOUGHERTY: No. You said there were differences between the two nominations, and you disagreed. But if you could explain what those differences were so that in the future we'd be able to think about applying those criteria. Suppose we had to vote against one or one that was going to go first if there was a long queue or something like that. I'd just like to understand what the reasoning is about those two differences between the nominations. Maturity and there was something else.

DR. GREEN: Sure, sure. No, that's fine. Again, I invite Rod and Piero to contribute to this. You're right, Denise. It's important to be very clear about our deliberations and where we had some disagreements.

Again, underscoring that both conditions had very well completed nomination forms, so we had sufficient data to at least advise that these would be ready for the investment in evidence-based review. So that was not at issue, but that was certainly an important primary consideration, in fact.

And then I don't want to represent the Pompe question, but maybe I could represent the issue about SCID. As we will hear later today, Wisconsin has initiated a pilot screening program for SCID, but from my perspective, since that program is really in its very initial phases, in fact, began at the beginning of this calendar year, it wouldn't be sufficiently mature in terms of the experiences, the false positives, the ability to detect disorders, and then who knows what vicissitudes come up with population-based screening. It did not yet capture that full experience.

Piero, perhaps you'd like to elaborate upon your reservations about Pompe.

DR. RINALDO: Perhaps I can bring Mike on this, but I understand that there is work in progress about defining ACT sheets for additional conditions, including the lysosomal conditions. So my understanding at the last meeting of that group, the latest update on the Taiwan results suggested a 0.5 percent false positive rate, and to have a 0.5 percent false positive rate for a single condition means that as we look at future expansions that can become a major burden. So that is really my reservation. You can summarize it very simply. The preliminary performance metrics may indicate that the approach used in Taiwan might not be a feasible one.

DR. HOWELL: So fundamentally, one had to do with the testing in Taiwan and the second had to do with the fact that the SCID community testing is early, et cetera. But they both have clearly a lot of data supporting them.

Any further comments?

DR. BOYLE: I have a comment.

DR. HOWELL: Coleen.

DR. BOYLE: I actually looked at both of the nomination forms last night, and I would request that in the future we'd actually have access to these before we come to the committee meeting because it would have been nice to be able to look at some of the references.

But when I looked at them, I felt like for SCID one of the criteria was the population-based screening. I didn't see that in there. I didn't see it in the references. Again, I didn't have access to the references, which I would have checked before I came here. So I guess I was thinking that it wasn't ready because of that information. But again, if we're going to just set it so that --

DR. LLOYD-PURYEAR: Yes. It needs to be (inaudible.)

DR. BOYLE: Okay. Again, when I was reviewing it, I just felt like there was the absence of that information.

DR. HOWELL: Any further comments about that?

The community studies on SCID that are currently going on at a state level we're going to hear about later today, but they're not published within this reference.

DR. DOUGHERTY: I'm sorry. I'm just going back to the Pompe, I guess, and trying to figure out, if there are disturbing results -- that's what I hear you saying -- from the Taiwan data about false positives, why that would necessarily put the Pompe nomination first or second. I mean, the data are the data. It's just the availability of data, not what it says, that should probably be the criterion for deciding, unless I'm missing something.

DR. GREEN: I think you're right, Denise. The intent is not to have an easy pass but, in fact, to look at all the available data. But I think it was the workgroup's commitment to recommend conditions for review that had the best chance of moving as far along as possible because, remember, while this is nomination live, this is real work from the committee, it's also sort of the first time to go through the process, as you know very well. Therefore, it's important to experience that review as well as possible.

DR. RINALDO: Just to address the question for Denise, I'm trying to be very practical here. If I take my own State of Minnesota and I think what would come out of a 0.5 percent false positive rate, that would probably translate in 1-plus false positive per day. So I would invite Dr. Berry, who will probably take the brunt of a situation like that, to comment if she would be satisfied with such a situation.

DR. BERRY: No.

(Laughter.)

DR. DOUGHERTY: I guess I just don't want us to be circular in reasoning and have the ones with the best chance of getting full approval by the committee go first and the other ones not.

DR. HOWELL: Peter has some comments I think.

DR. VAN DYCK: Well, I know this is the first time through this and we're wanting to move ahead. But I kind of expected we'd get a paragraph or a note about each of the six elements that you went through in the review or a summary of your concerns about each or positives or negatives about each. I kind of expected to have something to review that was written, very short, but just to get the thoughts down instead of just a copy of the nomination form because you've obviously put in a lot of time and looked at it and all the rest, and the rest of us don't have that.

DR. RINALDO: Well, we only saw two. We didn't see the other four yet.

DR. VAN DYCK: No. The six criteria that Nancy outlined in her slide, the process by which you reviewed. I'm not sure the best way to do it, whether it's a little summary paragraph. I'm not talking about a lot. But all we have now is a verbal report, and I'm having trouble deciding on a vote from a verbal report without being able to kind of review it a little bit.

DR. GREEN: I think, Peter, your request is entirely reasonable, of course, but we're just not prepared right now to give you that.

Rod, do you have some suggestions?

DR. VAN DYCK: I just wonder if anybody else is having the same issue. I'm just making a comment.

DR. DOUGHERTY: I think that's where my comments are coming from because I need more clarification of these couple of words on the slide.

DR. RINALDO: I think that was actually part of our discussion really in trying to find out where is the boundary between what we're supposed to do and what is going to be the job of the Evidence Review Group. I think at the end the conclusion was that we really want to stay at 30,000 feet and empower the Evidence Review Group mostly also to see what happens and how it works.

DR. HOWELL: Does anybody have any specific suggestions, Peter, about moving ahead with this issue?

DR. GREEN: I'll speak for the group. We could certainly submit a formal, terse report addressing those six issues in a very short turnaround time, but again, we can't do that -- I don't know if the break is going to be long enough for that.

DR. LLOYD-PURYEAR: I think the committee needs to decide what it needs to vote on today. Otherwise, we're not voting until May.

DR. VAN DYCK: This could be done by a phone call.

DR. LLOYD-PURYEAR: But it requires a Federal Register notice and a six-week -- okay. So the issue is how fast do you want to move forward, how fast do you want stuff to be turned over to the Evidence Review Group.

I think, if you remember, a lot of this was happening over vacation and moving things along with schedule conflicts. Those conflicts continue to exist in terms of scheduling another conference call to take a formal committee vote.

DR. GREEN: I'd be happy to volunteer three out of the four of us at lunch to come up with a terse report, if that's going to be helpful to the committee, so that it could still be considered at this meeting. There's not a problem.

DR. HOWELL: We'll come back to that recommendation. Ned has had some activity over here.

DR. CALONGE: I mean, I would wonder if the committee members feel they have enough information to vote already. I mean, do we have to vote? What are our options for actually making a selection? One is that we go ahead and say let's do both and then we'll prioritize one first and the other second. Or is it that we just want to move one forward? We're uncomfortable moving two forward at this time. I mean, I wonder how many people are ready to go ahead and say we can make a decision. I'm ready to make a decision.

DR. HOWELL: Let me point out that the group that met over the phone reviewed each of these six things in great detail and felt that these two recommendations both fit. And I must confess that we spent a lot of time talking -- for example, let me spend a little bit of time on the Taiwan thing again.

There's been a screening program in Taiwan that's been underway for quite a while. Taiwan has a health care program that permits them to be fairly sure they pick up everybody, and they've identified four children in their screening program who have the deficiency of alpha glucosidase. They purposely in their

report, which is published, said that they set the values at a level so they'd be absolutely sure not to miss anybody. Again, I don't want to go into evidence. That's their job.

But the bottom line, if you take that tack that you're going to set it at a level so you're very sure not to miss anybody, it would be likely that if you were going to do that in the States, you would want to tune up that value so you didn't have that positive. And that was the reason that -- plus the fact I'm very interested in Pompe disease -- I thought that that would be first, but I thought it should go ahead.

And there was no question among the committee that SCID clearly was ready to go ahead and we were aware of the fact that there's a public program going on that will be available to advise this committee. So that was the reason that we did that.

But I think if we were to list the six things, we're going to say, yes, it satisfies it very well; yes, it satisfies it very well, except for those two issues.

DR. VOCKLEY: Yes, I agree with Ned. I don't particularly need to see this in writing this time. However, I think Peter's suggestion is quite reasonable. As the number of these disorders increases, having a succinct summary in the future is the way to go.

So I think what we want to do here is keep the process going forward and test the system. I think we have two very good conditions that have been vetted, and sure, Nancy could go out and write something real quick, but the end result is that we're going to all know the same thing we know right now. I think it's worth moving this to the full review so that we can understand the process better with two excellent candidate conditions.

DR. HOWELL: I think Peter's suggestion is a very valid one, and I think certainly, going forward, that should really be the case so that that's written and it's provided to the people beforehand. There's no question about that, particularly as we look down the pike and we see some of the conditions coming along where I think the decisions will be a bit more -- you know, these are conditions whose treatments are widely publicized and known to be lifesaving, et cetera. And as we go down the pike, that will be less.

What's the sense of the group? I'm sympathetic with Peter's concern. On the other hand, I'm extremely sympathetic with moving head, for heaven's sake.

DR. WATSON: I think it's just an anomaly of time. I think your six criteria probably fell out after people were instructed about the nomination form. If they know what your six criteria are, they're probably going to get reflected in the nomination form. I think some of the criteria are very clearly already expressed here in a two-page document, and others like the 0.5 percent false positive rate -- you don't see that here, that Piero referred to on Pompe that there was 0.5 percent false positive. So I think that it will go away eventually as people align what they give you with what they know you're looking at.

DR. GREEN: I want to make very clear, to underscore the point that you made, which is that -- you're right -- those six criteria fell out after we designed the nomination form and the committee had approved it. But those criteria are abundantly represented in the specific topics within the nomination form. So I just want to make clear there's nothing new here. In fact, there is a section in the nomination form specifically addressing the characteristics of a screening test.

DR. WATSON: (Inaudible.)

DR. DOUGHERTY: If Gerry's was a formal recommendation, I'd like to second it, that we vote on these two and then have it as a principle for the next time that we have the nomination forms ahead of time and, if it's possible, the writeup from this group.

DR. HOWELL: So we'll consider Gerry's as a formal motion, Denise's as a second, that both of these conditions proceed with due speed.

Can we have any further discussion? I hope not a lot. Ned?

DR. CALONGE: My only issue is if we have to pick one to be the first. We don't need to do that.

DR. HOWELL: Let's do the following. We're going to vote on the fact that the committee voting members would like to send both of these nominations forth to Jim's committee with due speed. Can we see a show of hands on that?

(Show of hands.)

DR. HOWELL: Those who are opposed to that?

(No response.)

DR. HOWELL: Is anybody abstaining?

We have one abstention. Oh, I'm sorry. We have two abstentions and the other voting members all support that. Thank you very much.

Now, the other thing is can we have a sense of the group about -- Jim?

DR. PERRIN: So just two things about the choice of which is first. We're not talking about major time differences.

DR. LLOYD-PURYEAR: (Inaudible.)

DR. PERRIN: I'm just going to give you some background for that, though. It's not a major difference.

And the other is there was a discussion at the November meeting, based on Coleen's recommendations, that the one nominated first would be discussed first, to reflect on your discussions the last time around.

DR. LLOYD-PURYEAR: The order of a completed nomination, not the original.

DR. HOWELL: Let me be sure I understand. As I recall this conversation, if more than one condition came to the committee -- so if there were two conditions that came to the committee, at a meeting and they were both approved to go forward, it would be recommended that the first nominated go first. I don't know which one was nominated first. Which was the first completed nomination?

DR. LLOYD-PURYEAR: I'm sorry. I don't remember if it was Pompe or SCID. They came in very close.

DR. HOWELL: It's a profound detail, but does anybody have any feeling about not following that?

DR. RINALDO: I don't think we should go first come, first served. I really think that which one came in first is almost irrelevant.

DR. CALONGE: I would, again, recommend maybe a straw poll of seeing if there's -- since it was two to two the last time, is there enough votes to get one prioritized first?

DR. HOWELL: I did not hear what you said, Ned. I'm sorry.

DR. CALONGE: I wonder if we could just have a show of hands and see if there's a clear preference.

DR. HOWELL: That sounds like a very democratic process. Those persons who would favor sending Pompe first, raise your hand.

(Show of hands.)

DR. HOWELL: Three. Me.

Those for SCID?

(Show of hands.)

DR. HOWELL: Okay, SCID will go first, and very shortly thereafter, you'll get Pompe. As a matter of fact, they'll both come at the same time, but starting with SCID.

Thank you, Nancy, very much.

Let me also point out the following and that is this small internal formal group that Nancy just duly refereed from, it needs to be reconstituted of members of the committee. Piero and I served on the committee previously, but I would like to ask Kwaku and Becky if they would serve on the review for the future nominations so that you can dutifully file a written report for the next time and so forth. I see you're nodding. Thank you very much.

I'd also like to ask Nancy Green to continue to serve as a very active liaison because she's really done so much of the work, and Nancy, we appreciate that very much.

We now are going to have a brief report from Marie Mann. Yes?

DR. DOUGHERTY: This seems like a minor comment, but I'm not sure it is. In Nancy's slide, she calls what was the Criteria Workgroup the Nomination Workgroup, and it was called the Criteria Workgroup at one time.

DR. LLOYD-PURYEAR: It was two different workgroups.

DR. DOUGHERTY: But Coleen and I were appointed to a Criteria Working Group.

DR. LLOYD-PURYEAR: You were appointed to a Criteria Working -- oh, you mean the -- that's true. I thought you were talking about the most recent workgroup.

DR. DOUGHERTY: And I think it's important because we did discuss criteria, not just the way the form looks. It may be a subtle difference, but I think it's important to keep them straight.

DR. HOWELL: We'll try to correct that.

Marie, let's see how speedy you can be.

DR. MANN: Oh, this will be very speedy since, in fact, I think you have heard much of what I'm going to talk about.

So, in fact, I'm just going to run through the process of the administrative review. Basically when the nomination forms come in, the HRSA staff determines if all the requested information is present. If any of the information is missing, the nominator is contacted to supply the missing information. And then when all the information is determined to be complete, that completed nomination package is forwarded to the chair of the advisory committee.

The questions we specifically address are, is there a signed cover letter by the nominators and is all the requested information on the form regarding the condition, the test, the treatment present? And is there a signed formal conflict of interest statement for the nominators, and is there a list of supporting references? In fact, have the copies been included?

So for the progress, as of yesterday, five nominations have been submitted, and they have all been, as of yesterday, reviewed by the staff. However, in fact, because this is such a new process, all the nominations that came in had to be returned because of some missing information.

Through the process what we found was that the form seems to be very complete. That was not complicated. Everyone seems to fill in the boxes.

But the two areas that proved to be a challenge were having a signed letter from the nominator and the signed conflict of interest forms for all the nominators because, in fact, for some of the conditions -- we had encouraged that the nominations come through a team or from the multiple stakeholders who may be interested. So you may have one conflict of interest statement for the primary nominator, but we did not have it for, say, the two or three other persons who were listed as part of the team. So, in fact, we had to request that for all the nominators.

You've heard that two of the nominations have been completed and were forwarded which you're looking at. One, I think, should be completed shortly, and we're still awaiting completion of the other two.

Based on our experience, we did revise the form a little to be more explicit about the need for the nominators to submit signed letters of nomination and that, in fact, we need signed conflict of interest forms from all the nominators.

So, in fact, the nomination form can be accessed at the advisory committee website. In fact, just to remind you, there is a new website for the advisory committee.

Sharon, you have a question?

MS. TERRY: Yes. Could there be templates of the cover letter and the confidentiality agreements also put on that site?

DR. MANN: We could. We didn't have problems with the actual --

MS. TERRY: Okay. Just some consumers have asked us for that, but as long as you don't feel that's an issue, then --

DR. MANN: No. It's very straightforward, the letters.

MS. TERRY: I agree with you. It's just that some consumers have asked. We can certainly give some assistance in that regard.

DR. MANN: I think you had offered in the past to provide that assistance.

DR. HOWELL: But it was, obviously, not completely clear that these things were required to some of the people because --

DR. LLOYD-PURYEAR: To sign them.

DR. HOWELL: To sign them and so forth. I realize that sounds simplistic, but the point is that that has held up some of the recommendations which we hope, going forward, will be so clear that that won't happen. These are fairly simple things, but on the other hand, with the federal guidelines and all, we need to be meticulous with their being filled out.

DR. MANN: Right, and hopefully we've made it clear.

DR. HOWELL: Good, and I'm sure, Sharon, that you can be certain the advocacy community is fully aware of that too.

Jim?

DR. PERRIN: Given our interest, Marie, in the conflict of interest question, I'm just sort of wondering whether that information was shared with the Nomination Workgroup. I don't want to go into a detailed explanation, but the degree to which that could have been used to influence their -- or how that might have affected their decisions.

DR. LLOYD-PURYEAR: That information was irrelevant. They received a completed nomination package. So it was not shared.

DR. PERRIN: I guess I would answer it's probably not irrelevant, but it shouldn't have affected their choices a great deal.

DR. LLOYD-PURYEAR: It shouldn't have affected their choices, but it was irrelevant to the review. So that wasn't shared with any specificity. The internal group you're talking about? Is that what you're talking about? They certainly knew that there were problems with -- just like the committee knows, that there were problems with receiving packages with signed forms and signed letters, but the specificity was not shared. No.

DR. HOWELL: Jim's question was did the internal review committee get the letter about the conflict of interest of the nominator.

DR. MANN: Yes. They should have received the completed package.

DR. LLOYD-PURYEAR: Oh, I didn't understand.

DR. PERRIN: That was my question really because presumably the nominators do have conflicts and it's important to be aware of what those are.

DR. HOWELL: By definition.

DR. MANN: And that's why some of them didn't go forward because we felt it was critical to make sure everyone who was on the nominator forms to have submitted signed conflicts.

DR. HOWELL: Are there any further questions? Coleen?

DR. BOYLE: Back to the Nomination Workgroup. I was going to make the suggestion that we add the public health perspective, someone from the public health to the internal Nomination Workgroup. I feel like we have great representation from the clinical world but I would love to have some representation from the public health perspective.

DR. HOWELL: That sounds like a very good idea, and we will -- Coleen, would you like to do that?

DR. BOYLE: Well, I was wondering whether we could have someone from outside. Nancy is outside the committee, isn't she?

DR. HOWELL: That's why she's no longer on the committee.

Thank you, Coleen. So she's been added to the committee.

(Laughter.)

DR. HOWELL: Anybody else have any questions?

DR. FLEISCHMAN: Very quick. Just following up on Sharon's question, I understand why you wouldn't have a template for the letter, but is there a standardized conflict of interest form? Well, I think that's important because most people think of conflict of interest as financial, and I think as we're thinking about this, it's a much more complex level and it may well be helpful to provide areas in which there are conflicts that people would then relate to.

DR. MANN: I don't know the specific language. We did outline -- there was a brief description of the type of conflict that one should be including, and it was more than financial. But we can explore that.

DR. HOWELL: Thank you very much.

I think it's lunchtime and we've got a lot of exciting things this afternoon, including we'll have some results from the pilot screening programs for SCID, now that we have sent it forward. So we'll return here at 1:30.

(Whereupon, at 12:40 p.m., the meeting was recessed for lunch, to reconvene at 1:30 p.m.)

AFTERNOON SESSION (1:38 p.m.)

DR. HOWELL: Ladies and gentlemen, let's find our seats, please, and we'll begin the important part of the program of public comments. Our first commentator this afternoon will be Dr. Mei Baker, and Dr. Mei Baker, who is back there talking to somebody, you're on. Dr. Mei Baker is going to present her recent work on the newborn screening for SCID project in Wisconsin. Mei is a science advisor for the Newborn Screening Program at the Wisconsin State Laboratory of Hygiene, the University of Wisconsin in Madison. Dr. Baker?

DR. BAKER: Well, thank you for giving me this opportunity. I know I have a very, very short time.

I want to start by saying that SCID is -- I used a quote or a campaign slogan for newborn screening for SCID by Dr. Rebecca Buckley. I think it's more than 10 years now it is. "SCID is a pediatric emergency." We need to do something for this group of kids.

In general, we know SCID kids, because the maternal immunity grouping, at birth, with a routine physical exam, you will not be able to detect them. But later on, they will experience repeatedly fatal infection.

Another fact I want to point out is the live virus will do harm than do good for them just because of their unique situation.

Another piece I want to mention is SCID has, I believe, a very straightforward confirmatory test and we do have effective treatment. I do believe we should do the newborn screening for SCID.

Another piece, I think from the laboratory point of view, from the newborn screening point of view, is can we detect SCID using currently the newborn screening setting? I think Dr. Jennifer Puck published her work demonstrating the use of dried blood spots can detect SCID.

From that work, we started in early spring, about March sometime, looking into that and trying to refine the protocol and find algorithms. First, can we develop a robust laboratory protocol? Second, if this protocol can integrate the current newborn screening setting? It's been challenging but I think it's fun to involve this work.

Up to the end of last year, the phase we did is, first, we had to have the protocol. Second is we redo the deidentified newborn screening, the specimen.

I submitted written comments for the committee, and actually the number we screened, the deidentified, is close to 10,000. The reason I didn't put it together is because during the process, we refined the protocol further. I just don't want them mixed together and be misleading.

In this 5,766 screened samples, we referred to Dr. Puck's cutoff. In her work, I believe in the paper, she used two dried blood spots to do the DNA extraction, and her result is of the SCID babies, the TREC number is 30 or below for two spots.

If we use the criteria, we say if one spot is below 30, our initial screening, the screen positive is 0.4 percent. Our protocol is, we go further. We want to set up a cutoff higher so we're able to capture everything. Then we will do further analysis.

So far, actually I can safely say in close to 10,000 specimens, we just have one screening positive. And we just don't have the amplification there.

With this data, we feel very comfortable in terms of the laboratory protocol aspect, and fortunately, we got the department of health to approve going forward to identify newborn screening samples. We call it probation because the advisory committee will evaluate on a regular basis. We will report progress. Hopefully, after two or three years' trial, it will be formally recommended into the regular panel.

So in this period, I want to emphasize it has to be supported by research funding. We did have some funding through Modell Foundation and the Children's Hospital of Wisconsin started that and we hope we still can continue to work with different funding areas.

My time is up.

DR. HOWELL: Thank you very much, Dr. Baker.

You're running about 0.4 percent screen-positive samples at the current time.

DR. BAKER: No. The way we set it up is we -- just because the newborn screen, the throughput, we do the initial screening, which DNA extraction will be in the 96-well format and the single spots. And after the initial screening, if it didn't meet our cutoff -- actually currently we set it pretty high -- we will reanalyze. Another two spots have to be punched from the dried blood circle because some are saying maybe the distribution is not even. We will use real-time and other ways to do the TREC.

And then from that, with this protocol, so far we have just 1 in 10,000. We started January 1st to identify newborn screening. Every single baby that comes in, we'll do the screening. Up to now, with the data I saw, we will maybe have to revisit, in terms of cutoff, for the premature babies.

DR. HOWELL: Let me be very concrete. You have identified one positive patient so far out of 10,000 patients screened.

DR. BAKER: Correct.

DR. HOWELL: A patient that has SCID.

DR. BAKER: Yes, you're correct. Screen-positive. It's deidentified, the samples.

DR. HOWELL: They're deidentified? I thought you were doing --

DR. BAKER: We do. I'm sorry. The data I presented here is before January 1st, 2008. So that data set, close to 10,000 samples, we have one screen-positive.

DR. HOWELL: I think there are a number of questions we have, but I think, unfortunately, we need to move on unless there's a compelling question. I have some questions about the number that you're picking up as far as the ones that need follow-up and so forth.

PARTICIPANT: (Inaudible.)

DR. BAKER: Correct. Correct, because I was the one very close to the assay, but later on I found out actually this is a premature baby.

DR. HOWELL: Thank you very much, Mei.

There are a lot of folks on our list today. Our next presenter is John Adams and John is from the Canadian Organization for Rare Disorders. John?

DR. LLOYD-PURYEAR: You have about three minutes.

MR. ADAMS: Okay. Thank you very much.

For those of you who don't know me, now, the most important thing is I'm a PKU dad. I volunteer as Treasurer of the Canadian Organization for Rare Disorders. I have a full-time job in business development with a company out of Geneva, Switzerland and Dallas, Texas that specializes in database and information management systems. I serve on a CLSI working group that's attempting to write new guidelines for newborn screening of premature, low birth weight, and/or sick children. And Julie Miller, the newborn screening program manager from Nebraska, is the co-chair of that group, along with Judi Tuerck from the Oregon program.

My son is a beneficiary of a whole bunch of innovations in policies and programs and leadership and is a consumer of American health care and is the only non-American in the early access program for

the first-ever drug therapy, Kuvan, for PKU. His response is absolutely remarkable. So far, the latest lab results by my calculation is an 82 percent reduction in his plasma phenylalanine. That's after we started an incremental whole protein food load.

So I want to say this month is the 25th anniversary of President Ronald Reagan signing into law the Orphan Drug Act, and I want to say publicly thank you very much for the Kuvans and the other orphan products and the other rare diseases who are going to get attention and benefit from all of that. We hope to have an Orphan Drug Act in the not too distant future in the northern country.

I just want to briefly highlight the triple play that has led to a breakthrough because it's material in PKU but it's material to the world of universal newborn screening. Next year happens to be the 75th anniversary of the discovery of the condition of PKU by a Norwegian, Dr. Folling, due to the persistence of a mother with two retarded children. Then 55 years ago was the publication of the first-ever diet therapy for PKU by Dr. Bickel, his work in the U.K. Of course, then we have the third part of the triple play, Bob Guthrie's discovery of the means to do universal newborn screening, means which we're still using with the famous filter card today.

I just wanted to advertise all of those things and invite anyone who wants to to think about the ways in which we can all celebrate those milestones and, in particular for me, the discovery of PKU and what it led to in terms of the world of universal newborn screening and all of the benefits it's going to derive for lots rare disorders.

We're making some progress on your northern border. Next month we'll be having the first-ever national conference on newborn screening in Canada. Unfortunately, in my opinion, it's by invitation only. However, I have beaten down the doors and been invited. So I want to emphasize to you that at least reserve 5 percent of your mind space in this important deliberations of this committee and its emanations for the fact of what you're doing is very, very important outside the United States of America. Thank you.

DR. HOWELL: Thank you very much, John. I think everybody will look forward to some big celebrations next year, the celebration of the 75th anniversary of the discovery of PKU by Folling.

Now Kym Wigglesworth from the National MPS Society is next on our list. She's co-chair of the Committee on Federal Legislation.

MS. WIGGLESWORTH: Hi. I'll just take a few minutes of your time. This is the first meeting I've attended in person, but I've been following the proceedings of these meetings for years, and I have been very happy to be here the past two days.

I'm representing the National MPS Society. As many of you know, MPS is a rare genetic disorder. It's part of the lysosomal storage disease group. My daughter Maddie is 9. She has MPS-1. So I guess we fall in the consumer category, but I really hate that name. So I'm just a parent of a child who would have benefitted from newborn screening. So that's why I am passionate about this issue.

We are fortunate that Maddie was diagnosed relatively early on for MPS-1. She has a severe form. It took several months, but she was diagnosed. She was treated at Duke with a cord blood transplant. She's now almost 10 in fourth grade in a mainstream setting and is doing remarkably well thanks to early intervention, not only through transplant but through a myriad of therapies that she received, physical therapy, occupational therapy, speech therapy, hours and hours and hours of early intervention that were key to her success.

So the National MPS Society is a nonprofit advocacy group, family supports group. Our ultimate goal is cures for MPS and related disorders. In the interim, we help families manage and live with these disorders. Unfortunately, for several forms of MPS there are no treatments, but a lot of our families do

believe that knowing the diagnosis in the newborn period would benefit new parents greatly as far as managing the disease for the rest of their children's lives.

So I wanted you to know that as advocates the MPS Society is ready, willing, and able to be a support and be a partner in the newborn screening process. Thank you.

DR. HOWELL: Thank you very much, Ms. Wigglesworth.

Our next commentator is Andrea Williams, Executive Director of the Children's Sickle Cell Foundation.

MS. WILLIAMS: Thank you for the opportunity.

The newborn screening system with regards to the general public is almost the best kept secret. We have spent considerable time and resources preparing physicians via the ACT sheets to respond to questions that may arise from their patients but have yet to balance the time and resources to bring the message of newborn screening to the consumers and general public to prompt them to ask the questions. Expectant mothers, mothers of small children, and the parents of affected children and persons who are of child-bearing age who could benefit the most should be the focus of our educational efforts in a concurrent manner with continuous physician education. We must answer the question, who benefits most from newborn screening? Who can benefit more? Are we reaching our target audiences? And what can be done to maximize these benefits overall?

Each time I come before you, I hope that you will hear not only my voice but the voices of those that I represent, a representation not of institutions but of real children and real families. I have the honor of being the mother of one child with sickle cell disease and three others, two of which have sickle cell trait. If I pleaded here for them, you would understand why, but the privilege of being here to advocate for 347 other affected families that we serve is more precious because when I leave here, I return to these families, I will hear their voices, I will feel their pain, and I can take back hope, hope that the work that you do as a real committee that is addressing the real issues that affect the way their children are cared for is more precious. But work that you do here is a divine work and we're counting on you.

Newborn screening for autosomal recessive conditions has a natural byproduct, carrier identification. Follow-up with these families across the United States is widely ignored. Approximately 1 in 12 African Americans are sickle cell trait carriers. Approximately 1 in 400 have sickle cell disease. I state this because I want you to take notice yet again that this is not a rare occurrence.

Since 2005, I have had the auspicious experience to participate in a project that offers follow-up testing and genetic counseling to these families with babies identified as having sickle cell trait via the newborn screening program. Most families are receptive to the information over the phone and many come into the clinic to receive additional testing and genetic counseling.

I encourage you, as you meet and as you go about your daily lives, to answer the following questions. Would you want to know that there was a risk of having a child with a genetic disease? If so, what would this information do for you? How would it prepare you for possibility of disease? How would you feel if someone somewhere, even an organization, had a list with your name on it that stated this risk and decided to ignore it or didn't share it? How would you feel then?

Thank you.

DR. HOWELL: Thank you very much, Ms. Williams.

(Applause.)

DR. HOWELL: Our next presenter is Ms. Micki Gartkze. Micki is Director of Education and --

DR. LLOYD-PURYEAR: No. It's Sandy Simpson.

DR. HOWELL: We seem to be getting lists by the moment. Excuse me just a moment. Is there yet another list that is not here?

The next I have now is Sandy Simpson who is representing the Parent Project for Muscular Dystrophy.

DR. LLOYD-PURYEAR: She's gone. So then it's Kelly Leight.

DR. HOWELL: Okay. Kelly Leight, President and CEO of the CARES Foundation.

MS. LEIGHT: I'm here.

DR. HOWELL: Good. I think I had the right list all along.

MS. LEIGHT: Hi. I'm Kelly Leight. I am the President and CEO of the CARES Foundation, and I'm also the parent of a child with congenital adrenal hyperplasia.

This is the first time I've attended one of these meetings, and it's been very enlightening, although I've sat at the table for various other newborn screening workgroups and at various different committees. This is a very unique group in that it is really setting national policy, which is truly needed on many, many fronts, and has a direct link to the Secretary that can be extremely meaningful for the entire newborn screening community and for all the processes.

I do see a couple of gaps in the representation on the committee that I'd like to highlight.

First of all, as we move into an era where long-term follow-up is an integral part of the newborn screening system, the needs and concerns of families and affected individuals will need to be considered to a greater degree.

In addition, there need to be enough voices so that it's meaningful. Currently I see huge disparity in this particular type of representation on the committee.

I think also as we move into long-term follow-up, the committee would benefit by having representation from social services and early intervention and also from the insurance industry. I hope that as nominations are being put forth, that those particular types of members will be able to have a seat on this committee.

In addition, I understand that there is some talk about funding for travel expenses for subcommittee members being cut. I think that this will make a huge difference on the access, on the ability for subcommittee members to attend and for the committee members to have access to those voices. So I hope that there will be efforts put into place on a national level to secure permanent funding for these travel expenses for the subcommittee members because also I think it should be considered that conference call participation in these long, drawn-out, and comprehensive meetings is quite impractical.

So thank you very much.

DR. HOWELL: I thank you very much, Ms. Leight.

Our next presenter is Jill Levy-Fisch, who is President of Education and Awareness, Save Babies Through Screening Foundation.

MS. LEVY-FISCH: Well, thank you for the opportunity to speak today. I will be echoing many of Kelly's sentiments that we just heard.

I'd like to thank the committee for continuing to move this process forward and would especially like to recognize the efforts being made by the subcommittees. I think everyone is doing a wonderful job.

I'll start off by saying in December I had the opportunity to visit the Georgia newborn screening lab in conjunction with a visit to the CDC. While at the lab, it was brought to my attention by the lab workers themselves that many of the hospitals in the state are not utilizing the services of an overnight courier to transport their blood spots. In fact, I saw myself that there were specimens being run on samples that were already 11 to 12 days old. This is unacceptable as the lives of our children are directly being impacted in a negative fashion. Turnaround time should be five to six days, not two weeks. We've seen the benefits of a private/public partnership in other states, and we greatly support this, as it is our mission to protect the well-being of our children.

In addition, it is wonderful to see the addition of so many new committee members. However, I do feel the committee is lacking members who have experience as either a public health newborn screening laboratory manager or a specific follow-up manager. We feel the committee would greatly benefit from the addition of a professional public health newborn screening person and hope to see this addition made in the very near future.

I also respectfully ask the committee to help strengthen the voice of our families by inviting additional family representatives to the table. We need more than one voice at the table.

In closing, I ask the committee to please address the funding issues for our subcommittee members. I have heard rumors today, although nothing specific, that subcommittee members will no longer have their travel expenses covered. This greatly concerns me as it will directly impact in a negative fashion the ability of families, advocacy groups, and others to continue their vital participation in the activities being completed by the subcommittees and the committee itself.

Thank you for the opportunity to share this with you today.

DR. HOWELL: Thank you very much, Jill. Let me point out that the committee does benefit from the distinguished service of Mike Skeels, who is director of the laboratory on the West Coast.

MS. LEVY-FISCH: We've discussed this with other people. I mean, he doesn't serve the same function as what I'm referring to. He oversees but I think many people who we've spoken to feel that we could benefit from a specific person.

DR. HOWELL: A follow-up person and so forth.

MS. LEVY-FISCH: Yes.

I also have somebody else's comments. I don't know if she's on the list.

DR. HOWELL: What I would appreciate your doing, in view of the fact that we're running a little late, is if you would submit those and they will be a part of the formal agenda.

MS. LEVY-FISCH: This?

DR. HOWELL: Yes.

MS. LEVY-FISCH: They're handwritten. Is that okay?

DR. HOWELL: Yes. They have excellent translation facilities at HRSA even for handwriting.

(Laughter.)

DR. HOWELL: These, I assume, are the comments from Victoria Odesina -- is that correct -- who is from the Citizens for Quality Sickle Cell Care, Incorporated, who is not here. So if you would submit her comments, they will become a permanent part of the minutes.

I think that's the end of the list of public comments I have unless there's a new list that's recently arrived. So I will call an end to the public comments at this point in time.

We're really quite much on schedule now. It takes us back to the committee business.

Let me comment before we get away from that. Under tab 16, you have a variety of items, recent articles published about newborn screening. There is just an absolute flurry of articles appearing both in the scientific journals, as well as the lay press, including the Washington Post just last week, major articles about newborn screening and the value of newborn screening. It's interesting to see what a tremendous interest there is in this area.

The first item of business I would like to have Tracy, if he'd be good enough, read the resolution that his group reluctantly spent much of their break this morning drafting that will make a recommendation to the committee.

DR. TROTTER: Thanks.

Yes, we had actually a great time. A couple of lattes and we took off.

So I would like to make the motion or whatever it is, resolution, I guess, that the advisory committee acknowledges the importance of the American Academy of Pediatrics clinical report entitled "Newborn Screening Expands Recommendations for Pediatricians and Medical Home Implications for the System." Furthermore, the advisory committee recommends that the American Academy of Pediatrics and the American Academy of Family Physicians develop a seminar or workshop for their 2008 annual meetings and a series of educational initiatives to address the roles of the pediatrician in the newborn screening system to improve the working knowledge of genetic testing and systems of care. The advisory committee considers it especially important that the AAP considers newborn screening in their discussions of the future of pediatrics.

Second, recognizing the importance of the American College of Ob-Gyn and the American Academy of Family Physicians membership in prenatal education, the advisory committee recommends to ACOG and AAFP that under their CME or other educational activities that have a genetic medicine focus, the design of those programs should include newborn screening issues.

DR. HOWELL: Can we have any comments or discussion of Tracy's committee's work? Chris?

DR. KUS: Just to add that in the development of the training program that other participants of the newborn screening community be involved in doing that because I think it's important from a public health side to link what happens in the pediatrician's office with public health.

DR. TROTTER: Yes, I agree with that. In fact, we sort of made the resolution smaller and simpler, but the expansion of that would be that we would sort of provide a package of content, we hope, that would include all of the aspects of it.

DR. HOWELL: Kwaku?

DR. OHENE-FREMPONG: I just wanted to add just to make some of these educational materials available on a permanent basis that they use their websites as permanent displays of some of these educational opportunities so that when pediatricians or obstetricians come in contact with a specific question or an issue about a child, they can use the websites as referral sources.

DR. TROTTER: Yes. We would hope and expect that each of these groups would expand their use of this material to the multiple ways that they promote it, both on the Web and paper and newsletters, et cetera.

DR. HOWELL: David?

DR. LOUDER: I would imagine that a lot of the agenda has already been set for the 2008 NCE. Perhaps it would be better to recommend at the earliest possible occasion to institute this workshop so that we don't get lost with a specific year.

DR. TROTTER: I don't have any trouble with this. This is going to be an ongoing issue anyway.

DR. HOWELL: Further comments?

Is it the sense of this committee to support this recommendation? And if so, what will happen is that a letter will go forth to the involved people from the committee. Everybody is in agreement with that? Everybody seems to be nodding up and down. I don't know whether it's the time of day, but it looks like it's affirmative.

Since it's a recommendation from the committee, my parliamentarian to my right says we need a more formal vote rather than these sleepy nods. So those favoring this, raise your hand.

(Show of hands.)

DR. HOWELL: Is there opposition?

(No response.)

DR. HOWELL: It looks like it's unanimous. So we can proceed to send that ahead.

We'll get down to the items for the May 2008 meeting, but are there other items of business that should come before the committee before we get down to the agenda for the May meeting? Coleen?

DR. BOYLE: I also wanted to express some concern, at least on the part of my subcommittee, trying to try to move. I don't know the issues with regard to supporting travel for subcommittee members, but I do feel like we have made substantive progress, particularly during the committee meetings. That three-hour block really gives us a time to get together, coalesce around an issue, really discuss it, things that we try to do over a conference call but are really challenging. So I know that funding is always a challenge, but I would hope that we could find a way to continue to support travel of the subcommittee members.

DR. HOWELL: I think my colleagues to the right heard your recommendation quite strongly, as well as from two of our public presenters. And I think they'll have to go back to the purse and see what's there.

Is there any other business?

The agenda items for the 2008 meeting. Obviously, the agenda will be in flux until then, but can we have specific recommendations so that we hear about those now so that we can be planning on it? Barbara?

DR. BURTON: I'd like to suggest that perhaps we invite Maria Escolar or Joanne Kurtzburg to come talk with us about the long-term follow-up of patients with Crabbe disease treated with stem cell transplantation. I know that's one of the disorders that's going to be coming down the pipeline for consideration, and that's something I'd be interested in hearing about.

DR. HOWELL: Thank you very much. I think that what you're alluding to is there has been a good bit of discussion recently on the street about the long-term outcome of these children, and I think that it's absolutely essential that that become clarified. I must confess I think it would be desirable if there could be some sort of a workgroup before our next meeting of all the involved people so that you can find out really what's happening there. And I think it would be very nice if that were to happen, if the product of that could be at this meeting. I think that's the sense of what you're saying. Is that right? To find out what's happening?

DR. BURTON: Well, yes, and I think probably Maria Escolar is the person who is most on top of what's happening. She's been following them developmentally long-term. I think she's actually the person who really has the data. So she'd probably be the one most in control of that.

DR. HOWELL: Are there other suggestions for the meeting?

DR. DOUGHERTY: I'm going to suggest that Ned's group report back on where they are with looking at those various approaches to committee decision-making once we get the evidence review.

DR. HOWELL: Yes. I think that was implicit I think in the earlier discussions, but certainly we will have Ned on the agenda so that you can have a report on the various types of approaches this committee could take in response to Jim's Evidence Review Group and so forth. So that clearly will be on that.

DR. DOUGHERTY: And just FYI, Ned, AHRQ just had a training on using the GRADE system.

DR. HOWELL: Any other specific issues?

I think one of the things that was discussed at the Laboratory Committee that might percolate up to this committee will be the technology changes that might be under consideration for tyrosinemia type 1.

DR. VOCKLEY: Yes. I think we will pull that together for the subcommittee meeting, and then I don't know whether you want it to be a specific agenda item or just as part of the report of the subcommittee.

DR. HOWELL: My gut reaction is to have a specific working group at your subcommittee, and then I think it could be as a subcommittee report, but let's be sure we have it on the agenda of your subcommittee when it reports back to the full committee about your deliberations because it may well require some committee action of the whole thing.

DR. LLOYD-PURYEAR: Also a report from the Evidence Review Group.

DR. HOWELL: Will the Evidence Review Group have something to say in May?

DR. PERRIN: Absolutely.

DR. HOWELL: Well, there's no question that since our person is so confident, we will clearly have a report. As a matter of fact, if I look at my calendar, from right now till the first of May, that's certainly six months. It's a little tight, but I would think you should be able to be done with the first one. Right? And actually maybe two, since you're starting just a few weeks later. So we'll have a report from the Evidence Review Group.

Yes, Harry?

DR. HANNON: I don't know when the NIH grants or contracts or whatever are going to happen with the Translational Research Network, but it would be nice in the near future to hear something about what the intent and scope of the Translational Network will encompass and try to capture so that we can all have a better understanding of what the intent is for that project.

DR. HOWELL: Are there any comments about what Harry said?

A sudden missive has arrived over here that there apparently is an important letter that we're supposed to discuss, and I haven't seen the letter. So that's the first issue. Oh, it is here. Where is it? Under what tab?

DR. LLOYD-PURYEAR: Committee Correspondence, tab 5.

DR. HOWELL: Under Committee Correspondence, tab 5, dated October the 25th, is a letter to me that went over to HRSA from Bill Becker. Do you all have that?

DR. LLOYD-PURYEAR: Yes, you do. Everybody has that.

DR. HOWELL: It's under tab 5.

The bottom line is that this is a request from Bill Becker as President of the American Public Health Association, APHL, requesting membership as a liaison person to this committee.

Has anyone else read this letter before right now? Piero has read the letter.

I think many members of this committee are fully aware of the fact that the APHL is very involved in newborn screening issues. I think that goes without saying, and this letter is requesting -- they obviously are tied with the CDC and other organizing groups in requesting liaison membership.

Piero, do you have any thoughts or comments?

DR. RINALDO: I think we dealt with this request before, and I remember at one point we were having some discussions about the size of the committee, for one, and also it seems that it should be something different than first come/first served as a request comes in.

Obviously, APHL is a major player in the newborn screening arena. It would be useful to have Dr. Skeels here to also comment on it. It's interesting. Dr. Becker, I understand, is no longer the president. So at a minimum, I would ask whoever has replaced him in that position as president of APHL to reaffirm his request, which I think is likely to be.

DR. HOWELL: Can we have other members comment about the letter? You've read the letter. Duane?

DR. ALEXANDER: Well, they are certainly a major player in the things that we've been talking about. I think if you're looking for justification, it seems like a justified request. The only issue really I think is how big we want the committee to be and stay effective, but I think it's a legitimate request.

DR. VOCKLEY: Perhaps we need to ask the same question about committee membership as we do about the newborn screening panel. How do we go about adding new members and how do we take existing members out of the panel if they're no longer productive or appropriate to the mission of the committee? It seems a bigger question than just responding to one request.

DR. LLOYD-PURYEAR: The process is laid out in the policies and procedures, and perhaps I should make sure they're in every meeting notebook for every meeting so that we can review them and make sure that we're still in agreement with them. It actually outlines the number and ratio because that was one of the issues brought up, the balance.

The committee is limited to 15 members by legislation. You could have as many representatives as you wanted in the world theoretically, but there was an agreement on a ratio that we should limit ourselves to and that it should be less than the total number of committee members so that there would be a balance at all times.

DR. RINALDO: What is the current count?

DR. LLOYD-PURYEAR: Twelve. I mean, 11.

DR. RINALDO: So how many committee members? Fifteen and 11 --

DR. LLOYD-PURYEAR: Right now currently 11. I'd have to count for sure. Eleven. So we're one less than what I remember that we agreed to. But I think Gerry's point is probably the larger issue and what came up before is reassessing all the time what representatives you want. They're not necessarily permanent and to think about it that way. What are your needs as a committee?

DR. VOCKLEY: Are these positions essentially renewable? What are the ground rules? Once on, always on? Is this the last appointment that we'll ever be able to make? These are newbie questions.

DR. HOWELL: I'll turn it over to the committee experts to my right. Peter, do you have any comments about the renewability and the other things, the permanence, et cetera?

DR. LLOYD-PURYEAR: These really are outlined in the standard policies and procedures, and representatives are different than the committee members because they're serving at the request of the Secretary but really through the committee. And the representative is the representative of that organization. So the committee has a lot of leeway here.

DR. VOCKLEY: So by definition, you're saying if the committee feels that there's somebody that needs to be on and we're over our membership, that the organization representatives are here at the pleasure of the committee and can be asked to -- can be replaced.

DR. LLOYD-PURYEAR: Yes. If you find, for example, you no longer need SIMD on the committee because we just no longer need it, then you can say we no longer need it and we want to have some other organization.

But they're non-voting. They're always non-voting. So it's bringing expertise and organizational representation to the committee in a non-voting fashion. So you're bringing points of view that you feel are lacking.

DR. HOWELL: Let's hear from the other voting members of the committee. What do you want to do with this letter, which we almost forgot to even bring up? Ned?

DR. CALONGE: Well, I'd appreciate having the expertise within the operating rules of the committee. So I do think our public health laboratory partners are important to have input and to have around the table.

DR. HOWELL: Kwaku, do you have thoughts on the subject?

DR. OHENE-FREMPONG: Well, generally, I like to speak when I'm a little bit educated about the subject, but in this case, just in general, from what I know about the public health laboratories, I think that many of the things that we discuss bear on their work. So if there's a practical way that is procedurally correct that could get them here, that's fine. But I'm also sensitive to the larger question about just how membership gets constituted, and I think maybe it should be addressed in a larger context.

DR. HOWELL: I think the description of liaison members is really pretty well spelled out in the procedures. It's fundamentally that expertise that members of the committee would like to have represented. As Gerry put it, they serve at the pleasure of the committee. So if it's decided that the committee would like the expertise around the table of APHL and it would be valuable and the numbers are still below the members of the committee, then it's certainly completely appropriate to ask them to serve on the committee. I think that's clear.

Gerry and Piero, do you have anything to add additionally?

DR. VOCKLEY: Well, again, I'm information-gathering. I was questioning the relationship of this group with our current representation from the Association of State and Territorial Health Officials, and is that a duplicative expertise? Do we already have what this group would bring to the table?

DR. HOWELL: Ned is responding to that, and we obviously can hear from Chris too.

DR. CALONGE: I think Chris is great, but I don't think he's representing that group.

DR. HOWELL: Does Chris agree that he's great?

(Laughter.)

DR. KUS: Well, it's clear I'm not representing that group, but I think the representation for the State and Territorial Health Officials includes lab functions. So it's a matter of what parts of this. I'm saying, again, from your point of view, it's what you guys want, but I will say that public health representation is important, as I think that lab representation is important.

DR. HOWELL: Ned?

DR. CALONGE: I guess one of the issues that came up where it would be helpful for me is it's great to have Piero say, oh, we can do these extractions or we can do this or that. Having someone in a lab say, gee, I wonder how we could actually implement that new process and where does that fit and is PerkinElmer going to have a kit and what's the time line for that and how would we get access to that, those are issues that I don't know the answer to and that I would actually go back to my lab manager and say we're talking about this new extraction that's a double-methylated extraction of something and I don't

know what it is and can we ever do that, which would have some bearing on tyrosine screening, for example. Having someone at the table who says, yes, of course, we can, no matter what Piero does, we can replicate it, would be helpful.

DR. TROTTER: Well, as the end user who really doesn't understand any of that, I think the question I would ask is Dr. Skeels is not here this week, unfortunately, and does he in some way fill that role for the committee in terms of information that Ned was just talking about, et cetera? I don't know that. So I would say numbers do become a problem in terms of getting things done sometimes, but having the right information is way more important. I don't know whether we have it or don't.

DR. LLOYD-PURYEAR: The difference is Mike Skeels is here because of his expertise as an individual. He does not represent APHL and he cannot. That's a real distinction between what a member is and what a representative is. A representative represents their organization. Although he's a member of APHL, just like you're a member of AAP, you're not on this committee representing AAP.

DR. TROTTER: I understand that, but the definition that Rod used was does this person, whoever they are, or this group, whoever they might be, bring the expertise that we as committee members need.

DR. LLOYD-PURYEAR: It's not just individual expertise. It's organizational expertise and representation. If you need a message delivered to APHL, APHL can then facilitate that message. That's what the difference is between you and Tim, for example.

DR. HOWELL: Denise?

DR. DOUGHERTY: This is on a different issue.

DR. HOWELL: Let's stay on this issue, but you should comment on the subject since you're a voting member of the committee.

DR. DOUGHERTY: It sounds as if it might be good to have this organization represented here so we can get the organizational expertise.

DR. HOWELL: Duane, do you have anything else to add to your previous --

DR. ALEXANDER: I said what I had to say.

DR. HOWELL: Coleen?

DR. BOYLE: I would concur.

DR. HOWELL: I sense a concurrence of the voting members of the committee that it would be worthwhile.

I did not ask Dr. Buckley or Ms. Monaco.

DR. BUCKLEY: I would just be curious. You say that this is the second request from this person. Is that right? Okay. But you mentioned something about this had been brought up before. Maybe I misunderstood.

DR. LLOYD-PURYEAR: The discussion, the issues.

DR. BUCKLEY: I have no strong feelings about it, but I think that if we don't have this expertise on our committee, that it would be worthwhile having him here.

DR. HOWELL: Jana?

MS. MONACO: I have to agree. I think we need any connections to all the states that we could possibly get to disseminate the information to them and to get what all the states are doing back to us.

DR. HOWELL: In the discussions that I've heard around the table, I sense that there is an interest in possibly extending this group an opportunity to submit a liaison membership. Is that correct, Piero?

DR. RINALDO: Yes. I would like to add that I recall that in the period of public comments about the report, the ACMG/HRSA report -- my recollection is APHL felt they were not adequately involved in the process. The reality is that at the end of the day, implementation of any recommendation will require a substantial buy-in by state newborn screening laboratories. So I think it's probably not a bad idea at all to have them here, for one thing, to make sure that if there are concerns, they are not really presented as, well, we didn't have a chance to voice our ideas or concerns. So I would say that if it is feasible, that probably is a good idea.

DR. HOWELL: I've heard a sense around the group, but -- and this is an important thing -- we'll need to have a formal vote of extending an invitation to APHL to supply a liaison representative to this committee representing APHL. Can we have a vote on that? Those favoring that?

(Show of hands.)

DR. HOWELL: Is there any opposition to that?

(No response.)

DR. HOWELL: Thank you very much.

Is there anything else that we have to discuss?

DR. LLOYD-PURYEAR: Denise had something.

DR. HOWELL: Denise, I'm sorry.

DR. DOUGHERTY: The committee actually wrote a response, I assume, to the Advisory Committee on Genetics, Health, and Society on the report on oversight of genetic testing, and I was wondering if that's available.

DR. LLOYD-PURYEAR: Yes. I will send that to you. It's not in your books.

DR. DOUGHERTY: Okay.

DR. LLOYD-PURYEAR: I did.

DR. DOUGHERTY: Thanks.

DR. HOWELL: Jana.

MS. MONACO: Going back to your asking about recommendations for agenda items, would the work that the Follow-Up and Treatment Subcommittee is working on -- is it possible to consider having a representative who is an expert on formulas come and speak, whether it be from the companies that produce them, on their perspective on why there is a disparity with coverage or what's working in other states to make these possible and available to people?

DR. HOWELL: An expert on medical foods, as far as the coverage. Is that what your requesting?

MS. MONACO: The foods themselves. I think some of the problems is there's a lot of unknown with the formulas just for the fact that they are still considered food supplements, but in actuality we view them as a medication for our children. So I think somebody who is an expert on this who could shed some light on this to help guide the committee and the subcommittees in their work.

DR. BOYLE: I guess one thought is that we'd like to get some of the survey data in so that we would actually have that information to provide to the manufacturers, as well as the insurance industry. So maybe at that point. And I don't want to delay things either. I'm really trying to push things forward as quickly as possible, and I know the workgroup members feel similarly. But maybe just holding that until we have a little bit more information to be able to share with them. Those are my thoughts.

MS. MONACO: That's fine. I just thought this might have been something that would help move things along for you if we had somebody like that, but whatever you think would work best with the subcommittee.

DR. HOWELL: It seems like Coleen would like to have an opportunity for her committee to gather the data that they have in their survey and then add this at a later date. And that would be okay with you? Okay, great.

Any further comments?

(No response.)

DR. HOWELL: I think we're done, ladies and gentlemen. Thank you for your hard work and we will see you in the summer.

(Whereupon, at 2:40 p.m., the meeting was adjourned.)