U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
ADVISORY COMMITTEE ON HERITABLE DISORDERS AND GENETIC DISEASES IN NEWBORNS AND CHILDREN

Fifth Meeting

Thursday, July 21, 2005

Rotunda Room, 8th Floor
Ronald Reagan Building and International Trade Center
1300 Pennsylvania Avenue, N.W.
Washington, D.C.

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P R O C E E D I N G S (9:05 a.m.)

DR. HOWELL: Ladies and gentlemen, let me welcome you to the fifth meeting of the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. The name continues to be very lengthy. We have an exciting and busy agenda, and I'd like to get started by introducing Mr. Stephen Smith, who will be speaking in place of Dr. Betty Duke, who was not able to be with us today.

We're delighted to have Mr. Smith with us. He serves as senior advisory to Dr. Duke, who is, as you know, the Administrator for the U.S. Department of Health and Human Services HRSA organization since 2001. As senior advisor to the Administrator of HRSA, Mr. Smith really assists in all aspects of the agency's management, including budget oversight, policy development and program administration, and I think very important to all of us who are pediatricians by training, Mr. Smith worked at the Administration for Children and Families from 1980 to 2001. So he has an extraordinary experience there. He was most recently director of the Administration for Children and Families Office of Financial Services.

Let me introduce Mr. Smith, and we're delighted to have you here.

MR. SMITH: Good morning and thank you for inviting me to be here this morning. My job today is very simple. I want to welcome the committee members and the other people attending the meeting this morning. I want to tell you how much we appreciate the work that you have been doing and will be doing for the Department of Health and Human Services and, in fact, for the nation; and I want to express exactly how much we do need your advice and your expertise.

So I'm very pleased to be here with you today, and I do bring greetings from Dr. Duke, the Administrator of HRSA. She regrets that she could not be here in person. I know that you invited her to speak to you this morning, but she asked me to send you her best wishes and to thank you for participating in this meeting of the advisory committee.

I know the advisory committee has done a lot in the brief time, a little over a year, that you've been meeting. We're particularly grateful to Dr. Rodney Howell of the University of Miami School of Medicine for serving as the chair of the committee. I'd also like to thank our HRSA Maternal and Child Health staff who participate and support the committee, particularly Dr. van Dyck and Dr. Puryear. They have kept Betty Duke and myself and the Secretary's office well informed about the work that is important for you to do and that you have been doing on behalf of the Department.

I'm here before you today not as a clinician, not as a science advisor in the Department, but as a career executive. I started working in the federal government as a very young recent college graduate in the early '70s, and I thought I'd work for the government for a couple of years because I saw an opportunity — at that point I was working for the Social Security Administration — I saw an opportunity to provide some service to people. My grandmother at the time was receiving Social Security checks, and I knew it was important that people depended on the government. That was actually a very long time that my grandmother was able to receive Social Security checks. She died when she was 98.

So my grandfather's investments — my grandmother never worked under a job covered by Social Security, but my grandfather's investments in the Social Security tax paid off very well. My grandmother received Social Security benefits for 35 years.

I just have a strong belief that a career in which you're providing service to people, that you're helping people, makes a big difference. I bring that up because we can't do that alone. Neither the Department of Health and Human Services, even though it's large, a huge Department, cannot do everything it's charged to do by itself. We have to do it with partners. We have to have help. I think it's a very wise thing to have advisory committees. It's a longstanding tradition of the Department to have advisory committees, and I know that you have some very serious work facing you over the next couple

of days, that you have the comments, the public comments we got on the American College of Medical Genetics report, and we look forward to you reviewing those comments and advising us.

When I look at the number of advisory committees that there are in the Department of Health and Human Services — you may not know this, but there are over 200 advisory committees — that just tells you something about the breadth of work that's done in the Department, the number of issues that we face, and the very great need for us to be connected with experts, with people who have experience of working in the real world where these programs and where these issues do make a difference to the people that we're trying to serve.

In HRSA alone, we have 16 advisory committees. I think you're one of the preeminent committees. You have a big job that will make a big difference to many, many people in the country. We know that the general public is interested. We see many reports in the press about the issues that you're trying to grapple with, and we need your expertise, we need your experience, we need your good judgment. We are looking forward to receiving your advice, and you'll be giving that advice on behalf of the kinds of organizations and institutions you represent, on behalf of your professions, but you'll also be giving that advice on behalf of the people that we're going to try to serve as we improve the program.

Newborn screening is an example of an area where science has advanced, and public policy needs to keep up with it. As I mentioned, I'm not a clinician, I'm not a scientist, but I have been involved in public policy and I know we can't come up with good policy, good public policy, unless we find a way to work together to acknowledge and understand the best science. To provide the best quality health care, we have to get that science into practice. We have to do it in a way that's acceptable for public policy. We have to do it in a way that we can provide the best access to the services that are being offered in the most equitable manner possible, and we also have to provide those services in a way that the public can understand.

So I think if you think about what we would consider important in moving forward with the recommendations, we consider that the recommendations would be good if they improve access to the services, and that those services are high quality, high quality meaning they're based on scientific evidence.

We think it's very good if those services are accessible to even the most underserved, the most vulnerable populations in the country. We think it's good if anybody, regardless of where they live in the country, can get access to the same kinds of services. We think it's good if those services are provided in a culturally competent way that people can understand. We consider health literacy as part of the effort of explaining the services to parents who have to make decisions about treatment for their newborn children.

So there's a lot to consider. We definitely need your advice, and I want to thank you again for the efforts. I know it's hard to take time out of your busy schedules to do this, and I think this is a way in which you're providing a great public service. I know you have a lot to do, so I wanted to keep my remarks brief. I don't know if it's appropriate that we have questions and answers, but I'm quite happy to do that if there are any.

DR. HOWELL: Thank you very much.

Are there questions from the committee for Mr. Smith?

(No response.)

DR. HOWELL: Thank you very much. I think that we appreciate your comments, and I think the committee will be very interested in having your support and that of Dr. Duke in ensuring that the

committee's recommendations do move briskly through the process and up to the Secretary or wherever they need to go. So thank you very much.

We have a busy agenda, and let me make some comments about that before we begin. We have in the past been rather informal in having audience comments about questions, and we won't do that this time because of the busy agenda. We will have public comments, as always, in the agenda, but I'm talking about questions from the audience. We will not have those.

As you will recall, there was a lot of discussion at the last meeting about decision-making processes, and you see that the agenda is heavily slanted toward that, and we'll be hearing a lot about that. Mr. Smith has indicated that the Secretary is waiting on our comments and recommendations, particularly now that the public comment period has ended, and we're going to be spending a lot of time on that.

We're going to be looking at the proposed subcommittee charges. If you look at the agenda, we're scheduled to comment on subcommittee charges actually in this particular time, and there's not really enough time to really do that adequately. That's clear as we look at this a little further and think about it. So what I'm going to recommend is the following.

One is that Dr. Brower has had a lot of comments about her committee's charge, and she has made a few modifications. As soon as I finish these remarks, I'm going to ask Amy to talk about the modifications in her charge because it's a little bit different than what's in the book. Then if the committee agrees, we won't discuss the charges right now, but we will come back and discuss the charges, including Amy's modified charges, at the end of the day. We've allocated a big chunk of time on the decision-making process, and I think that we can allocate a little more time to the subcommittee charges at that time, so we'll plan to do that.

Now, let me also remind everybody in the room that the subcommittee meetings, which you will see on the agenda, are open, and we would invite anybody here to attend those and participate in a meaningful way. We also will hear from ACOG tomorrow, as you can see. But as we go ahead now, I think the first item of business that we will take care of at this time is the approval of the minutes. The minutes of the last meeting are in Tab 7. I wonder if this group has been great about reading these minutes in great detail. Historically, someone has said, well, gosh, I said something that isn't in the minutes. So these minutes are really fat. Michele, I think she transferred most of the spoken word in the minutes.

But could we have any comments about the minutes or any corrections to the minutes? I would find it remarkable if you can add anything to the minutes, but maybe someone can. Can we have a motion to approve the minutes?

DR. BOYLE: I motion to approve them.

DR. HOWELL: Thank you. So we have Coleen, and Bill seconds.

Those favoring that, say aye.

(Chorus of ayes.)

DR. HOWELL: Any opposite?

(No response.)

DR. HOWELL: Thank you very much.

So we will move now briskly to the next thing on our agenda. There is some correspondence to the committee which is in Tab 6, and that's really fundamentally just for informational purposes, and we don't need to vote on that. But one of the things that's in there is the letter under my name that went to the Secretary. As you can see, that letter is in there, and a notice to the registry and things of that nature, et cetera. There is a letter in here from Dr. Howse, who was unable to be with us, from the March of Dimes.

I think that that's all we need to do at this point, except we will hear now — if Dr. Brower would please comment about the changes in the charge to her committee.

DR. BROWER: Thanks, Dr. Howell.

Based on some discussion the subcommittee had following our last meeting and some feedback from the committee members as a whole, we wanted to make clear that the charge of the subcommittee in evaluating expansion of the panel or new tests, that will be serving as a role to make the structure for that to happen, and we propose to form working groups that no one on the subcommittee would be a part of. These working groups would be comprised of experts in fields like bioethics, epidemiology, having special expertise in the medical areas that we're reviewing, as well as other professionals.

The role of the subcommittee is really in providing the structure and doing it in a transparent way so that we can be facilitators to get the information to the committee as a whole for advice, recommendations and consent.

DR. HOWELL: Any questions of Dr. Brower? I think that there's been considerable interest in the process and the mechanism of any potential expansion in the future, and I think that really all the members of the committee are very interested in that, and Dr. Howse has pointed out in her letter that she does not think that those decisions reside in any specific subcommittee, and I think what Dr. Brower is saying is her committee agrees with that, to basically have a working group that would make some plans and that would come back, obviously, and focus through this committee as far as those expansions.

Are there questions about that?

(No response.)

DR. HOWELL: We will discuss that later. We really are not going to discuss that, unless you have a specific question about what she said. We will discuss that later at some length.

DR. BOYLE: Just clarification about what you mean by structure. That's all.

DR. BROWER: Well, I think we want to make a recommendation for how to provide the structure for this working group to meet. We need a fluid mechanism to evaluate new tests and technologies. So we want to put in place the structure for this working group to provide feedback to the committee as a whole.

DR. HOWELL: Dr. Telfair?

DR. TELFAIR: Mine was sort of on the same line. I have two questions. One is who will set the agenda in terms of what gets covered and what are the key questions to be answered for that committee. Then the second was related to who would be the liaison for that committee, if it's going to be made almost exclusively of those not on your committee.

DR. HOWELL: Why don't you put those questions on your list, and then we can just discuss it this afternoon. Obviously, that's a substantial discussion. If there's a comment about the general statement here, we'll hear from it. Otherwise, we'll discuss it later.

We're actually now ahead of schedule slightly, so Dr. van Dyck is going to bring an update on the ACMG report.

DR. van DYCK: Good morning. The committee at the last meeting asked the staff of the Bureau of collect and collate the public comments and get them out to the committee at least a month ahead of time so you folks had ample time to read them. We had 187 responses in the public comment process; 155 were submitted by the May 8th deadline, and 32 were submitted after the deadline. What we sent to you were those public comments and an alphabetized list of individuals or affiliations who commented on the ACMG report. I know it produced some paper, and I know it's probably hard to bring in your suitcases, but we hope you brought your copy with you for the discussion this morning.

So we did send those out about six weeks ahead, and I hope you've had time to review them. Thanks to Michele and her staff for collating them and making sense out of them, and putting them in a format that's really pretty easy to read through fairly quickly.

We've also begun an internal process in the Department to review the comments and to review the ACMG report, and that involves the main agencies in the Department that are affected or have programmatic responsibility for elements around newborn screening.

So I'd be happy to answer questions about any other element of the process, or if you have questions about the comments or the process. But otherwise, I think we're probably ready to begin the discussion.

DR. HOWELL: Bill?

DR. BECKER: Peter, could you explain the internal process a little more for us?

DR. van DYCK: Well, as we've always said, we want to take all the information that we can find around newborn screening and have a responsibility to recommend to the Secretary something related to the elements of newborn screening. So in the Department we have a clearance process which involves all agencies, and rather than wait and have HRSA develop something, send it up and then just blindly get reviewed by the different agencies, we thought it would make sense to have the agencies work together collaboratively to work out all of our different elements and responsibilities and in a sense form as much as we can a consensus document for the Department, which we feel would be much more useful to the Secretary, and much more timely eventually.

DR. BECKER: Do you have a time frame in mind?

DR. van DYCK: Our time frame is to move as expeditiously as possible. But a process this complicated I think is months, not weeks, the same as the committee's work. We look forward to the work of the committee as well, as another process that will inform our working group around the report and the other elements for newborn screening.

DR. HOWELL: Are there other questions for Dr. van Dyck?

(No response.)

DR. HOWELL: Would you comment a little bit about the mechanism? I'm aware of the fact that the federal agencies as a group convened at least by phone to review the documents, and the

mechanism — how do you see that working? I know you work with CDC, AHRQ, the NIH, and so forth, and have a consensus from the whole caboodle on the document. How exactly does that work?

DR. van DYCK: You mean how do we get together?

DR. HOWELL: No. For example, do you draft a document and the other groups approve it? I don't know exactly the mechanism by which that works.

DR. van DYCK: Well, Rodney, we're kind of exploring that. We've offered in HRSA, since we have the primary responsibility, to draft straw men for the group to review. But it may come that we decide that someone else would draft some section or some element that might be more appropriate. So we're not locked into a process. We're evaluating it each step of the way and as we go along.

DR. HOWELL: Would it seem logical to have the lead agency in there? I'm sure there are other advisory committees who do the same thing, that the lead agency would draft something and the other folks would tend to agree.

Are there other questions about that?

Piero?

DR. RINALDO: Yes, and the outcome of that process I presume will be shared with us, or not?

DR. van DYCK: The outcome of that process will be shared with you after clearance through the Department.

DR. HOWELL: Okay. It looks like that there is — I don't see any questions or comments.

Thank you very much, Peter.

That takes us, the committee, to the discussion of the public comments on the ACMG report. Peter has summarized those, and I think members of this committee got a freight shipment of these some time ago, and I think most of us have read them. It was personally very gratifying to me to see the large number of people who took time to send a comment in. An awful lot of people had done an awful lot of reading because the comments as a group, I think, were extremely thoughtful.

I've also given a considerable amount of thought to how we as a committee might comment on or review these, and let me make a few proposals, which you can think is a great idea or the worst idea you ever heard. But it would not seem to me to be useful of this committee's time to go through each of these 190 and say I agree with that and I think that this is really correct or that is not correct. But it seems to me that the vast majority of the comments that came in were either — there were a considerable number of comments that came in focusing on one area, and that was recommending newborn genetic testing for immunodeficiencies and so forth. So there was a recommendation that might follow some of the programs that have been set out in this document.

There were a considerable number that basically said this was a very good report and very thoughtful, et cetera. There were actually a small number of documents that were not supportive, that said they weren't supportive, and had specific reasons for lack of support. It seems to me that it would be helpful to think about the issues that were raised in these documents that this committee would be well served to address. In other words, rather than say you agree or disagree, to say that from these comments, what are things that we need to do.

I've listed a few of these, and I'm sure that others have. Let me make just a general comment. Before I list the areas of comments of need and that we need to work in, does the group think that it makes sense to think about what we should take on as our task to move this forward based on the comments that we've gotten about the record? In other words, we've gotten these comments, and people have said this is not right, this needs to be done. It seems to me we should focus on work of this committee that will improve the document, or the process I should say, and then I have a group of those. Does it make sense to approach that rather than to go through each of the things?

PARTICIPANTS: Yes.

DR. HOWELL: Coleen?

DR. BOYLE: I just had a further elaboration on that, and that is that when I was reading them, I was thinking specifically of some of the recommendations that would be specific to some of the subcommittees. I thought there were a number of recommendations that should be considered by the follow-up subcommittee, for example.

DR. HOWELL: Yes.

DR. BOYLE: So it may be that part of our charge would be to document those that are specific to the subcommittee and then somehow address them.

DR. HOWELL: I agree.

Let me tell you the ones that came out and that stuck out for me, and I'm sure others will have ones. I mentioned the immunodeficiency situation, but one of the issues that we will need to be considering is cutting-edge technologies, their development and validation, how these are implemented and things of this nature. That's one of the things that came out.

One of the things that was pointed out that needed to be worked on was the follow-up issue. In other words, we need a broad approach to long-term follow-up, data collection and analysis, methods of diagnostic confirmation and presumptive tests. That's an area that was pointed out.

Partnering with the medical home. In other words, how do you get these findings back, facilitating into adult care? These people are now growing up, and that's something that we will need to think about.

Also, the need to develop much better treatment. For example, we have treated PKU for a very long time with a diet that's complicated and difficult. It's effective, but we really need to think about new technologies for treatment. We really need to be very open and look at oral enzyme treatments and things of that nature.

We need to evaluate the health systems, and there's a tremendous need for outcomes research, and that was pointed out.

Better organization and functioning of our newborn screening and related health systems, the whole system. That is an issue.

Education is a big issue, and that was pointed out as a need for both families, professionals and the public.

Research. We need new and better screening technologies to include timing of screening; spectrum of diseases; ethical, legal and social issues; privacy issues; the sharing of patient data; other areas, storing of samples. Those are some of the things that surfaced out of the documents that I read

that I made notes of. It seems to me that thinking about these and I'm sure other things that you have in mind, we obviously are going to be discussing decision-making today, and how those decisions are made will obviously be one of the things that we need to look at.

But those are some of the things that we need to discuss, and I think that then we will end up with recommendations that we might look toward if we jump ahead. Those are considerations, but there should clearly be a uniform panel, we think, that all states should do. If someone says, well, why should all states do the same thing? I think that a consistent panel, if it should be done, it should be consistent. It should be done in Mississippi, it should be done in Minnesota, and having variations is, number one, scientifically not very sound, but it's also deadly for the families who move. We've had so many stories about that.

States must retain strong oversight over these programs. I think that's a recommendation we should be very strong about, and screening is a public health issue, I think, and who does the screening, whether it's done commercially or in a state lab I think is an issue. But the state has to have oversight over those programs to be sure that they're consistent.

There should be a national quality assurance program for this. There is a big program, an organized system for collection and analysis of data and so forth.

But anyway, those are some of the things that came out. You all have read all these things and have a lot of thoughts about these, too. So I'm interested in some comments about the notes that I've made here, and then how you think we should proceed to deal with this.

DR. TELFAIR: I would agree with Coleen in terms of looking at the recommendations' relationship to what we could do in the working subcommittees. But the other two issues to add to your list, one of the things was the issue of access, and I think it's complementary to something you brought up a few minutes earlier, looking at the systems, but also looking at the systems in terms of access from the consumer's perspective. We discussed that this morning. So I would add that to the list. The other thing is the point of literacy, being able to translate that information into an understandable way for the general public. So in terms of knowledge and information, those are other things that came up from what I was reading.

DR. HOWELL: Thank you very much.

Denise?

DR. DOUGHERTY: This may have been included in one of your categories, but one thing that leaped out at me was some of the issues that the state health departments or ASTHO and the labs raised about financing, even for doing the screening, not even considering follow-up, but financing and cost effectiveness. There was some comments on the lack of a true cost-effectiveness analysis in the actual report that they were reading. So I think they want more information about cost, cost effectiveness, and more help with that. I see Bill nodding his head, so maybe he can back me up.

DR. HOWELL: Interestingly enough, I don't know if these were distributed, but on my desk today — and I haven't had a chance to read it yet — is a brochure from ASTHO about financing newborn screening in an era of change and so forth. I look forward to looking through this.

Was this available? Does everyone have this?

DR. LLOYD-PURYEAR: All the committee members have it.

DR. HOWELL: All the committee members have it. It looks like a very nicely put together brochure. I look forward to reading it.

Bill?

DR. BECKER: Thanks, Rod.

I agree with Denise's comments. I think that one of the overarching issues that the committee is going to need to consider is that there is, at least from the reading of the comments received from the state health officials, we need to engage them more completely and more thoroughly on the nature of this report. I don't think they felt that it was compelling enough to be considered, in Dr. Hardy's words, a blueprint for national policy, which I think this committee might feel differently about if I were to poll it. It suggests that there is not sufficient engagement at the level of the health officials.

Given comments made a little earlier about the need for oversight of the programs at the state level, the practicalities that are involved in the operation of programs through the states, we need those guys as partners. Without that, it becomes more difficult to move forward in an effective manner. So I think this committee, then, needs to acknowledge that perception at this time, whether you agree with it or not — that is their perception — and work to develop ways to engage better the health officials from the state level.

DR. HOWELL: Now that you brought that up, how would you do that? What would be the mechanism for accomplishing that? Because I think that if our important partners have this as a major perception, we need to fix that.

DR. BECKER: Well, number one, in Dr. Hardy's comments before this committee, he made a request that a policy-level person from the states be made a part of this committee. It might be worthwhile to consider that request and move forward in that direction.

DR. HOWELL: This committee has little, if any, to do with adding members to the committee, I think zero to be exact. But the question of involving the state folks in the proper way — how can we do that? Peter, do you have some ideas? Because that's a very important perception. We can't let that pass.

DR. van DYCK: Well, I think certainly the committee could ask state health officers or propose to you state health officers that would be appropriate to serve on the subcommittees. The subcommittees could certainly hear from state health officers in the deliberations of the committee. Those are just two that come to mind instantly as ways to involve them more.

The committee charter doesn't allow for additional members. It's very strict in how many members there are, and the committee membership is full at the present time. People can propose additional members when people turn over, but those then go to the Secretary's Office, and it's the Secretary's Office that then decides what the ultimate membership of the committee is.

DR. HOWELL: Coleen, was that your bell ringing in the back of your head?

(Laughter.)

DR. BOYLE: That was my bell.

Peter, not even as liaison members?

DR. LLOYD-PURYEAR: They can't be members. They can be representatives, non-voting representatives. They can be part of the deliberations. They're appointed by the organizations. The Secretary doesn't determine who the member is, and they cover their cost and pay for their way here.

DR. HOWELL: Should we consider doing that, recommending that?

DR. RINALDO: Sure, but is that the only organization that should be given this option? How would we consider — I think it would be a legitimate question if somebody else said, well, that has been done; what about this organization or that other organization? I don't have any particular one in mind right now, but I think it would be worthwhile thinking about that possibility.

DR. HOWELL: Dr. Alexander is an experienced person in these matters.

DR. ALEXANDER: Well, we've had very clear suggestions for this particular organization. I think it's certainly acceptable and probably prudent to respond by utilizing the mechanism that Michele identified of inviting a representative of this group to be a person serving on this committee as a representative in exactly the fashion that she said. There may be others that come up later that we'd like to have in a similar capacity, but we don't have to do all of them at once. It doesn't hurt to start with one.

DR. BECKER: Rodney?

DR. HOWELL: Yes?

DR. BECKER: I'd like to make a motion, then, that the advisory committee recommend that a representative of ASTHO be added to this committee.

DR. HOWELL: As a —

DR. BECKER: As a representative.

DR. HOWELL: As a representative person. I think Dr. Alexander's comments — is there a second to that?

DR. BOYLE: I second it.

DR. HOWELL: I think that Dr. Alexander's comments are right on. I think there will be other agencies that probably should be appropriately considered, but the state health departments are such a critical aspect of newborn screening that you can make a fairly compelling issue that that group would be a proper place to start.

Any further comments about that? Denise?

DR. DOUGHERTY: No, I was ready to vote.

DR. HOWELL: Okay. Anybody else have comments before we vote?

Steve?

DR. EDWARDS: My comment is more to the general process than it is with this specific issue, which I happen to agree with and I'll vote for if it comes up. But I think the process of our trying to solve all these 15 or so problems that you've enumerated, and others probably have more, while we sit at the table for 30 minutes is probably not realistic.

What I would suggest we do with each of these issues that you've enumerated is not try to solve the problem, because I think they're all significant problems, but that we assign them to one of the subcommittees, to one of the groups, or it may be that some of them belong to the group as a whole, to

the entire advisory committee. But rather than trying to solve this problem now at this moment, that we initiate a mechanism for dealing with the problem, and I think that's what we can do in these 30 minutes, rather than try to get through each of these individually. It may be that as we reflect more on them, that we may have different ideas about what the appropriate solution is.

DR. HOWELL: Let me make a comment. The list that I gave is a list, but I would anticipate that working these through will be an agenda for this committee for literally years, because I think it really is the whole process. So I would think that we probably aren't going to solve any of these soon but that, I agree, we would look at them and try to identify subcommittees to work on them and move ahead. But this is kind of a roadmap, I think, of some of the areas that we'll be wanting to work in.

Do you want to comment specifically about the possibility of adding a person from the public health laboratory arena?

DR. EDWARDS: Well, my only thought on that is certainly it sounds like that would be appropriate, but maybe other people are appropriate. It may be that some group, some subcommittee, or maybe some committee or this committee should give more thought to it before deciding if we should have additional representatives. I guess the only way to have them would be as liaison members.

DR. HOWELL: Yes.

DR. EDWARDS: For example, at the last meeting, at the end of the meeting, there was discussion, as I recall, about having an obstetrician representative here. So I think in the context of this meeting, that maybe we're not considering all the options and that maybe somebody should be designated to do that and make specific recommendations.

DR. HOWELL: Comments about Dr. Edwards' —

(No response.)

DR. HOWELL: I think the discussion matter before we vote on this is would the committee rather have a more deliberative process, or would you like to go ahead and consider someone from ASTHO?

DR. ALEXANDER: I think the answer is probably both. I think that it makes such eminent sense and a clear need to be met to have somebody from ASTHO conveniently available to this committee, and there's no better way to have them conveniently available than to have them be a liaison representative. ASTHO makes eminent sense.

There may be others that come from time to time, and whether we want to wait until that needs become apparent or we want to deal with it prospectively by assigning to staff or to subcommittees the chore of identifying any other groups that they feel should be in this category of representative, we can do that. But I don't think that should interfere with our action on this motion to go ahead and invite somebody from ASTHO.

DR. HOWELL: Any further discussion on the ASTHO recommendation?

(No response.)

DR. HOWELL: Hearing none, let's vote on it. Those favoring the addition of a person from ASTHO as a representative to this committee, say yes.

(Chorus of ayes.)

DR. HOWELL: Any opposition?

(No response.)

DR. HOWELL: Thank you very much. We will do that.

DR. EDWARDS: I think there was a second for Duane's recommendation.

DR. HOWELL: Yes.

DR. EDWARDS: And I would suggest that we go ahead with that, too.

DR. HOWELL: Right. How would you do that, now that you've made that recommendation?

DR. EDWARDS: I think that you could make that an assignment. You've already asked the subcommittees to look at people that might be members of the subcommittee. I think it would be appropriate to ask each subcommittee to look at are there other organizations that should be at the bigger table and have them make recommendations, if that's the case.

DR. HOWELL: So your recommendation is that each of the subcommittees consider other folks. I think that we've got to be cautious not to think of adding a horde of folks at once.

DR. EDWARDS: Well, we could recommend them, but this group doesn't have to accept the recommendations.

DR. HOWELL: We'll make that recommendation, and the subcommittee chairs or their designees are here. So we will move ahead with that issue.

Now, what about the public comments? We still are in that discussion. Actually, we have a long period to discuss the public comments. We've allocated until 10:15, but then we also pick up with additional time after that to discuss the public comments and what we're going to do with them. So we need lots of wisdom from this group.

Denise?

DR. DOUGHERTY: Well, just to clarify, we're going to discuss these. People may have additions to your list and to what was just added about ASTHO and so forth. Then that's going to go into a letter to the Secretary saying we've all read the public comments and this is what we plan to do with them, which would need to be drafted at some point, and then what happens, because we're not going to send the minutes to the Secretary, I don't think.

DR. HOWELL: My thought would be — and again, I'm looking forward to your comments on this — that we draft a letter to the Secretary that says the committee has read all the comments, and I think the committee has indeed read all the comments, and we will make some comments about appreciating the comments, and say that having read these, we would recommend that the committee focus in the following areas to respond to these comments, and also for future directions of the committee to ensure that the process of identifying conditions and follow-up systems and new technologies are really advanced consistent with these comments and with the future mission of the committee. That would be my thought.

The Secretary will have gotten all the comments. The Secretary probably already has them.

DR. van DYCK: Rod, can I add or make a suggestion to add something to what you just said? And that would be put into the context of the original ACMG report.

DR. HOWELL: Yes.

DR. van DYCK: Because they're comments to the report. The committee, we have not yet sent a letter to the Secretary that's a formal letter talking about approving the report with the following comments or whatever. I mean, we've made the letter that you've suggested, but we've always said that we're waiting for the public comments to make really a formal statement about the report. So I think we have to do all that you said in recognition that they are in response to the report.

DR. HOWELL: Okay?

DR. DOUGHERTY: I guess the question is are we writing the letter today? Maybe we need to have, either on the computer screen or on a flip chart, what the recommendations are that we're making, what the areas are that we're saying we're going to work in. Or are we just going to have this list and then whatever anybody adds to it?

DR. HOWELL: I would suggest that we not as a committee try to write or draft a letter. I think that the committee drafts of that turn out as one is always expecting. But I would suggest that we have a considerable discussion about the points that you want in that letter to be sure that they're there, and that we draft a letter, and that we circulate that letter and so forth. I think that Michele and her folks can put that together and we can work on a draft and then circulate that for your comment, and then having gotten that we will send that forth to the Secretary. But that would be what I would suggest.

But I think that there probably are — I would certainly not suggest that the list I provided to you is all inclusive. There may well be other areas that we want to emphasize. Again, I think Peter has pointed out that we are indeed commenting about the report and the public comments in this report and how we would suggest responding to that as we move ahead.

Joseph?

DR. TELFAIR: Just a suggestion. I think it may be useful, even in thinking about what we're going to put together, if we all agree on what the key content areas are, or the key subject areas are that have come out of that.

DR. HOWELL: Yes.

DR. TELFAIR: And then once we all agree on that, then we can move forward with the next step.

DR. HOWELL: I would agree. We would certainly need to do that.

Do you have some thoughts about how you would like to proceed about the key areas of content that we would want to do?

DR. BOYLE: It would be helpful if we could see those. I know you listed them quickly, those 15, and I didn't write them all down. So maybe somebody could just quickly put the headings of those up there, because I know I read all the comments but I didn't take notes on what my issues are. I have some thoughts about that, and one was already raised.

DR. HOWELL: Okay. I think that we have just assigned a scribe who assures us that she has outstanding skills.

DR. ALEXANDER: Rod?

DR. HOWELL: Yes?

DR. ALEXANDER: While we're waiting for that, I'd make just a couple of general comments about my reactions to the comments and what we might do. First of all, the comments in general were very positive. Most of them clearly endorsed the concept of a uniform panel of tests that should be done across all states, and that this was a concept whose time had come, and urged us to move ahead with that.

The concerns that were raised dealt with a variety of things. Some of the concerns dealt with the process for identifying the conditions that would be on that initial list. I think we need to certainly be aware of those concerns, take them into account. I think the talks that we have lined up for this afternoon deal with that issue, and after we've heard those I think we'll be in a better position to respond to the criticisms about the process. Even the criticisms about the process did not necessarily quarrel with the end result of a list, although they called into question perhaps a couple of the disorders. The main thing was the process.

I think we'll be in a better position after we hear the presentations this afternoon that deal with how you go about a process, any kind of process, in dealing with the situation that we have where there is limited evidence and you need to make some kind of decision. So I would hope that we'd have an opportunity after those presentations this afternoon to address that issue.

The other issues deal not so much with the list but the consequences of having that list and doing the screening, and those are the consequences of how do you follow it up, how do you assure that when a parent gets a phone call that there has been a positive screen, that they are told what having a positive screen means and what they do next now that that process is in place to provide confirmation of diagnosis, counseling and care, the three C's, and the follow-up.

There was concern expressed from a number of corners that we not focus just on the issue of what we screen for but the follow-up of that, and that that process of the follow-up needs to be in place before we embark on markedly expanded screening. Unless that process is in place, we're in trouble. We owe it to the public, to the parents, to the practitioners, to be sure that that process is in place before we embark on such an expanded list.

The other components I think deal with issues of physician preparation, of parental education, of assuring that funding is in place to provide the screening so that there is equitable access, and other related issues. I think that each of those is something that we need to address, and perhaps we can assure the Secretary in our response that we consider these to be important too, that they need to be addressed above and beyond what is in this report from the College, and that it's the intent of this committee to pursue those in the course of its deliberations over the course of the next coming months.

DR. HOWELL: You know, it's very interesting. I think that Duane has made some very interesting points. The ACMG report had no commitment whatsoever to develop or suggest the follow-up. It was simply looking at a uniform panel, and many of the comments dealt with the consequences of that. So that's a little bit complicated as to how we couch that, because I think that does lay framework for this committee to do it, but it strikes me that perhaps one of the things we should put as the first line, as Duane has mentioned, in this note is that I think it would be appropriate to say that most of the responses to the report were highly favorable and felt that a uniform panel was very desirable. It seems to me that we should come out of the barn with that.

Actually, I don't think that list — those are just some notes I have, and I'm not sure that's the best way to start, with this one.

DR. DOUGHERTY: Can I suggest that we maybe group them under Duane's categories? Would that help?

DR. HOWELL: I think that may work.

DR. DOUGHERTY: Rather than a list of 15.

DR. LLOYD-PURYEAR: Except we were fussing around and I didn't hear half of what Duane said. If we can take a break, I can look at the person over there typing, and we can get stuff up. Why don't we take a break?

DR. HOWELL: Why don't we take a break a little bit early and try to organize this a little bit more. We've got to get the typist going and decide what we're going to do here. We'll take a 15-minute break and we'll come back.

(Recess.)

DR. HOWELL: We have a starting list here that we will look to have your comments about as we try to use these as bullets for our letter.

Duane had to go back to the NIH to introduce an important person at a meeting, and he'll be back at 1 o'clock. So we'll proceed.

Here are some of the starting points for your comments and discussion. It seems that fairly early in the document we should make a comment about the fact that there was considerable discussion about the process. Let's have some comments about these, because what I would hope we could do in the next period of time is go through these, come up with some bullets and so forth from which a letter will be written that will go to the Secretary, again referring back to the ACMG report because that's what we're commenting on. Let's remember that.

DR. RINALDO: I have a question. When he says, "The following issues were identified by the expert panel and persons who submitted public comments," I thought that here we were summarizing the public comments. So why do you have both? The expert panel means the group that generated the report, or this panel, this committee? So are we merging them? I'm just asking to know what exactly we are doing.

DR. HOWELL: I didn't write this sentence, so let's start with that. I think that the bottom line is that the ACMG report, as you very well know, did discuss many of these issues, and they also were in the public comments that came. So I think that that's where those combination comments came from, frankly.

DR. EDWARDS: But I thought that here we're responding to the comments. So shouldn't this be identified more by the persons who submitted public comments? Because we're actually responding rather than raising issues. We're responding to the issues. So I would see this as that these issues were raised by persons who submitted public comments, because that's how we got these issues.

DR. HOWELL: Okay, let's take out the expert panel. Is that what people are saying around the table? Okay, let's do that.

DR. LLOYD-PURYEAR: It's both persons and organizations, right?

DR. HOWELL: Michele points out persons and organizations, because a number of the comments came in from organizations. So it should be persons and organizations to be correct.

DR. LLOYD-PURYEAR: In number 1, can you put a colon after "cutting-edge technologies"?

DR. DOUGHERTY: Could I just make a comment on the second bullet about the ACMG report and its scope? I think it was charged with addressing the total newborn screening system, because there are recommendations in there about follow-up and systems and financing. They didn't, because of time and other issues, didn't go into as much depth, but I think the charge was that they were addressing the entire system.

DR. BOYLE: I was just looking at the executive summary, which is under Tab 6. There's a list of the charges, and one of them is Model Policies and Procedures for State Newborn Screening Programs as part of the charge. So maybe we just want to say that the main focus of the ACMG report was on recommendations for a newborn screening panel, something like that.

DR. HOWELL: Yes, I think that's accurate. I think the situation is that in the initial thought, that was going to be a part of it. But that was such a vast project that that did not really get much attention.

DR. RINALDO: But there was a significant contribution with the new overarching principles, which I think do address, although at a high level, I agree. They clearly identify issues related to each and every component of a newborn screening program.

DR. HOWELL: Yes, as an overarching principle rather than any recommendation of solving that.

DR. DOUGHERTY: I guess if we're sending a letter to the Secretary, I'm not sure how to put this but there may need to be some language about — you have "the following issues were identified," but we have to say something about characterizing what the issues are, I think, concern about cutting-edge technologies, concern about long-term follow-up, that kind of thing.

DR. BOYLE: Maybe we can say something like some of the key challenges to implementation. I don't want to wordsmith here, but that's the idea.

DR. HOWELL: How would you like to put that in there?

DR. BOYLE: I was just saying the following key challenges to the implementation, to the continued evaluation or implementation, those two key issues that Duane talked about before he left. One was an overview of the process; the other one was the actual implementation of the recommendations.

DR. HOWELL: Our scribes are still up in that first thing, and we're down below. So, scribes, let's move below, and we can wordsmith that first thing a little bit later.

DR. LLOYD-PURYEAR: Just to acknowledge, I wrote the contract, Marie was a project officer, and they were not charged with addressing the whole newborn screening system. So just to clarify that.

DR. BOYLE: I'm just reading what was here, Michele.

DR. LLOYD-PURYEAR: Yes. Well, it doesn't say to address the whole newborn screening system. So that was clarified.

DR. RINALDO: Could you go back up there and look at that? So perhaps you can say —

DR. DOUGHERTY: Could I just read from the executive summary under Section 2? It says, "Because the appropriate functioning of the system is critical to realizing improved outcomes, the full

breadth of the components of a screening program and system was examined by the expert group over the course of the project."

DR. LLOYD-PURYEAR: But that was not their charge. Those chose to do some of those, but that was not their charge.

DR. RINALDO: I think it was examined to basically pursue the primary goal. That's not to do it out in a vacuum. In fact, I would add there some qualifiers, like "the focus of the ACMG expert panel was primarily to develop a uniform screening panel," and it was not charged with addressing general consideration of the needs and issues related to a total newborn screening system.

MR. ROBERTSON: Rodney? I apologize for coming in late after the break, but could you just clarify what we're trying to do here? I thought that you said we weren't going to try to write the letter as a committee, and I agree with you, and what we're going to get up here is some of the issues that you raised this morning.

DR. HOWELL: Yes, yes.

MR. ROBERTSON: So I really don't think it's a good use of time to wordsmith these things. I mean, if we just get the points up, then we can talk about trying to group it based on the three C's that Dr. Alexander had mentioned. We should probably just do that.

DR. HOWELL: I think Derek's point is well made. What I would hope we could do is get the points that the people would like to see, and Michele and folks are excellent at wordsmith, so we can then wordsmith. So let's not worry too much about the exact wording, but let's be sure that the key points that you want in the letter are there.

I think that a key point that must be in the letter is, number one, we need to, as a committee, be very clear that the committee has reviewed the public comments and the report of the ACMG, again looking at those together, and supports the overall recommendation. I think that needs to be at the first of the letter. Does anybody have any qualms with that?

(No response.)

DR. HOWELL: Then there are going to be these other considerations that came out in the public comment that we need to be looking at in the future. What's the wisdom of the group on that? That's an important thing. That's a key thing. So we need to at least put a bullet in, any words you want to put in there. It ought to be the very first thing you put.

DR. DOUGHERTY: Rod, could I have time to think about that recommendation?

DR. HOWELL: A short while.

DR. DOUGHERTY: Well, I guess the issue is still the evidence base and the process. So recommending that all of these conditions be adopted by every state given concerns about the process, I'm not sure, but I'll think about it. Is that what the statement is going to be, that the committee recommends that every state tests for these 29 plus 25?

DR. BECKER: Well, rather than go directly to that specific point, maybe it will be helpful, Rod, to clarify. Once Michele and staff formulate the wording around these specific items that we've identified, will that draft letter then be distributed to the committee for further input? Because I think at that point the specific comments like what Denise is talking about and what Coleen is talking about, maybe some points of clarification that might need to come out. There will probably be some conversations that may occur

electronically, but is it your intent — I guess I'm asking a process question — once a draft document is developed, to disseminate it to the committee for further consideration?

DR. HOWELL: The answer to that I think is yes. On the other hand, I think a key consideration, however, is we need to make a recommendation to the Secretary about this document. It will have some conditions under it, but we must say that we're going to support the document, and these are concerns that we will be working on in the future and so forth.

DR. BECKER: I guess I agree with your ultimate intent for the document. But until we have the document, I'm not sure that anybody around the committee can actually support something we don't really have in body at this point. But I agree with the process that you've described.

DR. HOWELL: Any comments about that?

MR. ROBERTSON: Again, I would focus on what's actually at the fourth bullet, the following issues were identified, because I think that's the section that we're in. We're supposed to be discussing the public comments. I mean, isn't that what we're supposed to be doing during this time? That's how you opened it. You kind of mentioned a few things that came out in the public comments, and if we could talk about those, then I think the second step is how we draft the letter and what's in the letter. But I think right now we're supposed to be focusing on a discussion on the public comments, not on our own views about the report but about the public comments.

DR. HOWELL: Peter, comments about what we should have in this document? We're clearly discussing the public comments, in the context, however, of the ACMG report.

DR. van DYCK: I think we should focus on the public comments as well, as Derek has suggested, and let the staff kind of put together the preamble to the letter. I think there's enough up here as an outline of what should be included in that preamble that I think they can write that. We ought to be now, in the time we have, discussing how and to what extent the public comment areas concern us in relation to the overall report, and if we're going to acknowledge some of the public comments and say we're going to work on them further or develop them more.

But to go through these highlights that I think you so ably put up there with the additions from the committee and describe or get a sense of the committee of how those affect our overall opinion of the report — as you suggested, the conditions, more or less — I think that's kind of where we're going, but I don't think it's worthwhile to work on the preamble pieces of the letter.

DR. HOWELL: Okay. Do people agree with that? Well, then, we'll go back to the public comments section and see if these things cover the major things that we should comment about.

Amy?

DR. BROWER: And I just wanted to add, for the cutting-edge technologies, there's also the utilization. So not only the development and validation and implementation of new technologies, but also new applications of existing technologies or new areas. So the clinical utilization, which diseases, which populations are we focusing on. I would pick up on comments before the break that we decide if some of these points get charged to the subcommittees to then follow up on. So this one seems like a logical one that would fit in the Laboratory Subcommittee.

DR. van DYCK: And I think it's helpful for the committee to think if they were drafting these comments to the Secretary, what is it they'd like to know about what it is the staff is going to say about this issue, for example. So what is the staff going to write about cutting-edge technologies? What is the sense of the committee that they want the Secretary to hear related to the report in this comment? So if

we could just get a couple of succinct comments that the committee can agree on about how this relates to the report or should modify the report, or how the committee is going to respond to these, that's what I think is most helpful.

DR. HOWELL: Steve?

DR. EDWARDS: If I were the Secretary and receiving this report, the first thing that I would want on the list would be the most inflammatory thing that's come up. The questions that have been in the press and the questions that have inflamed the issue the most are those about the question of scientific validity and process. I think we need to hit that head on right at the start. I think that should be the first response.

Then I think that if you look at our discussion last time, in fact we had an extensive discussion last time — it's in the minutes — about this very question. We're going to have discussion later today about the scientific process and so forth. But I think that that's going to be the most inflammatory thing, I think, that the Secretary will see, and I would hit that head on and not try to hide that in any of the discussion but say that we have discussed that and reached this conclusion. But I would put that first.

DR. HOWELL: Okay. Well, you want to back up and erase scientific validity? Put it up as number 1.

Now, what would you like to say about that? How would you like to couch that, since you have some strong feelings about that?

DR. EDWARDS: Well, I think that I'm not the one to respond to that. But we had a long discussion and there's a good summary of that in the minutes of this meeting, the minutes of the last meeting, and that should be summarized. But in addition to that, I think the comment should be made about what happens this afternoon. There will be several speakers talking about the science of evidence-based medicine, and I think that that should be a part of the response too.

DR. HOWELL: So you would say that —

DR. EDWARDS: I don't want to give you the verbiage. I cannot give you the verbiage.

DR. HOWELL: But so that we can think about this, you would say that there's been considerable discussion about the process at the committee presentations, blah, blah, blah, and so forth. So you would like to have that as number 1.

DR. EDWARDS: Yes.

DR. van DYCK: I agree with that. We have a period of time after the afternoon discussions to discuss that issue.

DR. HOWELL: Yes.

DR. van DYCK: I agree that it should be number 1 and we should address these issues in some kind of priority order, and that we hold the discussion on this one until after the presentation this afternoon.

DR. HOWELL: Okay.

Any other hot-button issues that should be here?

DR. LLOYD-PURYEAR: Do we have Duane's issues?

DR. HOWELL: Greg?

DR. HAWKINS: One issue I saw pop up in a couple of the comments is whether the tests will be mandated or whether there will just be recommendations. I think there was some concern that this could go to the process of where these tests could be mandated in the future, and there was a concern about whether states would be able to handle that without having the financing. So I think that's one thing that I saw pop up a couple of times. That may come up as an issue in future discussion. I don't know who would decide to mandate tests like these, and I know it's coming as a recommendation and not a mandate, but I think there might be some concern that that may be a future direction.

DR. HOWELL: Any comments about that? Obviously, the federal government can't mandate newborn screening, which is a state operation anyway. So I think the recommendation was that the states mandate it. Any comments about that?

DR. van DYCK: I'd just like to say that that's correct. It's never been very clear that this will not generate a mandate from the Department on what must be screened. Rather, if the Department issues something, it will be in the form of guidelines or recommendations. But if it's a concern and it's stated in the comments, then I think it's fair to mention that in the comments.

DR. HOWELL: Other stuff that should go on this list?

DR. BOYLE: This is not my area of expertise, but I felt like there was clear indication from some of the laboratory directors about some of the challenges that this panel might provide in terms of their actual implementation, cutoff values, the relevance of some tests, tests that were not included, a number of laboratory-related issues. I don't see lab here other than methods of diagnosis, but I don't consider that so much laboratory screening-related challenges.

DR. RINALDO: If I can comment on that, I'm completely with Dr. Edwards. I think that we have looked at, as a whole, these comments, and clearly, as was said before, when you look at what side these comments are taking, there clearly is I think a significant majority of positive comments and endorsement. I really believe we should look separately at the comments that come from professional organizations versus the ones that come from individuals.

But besides that, there is no doubt that there are some extremely negative comments, some probably close to being vitriolic in the intensity of the comment, and I agree with Dr. Edwards. We cannot avoid discussing that. I read them carefully and clearly. When somebody tells you that this has been a colossal waste of time, you take it with a grain of salt and say, okay, there's somebody clearly unhappy. I think we should address the issues of all the perceived deficiencies in the scientific process or the approach. Some people feel that we didn't use a standardized evidence-based approach, and there are perhaps reasons why that didn't happen.

So I think that what we should really do here, and besides a brief preamble, this many comments, this many supportive, this many negative. So that, I think, sets the tone. Then you say the negatives made these specific points. I don't think it will serve any purpose here to pretend it didn't happen or they're not there. Then see what the response or the assessment of the committee will be of these comments. Are they justified? Is it something we should take into consideration, something we should even suggest the need to make some changes?

I found it interesting that in most of the negative comments, maybe I can be proven wrong but it seems to me that rarely, if ever, there are comments on the key purpose of these reports and on the recommended panel, and that is uniformity. Nobody seems to appreciate the fact that that really was the driver. The driver, in response to what is really a mounting amount of evidence from the public, from

public health, is that it cannot continue to be so different and go from states with a few conditions to others that have much larger programs.

If anything, I think it's also fair to say that it's also a way for us to assess and perhaps make comments on the comments. To me, that is a deficiency, and perhaps it wasn't conveyed well enough. But if you look at the title of this report, you can clearly say towards a uniform panel. That's the key. Now, as Dr. Boyle said, some of the comments on the laboratory side — I'll be happy to get into that discussion. I really think that another thing that hasn't been fully appreciated in the process is — there was a lot of attention, actually, on the secondary targets. There has been a lot of steam, a lot of criticism.

Still, I found it quite interesting that the thing that is irrefutable evidence that nobody seems to appreciate here is that all but three of the secondary targets are required for the differential diagnosis of the uniform panel. So you can't really — they are in because you need to know if the patient has Condition A or Condition B. Some of you may have seen recently that there was some attention given in the media about the decision made by Germany, where Germany is comfortable with this course of action, that if the screening indicates one of the conditions they have decided not to actively be screening for, the data will be destroyed and nobody will be told about it.

Switzerland, on the other hand, collects all the data, doesn't destroy anything, but once are told that a child fell ill and is probably suffering significant morbidity, or even mortality, then the lab will go back to verify that, indeed, he has that condition.

I don't know if either of these two models will really be acceptable here in the United States. Ethically and morally, I don't think it's the case. But I really want to make the point that those comments, in my opinion — and I think we are entitled to somewhat criticize the critiques. I think it's just a fair process. I think they completely miss the point.

DR. HOWELL: How would you like to modify this list in view of your comments?

DR. RINALDO: I would start making the list, and again, I think Derek is absolutely right, and Dr. Edwards. Let's not pretend it didn't happen. Let's make a list of the criticisms, starting from the worst ones or the most intense ones, and then decide if and how we as a committee decide to include a commentary on what we feel is the case. If not justified, maybe it's driven by all sorts of possible issues. I don't think I would generalize but rather take them one by one.

DR. HOWELL: Coleen?

DR. BOYLE: I was just trying to think of a way to simplify this for us, and I guess maybe I'll make this suggestion. One of them is that this letter be fairly general, that it talk about the fact that this committee is considering the ACMG report and other things that are within its purview, and it's deliberating about its process, which we'll hear more about this afternoon, and it will come up with a way, with guidance and experience that has been learned from the ACMG report and the public comments, it will come up with its own way of evaluating conditions and making recommendations.

There were a number of issues that were raised through the public comments, and we list some of what those key challenges are, and that information would be turned over to the subcommittees, and they will try to address those specific challenges within the work of the subcommittees, rather than getting into the specifics and the details here. I don't feel like as a group we can do that. I feel like this letter has to be pretty general, and I thought what we were trying to do is take what we've learned from the ACMG report, take what we've learned from the public comments, and move on from that process.

DR. RINALDO: And I really want to second that. What I would like to have a better sense of is a timeline. Are we going to digest this report, the comments, and forever? I really wish that this committee could reach some closure. Nothing that I can think of is perfect. We're not talking about here making

something like a perfect report, the perfect conclusions. But I really think we should reach a point to say this is what the report concluded, these are the recommendations of this committee, and then move on. There are many things that we can talk about and bring on some positive changes or initiatives without continuing to digest. This is approaching rumination. I'd rather move on.

DR. BECKER: Rod, part of me agrees with Piero because it obviously is something — I think the advisory committee will probably move on past the report faster than the internal process will, and by that I mean there are a lot of things, as Peter described — it's not going to be a fast process moving things through all of the agencies within HHS, and we're still sort of in the throes of that as well, because we still have to develop our comments to the comment period that was part of the HHS process.

So on the one hand, I agree with Piero in the sense that there are things that I think we're all eager to move forward with in due diligence and quickly, but I think we are a little bit stuck in the process that we need to adhere to, and so we do have a few routine activities that need our attention, and the public comments are certainly those.

One thing I would like to add to our list of things that were concerns that were cited, since that seems to be sort of what we're generating, is the policy setting process was a concern that was cited by a couple of commenters. So that is something that we need to probably acknowledge or consider acknowledging in our response, the Secretary's committee response to those comments.

DR. HOWELL: It seems to me the committee has spent a tremendous amount of time on the ACMG report, and have reviewed it extensively. The second thing is the public comment period is over. We have all those comments. We've read them, and I would agree that we really should make our comments on the comments. They're here and they're not going to change, and comment about the report and, for heaven's sake, move on to another period. I think that there's a tremendous amount of work to do, and I think there are so many areas that the subcommittees have already identified that we need to do.

But I would certainly hope that we could put this public comment period to bed and a note to the Secretary about the report, and then see what we need to do.

Derek, do you have any further thoughts over there?

MR. ROBERTSON: Not in particular. I think we just need to keep it simple. I think the Secretary would expect us to comment on what people said about the report and what do we think about that. I think the most important discussion will come this afternoon because that was the primary concern, and we'll just move on from there.

DR. HOWELL: I see lots of nodding, and I think then we need to think about — wordsmithing as a committee is a deadly process, and I don't want to get into that. But we need to get the stuff up there that this group wants to see in the letter, and I think that that's the key thing.

Are there key areas? Again, I think it would be a mistake for us to try to point out — there weren't an awful lot of negative comments. They were focused in a few areas. We really ought to probably identify those, not wordsmith them, to be sure they're there, say we heard about this, et cetera, and move on from that point.

Let's go back up to the top of the page, if we could. Let's don't worry about the wordsmithing. We'll just get the big things up there and we'll worry about the details later. Could we go back up to the top of the page?

MR. ROBERTSON: Rod, is this list — are we developing a list of things that were lacking in the report? So if I see literacy, saying that the report didn't address the comments —

DR. HOWELL: No.

MR. ROBERTSON: Because I thought what we wanted to focus on was not necessarily all the good things the report said but some of the comments that critiqued the report. So, for example, the scientific evaluation and process. If people commented that the report lacked some other aspect, that's what we want to see because, like Dr. Edwards said, if the Secretary looks at it and says what was the main complaint, these were the complaints, and the committee agreed with them or the committee doesn't really think it's a valid complaint because of A, B, C; because a lot of those things to me, I was looking and I said, well, we kind of did address that in the report. So I thought that what we wanted to try and focus on and have the committee comment on was those issues that people felt the report was somehow lacking or could have done a better job on, and then we would comment on that.

DR. RINALDO: But I would keep it in the context of really not losing perspective. If this report in any way will make a difference or will be remembered, it will be for those conditions, no matter how you got there, but how this panel has been assembled and recommended. So I really think that every negative one should be assessed, any negative opinions should be assessed really in respect of does it really change anything in terms of what should be included, and if so, then comment on it. In the end, it will be those 29 conditions and the others as secondary targets. Everything else, again, is a frame, but the substance is in that list.

MR. ROBERTSON: And I think in terms of process, what Piero just said is a second step. In other words, we put them up there, whatever the concerns were, and then let's say we agree with Piero's comments, or we don't agree, but the second step is that would be a response to the comments that are up there, that this particular criticism is not valid — or not that it's not valid but we don't put too much weight on it because it deviates from what we think gets to the core of the project, or we may disagree. I'm just saying that that would be step 2. Step 1 is you get it up there, and step 2 is you comment on it. Step 3, you have a recommendation.

DR. HOWELL: Amy?

DR. BROWER: And I would just say that Piero is right that the end result doesn't change by the comments, but the comments certainly inform us of how to do it in the future so that we can listen to what people see it was on the process and include those points in our process going forward. So the end result of this panel of 29 conditions and secondary targets doesn't change based on these comments, but as a committee we've heard those comments and we're going to act on those in our future processes and recommendations.

DR. DOUGHERTY: I think I was about to say the same thing. There's an approach to doing this where you don't get into a fight in your recommendations to the Secretary about who is right and who is wrong but just say we've heard those comments and we have already formed a whatever we're going to do this afternoon in order to address the comments about scientific validity, and the same for the other things. We're already inviting ASTHO to the table so we can get more input on this, rather than get into an argument over who is right and who is wrong. I just don't think that that's a profitable way to go because this committee is moving ahead on a number of these issues.

DR. HOWELL: The bottom line is I think that this is the sense that we need to get. One is that we need to identify, as Steve pointed out — this is a concern that was probably one of the main concerns, the method by which you got there with this system. The typing is not nearly as effective as Michele's notetaking here. But say what you would like to have Michele say about this first thing, the scientific validation process. What would you like to hear?

DR. DOUGHERTY: Well, I think it's been proposed that we don't say anything specifically about how we're moving forward. I mean, we could right now say we're moving forward, we're examining the issues, but then based on this afternoon's discussion try to say how we're moving forward on this in a little more detail.

DR. HOWELL: Right, we've heard these concerns, we've had experts come and discuss decision-making when information is meager, et cetera, and we're going to use that in our process going forward.

DR. LLOYD-PURYEAR: And your recommendations are? Are you moving to a step 3 to make actual recommendations?

DR. RINALDO: Recommendations in general or about the report?

DR. van DYCK: At the end of the discussion this afternoon on the first one, the committee should come to some decision about the way the report was crafted and developed. We feel comfortable, we're a little uncertain, we think it's not useful. I mean, there should be some sense from the committee what the committee's feeling is at this point. If it's very satisfactory, then it's very satisfactory and it's over. If there's areas for improvement, then you have the report, we recommend going ahead with the report and in the future doing this, or we're concerned about this piece of the report and would like further development until we can recommend it, or whatever.

But there has to be some recommendation from the committee that the staff can then craft a paragraph around. I think anything short of that is not useful to the Department, and I think there should be five or six issues. I mean, 15 or 20 is way too many. There should be five or six really outstanding core issues. I mean, we know what most of them are, and those should be highlighted in a sense of the committee to the Secretary. I think that's important for him to hear.

DR. HOWELL: Steve?

DR. EDWARDS: I agree with that. I think that if you will allow us to wait on number 1 until after the discussion this afternoon, that we should do that. But then I would take the rest of these responses — and I agree that 15 is too many. But as I look at the rest of the responses, most of them were not so much criticisms as suggestions of things that need to go into the process, suggestions of things that might have not been fully explained in the report. I would divide them — and I think it's totally open to discussion as to how we list them, but follow-up, for example, was a big issue which wasn't totally addressed in the report. I think we all would agree with that. I think follow-up was an issue that was raised in the critiques that needs to be addressed and is going to be addressed, and we can say that.

The medical home was an issue. System organization, including the dynamics of the system and how tests are looked at, was an issue that was raised. Education. Privacy. State oversight. Financing. I think those, to me, were like the key issues, and almost none of them was raised. I read all the reports, and I didn't see any of them being raised as strong criticisms but as suggestions of things that needed to be incorporated into the recommendations. I think we could take those as such and just list a few of them, and we don't have to list all of those I suggested, but some of those I think are core issues from the critiques that we got, and many we've been planning to move ahead on in many cases already.

DR. HOWELL: Those are fundamentally the list that I read out earlier. They were not criticisms so much as the fact that this is a problem and we need to figure out how to do that. So that, basically, I think is a core charge for the committee and the subcommittees as we move forward.

DR. EDWARDS: But the only thing that I would recommend on that relative to what Peter said is that I think that's too many. I think you listed probably 15 to 20. I think that's too many. I think what we should try to focus on is on the more essential elements of that list and then not comment beyond that.

DR. HOWELL: Actually, there were seven on my list.

DR. EDWARDS: I wrote 15.

DR. HOWELL: But they were basically technology, follow-up, management, evaluation, education, research and privacy, and each of those had little verbiage after them, but those were culled out. The criticism of the document focused almost entirely, not completely, on the process by which the conditions were identified, and many of the comments said that although the process was not transparent and it's not clear how that happened, it seemed like the final product seemed to be fairly sensible. It was an interesting thing that the process was unusual, but it does seem like that at the end of the day I believe that's what — and these were the ones that were very critical in that particular area.

Greg?

DR. HAWKINS: I just wanted to make a quick comment. Some of the comments that I read, it seemed like people when they read the report were expecting it to be this all-encompassing document that was going to solve all the problems at one time and cover every topic comprehensively, and that was not the target, as Piero said. That was not the target of the study. So some of these comments, you just say this is off target, this is off target, this is off target, and make sure that we really hit the fine points. As Piero said, this was a report of a recommendation of tests. It wasn't to go into great detail about education. That's what the subcommittees are for. So to say that up front, we said that earlier, that at the very top we should emphasize that comment.

DR. HOWELL: Bill?

DR. BECKER: I agree with Greg completely, and also to expand on Steve's comments. To a certain extent, the committee has already done that work of identifying the core issues, okay? If you look at the public comments and the list that we've generated here now and think back to a couple of meetings ago when we were deciding what to do with the subcommittees, what were the topics? Follow-up. It's on the list. Education and training, on the list somewhere. Laboratory standards, on the list. And our cross-cutting issues: finance, IT and new technologies.

There was some discussion a little bit earlier, and I tend to agree with that, that those were the areas from which major concerns, or some comments if they weren't actually concerns, came from. I think that is the flavor of the response that Peter would be looking for in the response to the Secretary. So clearly, the first thing we have to address is the evidence base commentary. We have to have a discussion about that. We'll have some more this afternoon. That has to be part of our comments on the received public comments.

Then secondly, communicate to the Secretary that there were these other issues, but we already have identified — we agree with them to a large extent because they're core issues we've already identified, and we have standing subcommittees whose charges are to review these particular areas, as well as in the sense of these other cross-cutting issues as well, and there may be more that we identify as the process continues forward.

DR. HOWELL: I think Bill's comments are very appropriate because the committee has, indeed, already identified these and agree with the comments that actually follow later. I don't think that any of the issues that are on this list we would disagree with, because they're things that need to be done.

Piero?

DR. RINALDO: Indeed, the point is that we are ahead, in a sense, of these public comments, because we have already recognized that there are these specific areas, and that's what the subcommittees are all about, and the cross-cutting issues that affect everything.

What I think really is the point that we should stress is the fact that whenever we deal with each and every one of these issues, and that was also brought up earlier when we start talking about cost/benefit analysis, I really think that people should begin to recognize or realize the enormous benefit of having a level field of conditions. We will always be comparing apples and oranges when we're comparing the effectiveness of a program with five conditions and the effectiveness of another program with 30 or 40.

So I want to say it one more time: the fundamental and perhaps only contribution of the report is the uniform panel, the conditions that you can have and set up in every program so that when we compare testing, the performance, the costs, and all the other components, we are talking about the same thing. As long as we have those maps of the country where such a variety of colors and differences, we are just preventing the collection of objective evidence because we have a variable built into the system that will maintain somewhat of a status quo.

We often hear the difficulty, or sometimes the impossibility, of comparing programs. I think that should be very much high on our list of the things that we should try to facilitate and change. We have to create a level field.

DR. HOWELL: Derek?

MR. ROBERTSON: I think one thing we have to bear in mind is that this is not the report of this committee. I don't want to get the sense as though we have to justify or accommodate what was in the report or not in the report. So I think as we develop the comments to the Secretary, I don't think the approach should be this is missing and here's what we're doing about it, because it's not our report. We're commenting on a report that was done by a separate group, although a number of us were on that group as well.

So I think the approach should be just simply answering the questions. If you think about a decision tree, it's like how does this criticism affect the report? What does the committee think? So it's as if the Secretary read the report, read the public comments, and there is this issue on scientific validation and process. I think the Secretary is basically asking what do you think about that? That's the question the committee has to answer. Yes, we think it's a problem, but we don't think it takes away from the core report. That's why we still recommend it.

The other ones we could say we looked at these comments and we grouped them but we don't comment on them specifically, and then I think it would be more a sense to the Secretary don't we too concerned that these things weren't in the report because this advisory committee is addressing some of these very issues moving forward.

But we can't get away from the core question, which is how do these public comments affect your recommendation about the report, your thoughts on the report. I think that's what we have to focus on.

DR. van DYCK: Yes, and I think that last comment is important, because at the end of the letter from the committee, I think we should have an action step. I mean, the comments on the report and the public comments should result, then, in an action step, a recommendation for an action step from the committee.

DR. HOWELL: I think that I agree with that. I think that it's been discussed adequately. The time has come at the end of this discussion, at the end of the meeting, to have a commentary and send that

forward, and then we will move on to the committee's business with the subcommittees and all the things that are on our agenda.

I think, Derek, to go back to your original thing, we've got these recommendations at the bottom, these comments that people have said we should do this, and we'll comment that the committee is already working on them. But we do need, I think, as a thing to talk about, specific criticisms of the document and what we think of that. I'm not talking about every little detail, but as a general group.

We've talked about the mechanism, the scientific validation, which is the mechanism of decision-making. We're going to talk about that. Is there another generic area that you saw in the public comments that we should identify?

Denise?

DR. DOUGHERTY: It's not a broad area, but I think it would serve us well to signify that we're taking the comments seriously to deal with some of the possible errors in fact that some people pointed out. Like there were some on the CF fact sheet. I don't know whether those comments are correct or not, but I think we need to take them seriously and say whether they're going to be corrected or not.

DR. HOWELL: I would think it would be prudent to say that certain comments were made about potential errors in the report that are being looked at and, if necessary, corrected, because some of the comments were wrong, but they all need to be looked at to be sure they were correct. I think that's a good point, because we would not want any technical errors.

DR. RINALDO: But as in any field where you can identify — no, you're right. Remember, there was a process of validation by recognized experts. So it might happen that the person who validated those things has a difference of opinion with another equally respectable expert in the field. Then again, I wouldn't be dragged into a debate of who is right, who is wrong, and I would focus on answering the question. Should CF be included or not?

DR. HOWELL: Well, I think you're correct. But if people pointed out actual technical errors where there was a misspelling or something, we will obviously correct that. If there's an error in fact, we will also correct that. Piero was very upset that a recently published map has his state wrong. So those things do indeed happen.

What other wisdom do you have, Derek?

MR. ROBERTSON: I don't know if we as a committee can correct the report. I think we can just simply comment, again, that these statements of fact which may not be correct we don't think substantially take away from the report, and then maybe staff in their response to the comments may make a statement that in the hemoglobin disorders this was stated. But it's not our report to correct.

DR. HOWELL: You're correct. Then we cannot correct the report, so we'll comment on that.

Steve?

DR. EDWARDS: I like your list of seven better than your list of 20.

(Laughter.)

DR. EDWARDS: The list of seven that you gave us earlier, I think for most of those you can say that we've heard the criticisms and we agree with them and are addressing them, and I think let it go at that.

DR. HOWELL: We'll use the seven if you'd like, that we've discussed those, and I actually have them written here, and they're longer. The reason it sounded like a lot is that under management I had a lot of stuff, but they are just a single point.

Anything else?

(No response.)

DR. HOWELL: Again, it's great to have all of my bureaucratic expertise here. We obviously can't correct the report, even if it does have a typographical error in it. It will have to remain because it's not our report.

Any other comments about this? I think that at the end of the day we need to come up with a document, but before we finish this we will need to have a specific recommendation to send to the Secretary about this report, and for heaven's sakes, the time has come to do that. Every state will have adopted the report before we get through. I mean, it's changing every day, and I think that it's kind of an interesting place to find ourselves.

Is there any more comment about this?

(No response.)

DR. HOWELL: We will come back to this first thing at the end of the time after we hear the tremendous wisdom that's coming up today about decision-making. As you know, there was a great discussion about having some folks present today, and we've got an expert group that are going to be speaking this afternoon.

Michele or Peter, is there anything else we should do on that list except move on?

DR. van DYCK: During lunch, they'll make a separate list of the seven you have, and then we can —

DR. HOWELL: Then we can look at that again.

DR. van DYCK: Perhaps be a little bit more succinct.

DR. HOWELL: We're ahead of schedule, which is always great, but Brad is here.

Excuse me, Derek.

MR. ROBERTSON: I would just encourage the committee members on the comments and this afternoon, I would particularly want to hear from the folks who were not involved in drafting the report who are on this committee, because to me you can get your most objective evaluations. So I would just encourage the members of the committee who were not involved in drafting the report to really weigh in on that.

DR. HOWELL: They have weighed in.

MR. ROBERTSON: I mean this afternoon.

DR. HOWELL: I'm sure they will continue to weigh in. But I think your point is well made and so forth. They're a considerable group around the table who were not a member of that.

It's always interesting to hear about the state of the states, and we're glad to have Brad back from Texas to tell us what's happening in the states at the current time with the various newborn screening programs and so forth.

Brad?

I think everyone knows that Brad is the director of the National Newborn Screening and Genetics Resource Center. That's a HRSA-funded program, and I'm sure most of you know his website, but it's an invaluable place to go to see what's happening and who has done what with the system.

DR. THERRELL: Well, thank you and good morning. There are two handouts that you should have had on the table this morning. The first one I'd like to call your attention to is the one that looks like this with a list of all the states. That is from our website, and so you can grab that whenever you want it and try to get an updated version. This is the version from a few days ago.

If you'll notice, the first two pages are the core 29 conditions, and the last page is the secondary conditions. On these are indicated through some codes what all the states are doing. A dot means that it's universally mandated in the state. The letter A means it's universally offered through some sort of an optional program but it's not yet required. B means it's offered to select populations or by request from a physician. C means the testing is required but it has not yet been implemented in the state. Then D is special from the Massachusetts group. It's likely to be detected and reported as a byproduct of MRM screening targeted by law or rule. So this, we think, covers pretty much all the options that the states have right now.

So what I'm going to show you for the next little while are some of the maps that you have in your second handout. The first of those maps is sort of using the traditional counting systems that we've been using before. So this one shows you by color coding those states that do more than eight disorders, which is the way we traditionally have counted them, and there are 35 of those states, and then we've got them listed out there with the numbers of how many of them are actually doing those. I think this is not so informative, but I just want to show you what it looks like if you look at the old way we did this. If you look at the way it was a year ago, you subtract off a bunch of things.

This is the way it is now. This is the way it was a year ago. You have these maps, so you can look through them and digest them over lunch. This is a bar graph that shows you the number of mandated conditions across the states, where the red lines indicate mandates and the candy stripe lines indicate optionally available or pilot program. This is by disorder. It doesn't include all of those disorders that come from mass spec, but it uses MCADD as the indicator of those.

Now, this is the way it was a year ago, and this is the way it is now. Again, you see a growth in some of those bars, and we've added out to the far right hearing screening, which is included in the 29.

DR. van DYCK: Brad, say that again, what you said about MCADD and —

DR. THERRELL: There are — I forget now — 12 or 14 MS conditions which are included which we didn't line out here. We just used MCADD as the indicator because most states, when they do MCADD, they're doing the other 12 with it. So there'd be another longer graph with all these indicated if I wanted to do the 29.

DR. van DYCK: So is it a reasonable assumption when we're talking about this that MCADD stands for doing mass spec?

DR. THERRELL: Right, that's correct.

Now, Piero indicated last time that it would be nice if we could look at this in terms of percentage of babies rather than just numbers of states or numbers of programs. So this is actually the graph converted over into percents of babies assuming that 100 percent of the babies in a state are being screened.

So you see the red lines again show you the ones that are mandated screening conditions, and the candy stripes are ones that are optional to 100 percent of the population. So we're assuming that 100 percent of the population had access to it. So if you go across, you see that even for the hemoglobinopathies, where one state doesn't mandate it and doesn't universally offer it, still 99.7 percent of all the babies in the country get that. So the babies in New Hampshire don't account for that much of the total population of the country.

Likewise, is you look over at HIV, the 6.3 percent indicates the babies in New York State. So there's 6.3 percent of our population of babies are coming from New York State, and so on. You can see that for MCADD, 72.7 have mandated screening, and in addition to that another 5.4 have it universally available as an option, which means basically the whole MS panel.

Go ahead.

DR. RINALDO: California is included in this?

DR. THERRELL: In the mandate? Yes.

DR. RINALDO: Okay. So it's with California.

DR. THERRELL: If it's been mandated, whether they're doing it or not, we put it up here. If you actually want to look at all those mass spec conditions, if you go back to this one and look at page 2, that breaks out and you can look across the dots and actually see which ones are doing things in addition to MCADD. But I didn't want to go through all the details, but you'll have it there to look at.

MR. ROBERTSON: Brad?

DR. THERRELL: Yes?

MR. ROBERTSON: So you're saying 41 percent of the babies are not getting hearing testing? Is that right? Or it's optional.

DR. THERRELL: What I'm saying is it's mandated in 46.2 percent of the babies. It's universally optional for another 40.7. So if you go to the top, 86.9 have it basically available, 87. So the other 13 percent of the babies don't seem to have it available based on what we know. They may have it available, but it's difficult to get a handle on those because it's not exactly mandated in all those states.

DR. EDWARDS: What do you mean by optional?

DR. THERRELL: That means that the states that are reporting in are saying it's available to all their babies but it's not mandated.

DR. EDWARDS: Does that mean (inaudible)?

DR. THERRELL: I don't know the answer to that. We're assuming that when it's available to every baby, even though it's not mandated, it's still what we want to accomplish. We want it to be available to everybody, so that's what we scored here. Payment is a different issue, and we don't have the data on payment. Actually, we don't have the data on hearing. Our center is not really charged with

looking at hearing. There's another center that does hearing, and we have extracted information from their center and from some other centers, and from state information to get these numbers for hearing. So I'm not really the expert on hearing.

DR. EDWARDS: But I think there's a point here. It may not really be available to every baby if people have to pay for it and can't afford to pay for it. You see the distinction?

DR. THERRELL: That's correct. For metabolics, I know the answer to that question, and the answer is that the ones in which it's optional, it's also paid for. But for hearing, I don't know the answer to that. It's probably the same for hearing.

MR. ROBERTSON: When you say it's paid for, you mean it's paid for by the parent?

DR. THERRELL: No, it's paid for by the system. That means if the parent can't pay, it's taken care of another way. Payment is not an obstacle.

DR. BECKER: Steve, I can tell you — and again, this is only addressing the metabolic screening programs that offer either voluntary or supplemental testing or have pilot projects in place, where a person could opt in or opt out, whether they're using consent or dissent. First of all, the issue of fee or payment, at least on the metabolic side, is not an issue. It's no more blood. It doesn't cost them any more if it's part of a voluntary program or opt in or opt out.

Secondly, there's a high percentage of participation or consent or opt in or whatever, a high degree of participation for those programs in the states. Our program had a voluntary expanded MS/MS panel. It didn't cost the parent a dime, no more blood was taken. We had 96-plus percent participation by the parents, and Massachusetts State is even a higher percentage than that.

So if it's optional, and assuming it doesn't cost more, I think it's safe to assume that a high percentage of babies born in those optional states or states where hearing screening is optional, I think a high percentage of those births are probably being screened.

DR. THERRELL: Essentially, the ones that we've called A, that means it's universally offered to everybody. The ones we've called B are the ones where it's offered if you can pay or it's offered if your physician wants it or that sort of thing.

I guess I'd point out here that if you look at the core panel, all of those on the core panel are well into the 70 percent, close to 70. I guess biotinidase is 66 or 67, except for cystic fibrosis. Cystic fibrosis is still on the rise. It's now 33 percent or so. But all the rest of them are well into the 60s and 70s and 80s, regardless of how long it takes the committee to deliberate.

So let me just run quickly through this. We sent out a message to the states by several different mechanisms and asked them to let us know if there was something they wanted you to see in terms of what they've been doing over the past six months. So those next few charts are from those states, and I'm just going to run through those fairly quickly. If a state is not included, it's because they chose not to send us the information.

So California actually began screening for all of the MS/MS conditions and CAH on July the 11th. They still are not screening for biotinidase, CF, and they don't have a mandate for hearing screening. I talked to Dr. Cunningham the other day and he basically said he's going to refloat this to the legislature, but without outside support and help from parent groups and advocacy organizations, it's an uphill battle with the legislature.

Colorado has mandated the full screen of MS/MS disorders. They're currently working on implementation and expect to have it implemented in the spring of 2006.

Connecticut in January added 13 additional MS/MS conditions, which raised it to the full panel, and they're doing CF, it's just not mandated. They are doing hearing screening. In February they changed over to a total galactose kit. There were some problems that states have pointed out over the past year with manufacturers of some of the kits, and so galactose was one of those kits that was taken off the market, total galactose, which had some impact into the secondary conditions listed in the panel. So they made a point that they have been able to switch over to another kit.

Georgia, on January 3rd, they added MCADD and PKU, homocystinuria, MSUD, tyrosine, and they changed over to MS/MS. On June 27th, they actually changed their rules that said it was invalid if you did a test before 48 hours to now say it's invalid if it's before 24 hours. Currently they don't have a fee in Georgia, but they're working on one. So there are five states still without a fee. That will make four.

Iowa began CF July the 18th, so they now become actually the second state to mandate all 29 conditions, and I'll show you that in a few minutes. The lab has courier service and they're operating 24/7, which most labs in this country don't do for newborn screening. They've had a lot of personnel turnover, especially in the follow-up area, and that's being remedied with some new people. They have comprehensive use of their fees. So they use their fees for a lot of different things in support of services.

Kentucky mandated the addition of CAH, biotinidase, CF and the full scan MS/MS in March, and they are adding CH in August, MCADD in December. So they're sort of going through it stepwise, CF and biotinidase to follow. They have not yet mandated those two.

Michigan universally is piloting 11 additional MS/MS conditions. So they've expanded their panel up to 29, but it's just a pilot right now. They're working towards a fee increase to pay for the comprehensive program and services, and for CF.

Minnesota mandated CF, with an anticipated start by spring of 2006, and they're moving to a new laboratory facility in October of this year.

Missouri added 20 disorders after a five-month pilot. They've increased their fee from $25 to $30 — I'm sorry, from $25 to $50, and their biotinidase pilot is to begin late this year, and a CF pilot next year.

Nebraska has gotten into some lawsuits, and so let me just take a minute to talk about those. Nebraska has a law which says you must be screened and there's no option for dissent. They're one of three or four states that has that kind of a law. That's been challenged before in the courts, and the state continues to win those suits. The latest one was a challenge that was appealed to the Supreme Court, and the Supreme Court ruled recently that the state has the right not to offer dissent. So that one has ended again.

In the federal court, a suit was filed over "silent birth" by a Scientology group or by parents who were Scientologists. Their complaint was that in the law, it allows for babies in the intensive care unit to be screened at seven days, in opposition to the other babies that have to be screened in 24 hours, in the first 24 hours or before they leave the hospital. So this group said that discriminated, and they felt like their baby, because of their principles about silent birth and needing to recover from the birthing process and needing to have a silent week there, their babies should also not be screened until seven days or later. They filed that suit in federal court, but they've now dropped it. So we don't know what's going on there.

They've added another follow-up person. They're anticipating adding CF and CAH in 2006. They're doing expanded MS/MS as an option, and 95 percent of the people are accepting that option. It's a free option.

New Hampshire — and you'll see in a minute, New Hampshire now is the state with the least number of mandated disorders. Their advisory committee has actually recommended expanding the panel. But the way the law is written in New Hampshire, it has to go to the legislature and the governor has to sign off on this, and the legislature kicked it back. Now a new law went through, and that law actually gives the commissioner a little more power in terms of setting fees, and gives the advisory committee a little more power in terms of expanding the program. They're hoping that that will be signed, and then the advisory committee will move forward and expand the program by next year.

New Jersey currently does not mandate 13 conditions that are available but screens for them anyway as part of the differential diagnosis, as Piero indicated earlier. They also have a new law which requires that the state inform the parents about testing that they don't mandate in New Jersey and where it's available. They also have changed their rules to say that a sample is valid after 24 hours instead of 48 hours, like it used to be.

North Dakota is adding CF early in the fall. They're increasing their fee from $36 to $44, and they continue to send their samples to Iowa. So generally when Iowa changes something, North Dakota follows right behind.

Oklahoma added CAH and CF earlier this year.

Rhode Island is expanding — they're trying to expand to the 29 core conditions. They're anticipating expansion by next year. They currently are only doing MCADD and the amino acids, and they're finishing preparation of their rule changes for the fee increase and monitoring for babies over six days of age without a screen. So they actually have an active program that goes through and looks at all those babies by day 6 to see who has been screened and who hasn't been, and then they track those babies and try to get them back in. It's a little bit easier to do that in Rhode Island because of the size than it is in most states.

South Dakota. They have expanded their rules to include a lot of different disorders. Previously, South Dakota only mandated three disorders. So now they've moved into the bigger offering. They're doing a full scan MS/MS. Interestingly, they're sending their MS samples to Texas still and their CF samples to Massachusetts, and then they have a private laboratory that provides the rest of the testing in-state. They've updated their practitioner manual and distributed that.

Texas has had sort of an uphill battle over the year with the legislature. The legislature finally has agreed to allow start-up funds for expansion, and they can expand to whatever they can do within the funds available. That means within the fee structure. Their fee structure right now is at $19.50 a sample, and they have authority already to raise that to $36. But before they can do this, they've got to respond to a written review that our censure did of the program, and that review has to be accepted by the commissioner and the Texas Medical Association, basically. They have to respond by October 2005. They have to perform an in-depth cost analysis by early 2006. If all of that works out, then they can expand the program, and expansion is anticipated by October of 2006. So they still have a ways to go.

Utah has begun a pilot with expanded MS/MS using the local private laboratory, ARUP, and they have a fee of $31, but they have permission right now to go to $35, and they're going to raise that permission to go to $65. They are anticipating all of these additions by 2006, except for CF. So they'll be doing the full 29 and the secondary targets, but not CF.

Virginia's Board of Health mandated screening to include the full ACMG panel. Anticipated start is March 2006. They're currently not doing CF or expanded MS/MS, only MCADD and the basic amino acids.

Washington State just had a meeting last week of their CF advisory committee, and that advisory committee has now agreed that CF meets the criteria in Washington and will recommend that to the board of health, and they expect to expand to CF next year.

So that's the states. Let me just show you a map again. If you take what's available in a state, not necessarily what's mandated but what's universally available, either by mandate or universal option, then these are the states that mandate less than 10 disorders currently. You see that the lowest number is six disorders, and that's New Hampshire right now. But there are several that are close.

Then this is the group from 10 to 19 disorders. Again, this is using the counting that ACMG had. So we're looking at the 29 conditions. You see that it's sort of down through the mountain states and the south where the lower numbers are.

If you look at 23 to 25, there's two more states. Four more states do 26. Five more do 27. Thirteen more do 28. Then there are nine states that do 29 disorders. But again, only two of those actually mandate all 29.

You have all these maps available to you.

Yes, sir?

DR. EDWARDS: Is this in response to the ACMG report or the March of Dimes recommendations or some other recommendations out there, or is this something that just happened spontaneously even before the ACMG report was released?

DR. THERRELL: It was happening to some extent before the ACMG report, but the ACMG report and the March of Dimes report card have certainly driven this. I mean, there are a number of advisory committees that just refer to this as the ACMG panel, we're going to mandate the ACMG panel, we're going to do the 29 disorders and so forth.

DR. EDWARDS: Well, that's pretty fantastic, because this report was just made public in March. So to have that sort of response —

DR. THERRELL: They were waiting for it. They've been waiting for it for a year or so.

I think that's it.

DR. HOWELL: Questions from the panel for Brad?

DR. BROWER: I just have a quick question on the hearing screening, that it's in a different database. Because it's one of the first physiological tests, and there may be more added in the future, do you recommend that those all be brought into one central database? I'm just concerned about two different databases, because this is such a great wealth of data. I want to make sure as we recommend new conditions or a system, that we have one database that stores all the information. Just was wondering what you thought.

DR. THERRELL: That certainly makes sense to me, and I've advocated for that. The problem is that the programs inside the health department are often set up in two different areas, two different silos if you will, because the funding streams initially came down in two different silos. Actually, the CDC

maintains the data for hearing screening, or maintains a lot of the data for hearing screening, and when that was being developed I suggested that we might put those together. But that didn't get to the right people, apparently, and that was not the case.

So the states report their hearing data to CDC, and they report their metabolic data to us, and there are between 15 and 20 states that actually collect their hearing data on the newborn screening metabolic form, if you will.

DR. HOWELL: Your point is, I think, extremely interesting, because we've talked about the newborn screening in the early period here, but there are other technologies that are going to be of interest in congenital heart disease or in Wilson's disease or something, where the time frame is not in the usual 24 to 48 hours. So thinking about those prospectively I think is a very interesting thing.

Piero?

DR. RINALDO: I'm glad you incorporated the graph that also shows the percent of births.

I'm wondering to also address a question raised by Dr. Edwards. It would be interesting to see a map in 2002, because I think that somewhat was the time that the ACMG/HRSA panel began to be developed. It's clearly a combination of spontaneous combustion, but I really think you can see quite a dramatic difference, especially when you can compare over what happened in the prior three years, from 1999 to 2002. I believe there will probably be fairly modest activity, and then to see what has happened from 2002 to 2005. I think you can make a pretty objective case that there has been an acceleration.

DR. THERRELL: Right. I have some of those maps, and maybe the next time I come I'll try to do that real quick.

DR. HOWELL: Some of the press releases that I have personally seen about states adding things have specifically said that they're adding the ACMG panel in the press release, which I thought was kind of interesting.

Any further comments? We always appreciate Brad coming in and bringing us up to date with his maps that change every day, et cetera.

MR. ROBERTSON: Brad, I guess I was just wondering about D.C. It seems as though they had a few, the District of Columbia.

DR. THERRELL: D.C. is 10.

MR. ROBERTSON: What's happening on the MS panel? Because just looking at your dots —

DR. THERRELL: In D.C., they have a contract with a private laboratory which offers expanded testing through the hospitals. So it's sort of at the option of the parents. I don't know if there are some people here who could answer that. D.C. does not have a fee for newborn screening. They pay for it out of the government funds, and I think payment has been an issue over the year.

DR. HOWELL: Further comments?

(No response.)

DR. HOWELL: I've had a recent personal experience. I don't want to bring up personal experiences, but I recently had a granddaughter born in a nearby state that has a very modest screening program, and you have to really be on the ball. She was born in Virginia. You have to appear at the

birthing center, the hospital, with your card that you have bought beforehand and send it in the mail. Although that worked very great for her, that's clearly not a system that we want to have around the country. I mean, that's the absolute opposite end of the kind of access you need. You need access for everybody, and you obviously need to be sure that everybody knows about it and that they don't have to pay for it, et cetera.

Personally it worked very nicely, but that clearly is not the way we want it to go. Virginia, it appears, is moving into the modern era.

DR. THERRELL: Let me say also that it's not just parents who need education here. It's physicians as well, because I've heard many different examples of physicians within a state not knowing that their state actually did more than PKU or more than a couple of tests. So that's been an issue.

DR. HOWELL: The Education Committee has a lot of work to do, and it's not just with the public. Actually, the public is probably better informed, as a matter of fact.

Are there further comments from the committee for Brad?

(No response.)

DR. HOWELL: We've ended right on the moment. Congratulations. It's lunchtime, and we'll be back at 1 o'clock to have a series of wonderful talks about evidence.

(Whereupon, at 12:00 noon, the meeting was recessed for lunch, to reconvene at 1:00 p.m.)

AFTERNOON SESSION (1:06 p.m.)

DR. HOWELL: An area of central interest to this committee, and actually the public at large, is how one makes decisions when using evidence and other factors in decision-making, and particularly the issue that has to do with newborn screening has been to make decisions when the amount of information is limited because of the rarity of the condition and so forth.

We're pleased this afternoon that we have three outstanding speakers who will address various aspects of this. Our first speaker, whose presentation is "Evidence, Politics, and Technological Change," Dr. Sampat, is from the International Center for Health Outcomes and Innovation Research at Columbia University in New York.

Dr. Sampat, welcome.

DR. SAMPAT: Can you hear me okay?

DR. HOWELL: Yes.

DR. SAMPAT: Probably better than you want to.

Thank you and good afternoon. On behalf of my colleagues at Columbia, primarily Annetine Gelijns and Alan Moskowitz, who are the primary authors on the paper on which this talk is going to be based, I'm going to discuss the interplay between evidence and politics in managing technological change. I should note that our background is not in genetic screening — in fact, most of what I know about that is what I learned this morning — but rather in thinking about technical change in medicine more generally. However, we think that the issues I'm going to raise today are critical to the development of many medical technologies, including new genetic screening technologies, but would very much welcome your feedback on that front.

So I'll just begin by noting that it's a fascinating time to explore the interface between evidence and politics for three interrelated reasons. First, policymakers feel an increasing imperative to manage the health and economic impacts of technological change, and many find this task both conceptually frustrating and elusive.

Second, decisions on how to handle the explosive field of medical innovation translate quite directly into regulatory and reimbursement decisions; that is, the very important decisions about who gets what medical care and on what terms.

Finally, as a result, these sometimes arcane analytical issues often make their way quite quickly and directly onto the radar screens of public opinion. So, in other words, managing innovation is a formidable task, and many new technologies, of course, we know are beneficial and desirable in the eyes of patients, providers, and policymakers alike, but it's important to remember that the fruits of medical progress do not appear in final form on the physician's or the policymaker's doorstep. Adoption decisions are inevitably made in the case of considerable uncertainty about indications, populations, risks, effectiveness, and those sorts of things, and new technologies also raise important economic questions.

Since they are costly, they trigger debate about what economists like myself call the opportunity costs of the marginal dollar spent on health care; in English, whether a particular technology is the best way to spend our scarce health dollars. The resulting dilemmas have to be managed politically, and policymakers often turn to scientific evidence to inform and legitimate these decisions.

So for these and other reasons, in recent years industrialized nations have increased their investment in the clinical value of research. One manifestation of these trends has been the creation of various analytical infrastructures to interpret evidence for setting policy. For example, in this country we have the advisory panels for Medicare and Medicaid. However, one thing that's often overlooked is that scientific evidence alone rarely has the final word in these decisions, and let me just show you some pictures.

Basically, one thing we're learning is that interpretation and application of analytic findings varies considerably among agencies, and more so across nations, and this is in part reflected in variations in the use of technologies themselves. So consider CABG or coronary artery bypass surgery. Many of you are familiar with this. This is among the most widely studied surgical procedures out there, lots of evidence on it. Yet, as this slide shows, utilization rates vary two-fold among advanced industrialized nations, from 41 per 100,000 people in France to over 100 per 100,000 people in the United States.

A similar picture emerges for pediatric procedures. So here is a chart showing utilization rates for in-patient tonsillectomies, again stunningly different rates across advanced industrialized countries. So in each of these cases what we have is the same evidence with different adoption decisions. I've just sort of shown you some averages here, but more sophisticated work shows that these variations aren't explained by differences in disease prevalence alone. Rather, other factors such as professional uncertainty, economics, and sociocultural value judgments also play a role.

So this is sort of our starting point. Empirical analyses do not provide off-the-shelf policy decisions, or at least rarely do. So what, then, are the challenges in transforming evidence into policy? We're going to explore three underexamined challenges in this respect.

The first challenge arises from the dynamics of technological change itself; second, those inherent in the analytical enterprise; and third, inherently political factors, especially those dealing with the preferences of stakeholders that helps shape the translation of evidence into policy decisions.

So we'll begin by talking about the challenges inherent in the dynamics of technological change. One thing that makes evidence-based policy difficult is that many areas of medicine are characterized by extremely high rates of innovation. So in 2002, for example, the FDA approved some 90 new drugs and

biologicals, 172 new indications for use, and over 4,000 new or improved devices. This is in addition to many advances in clinical procedures which were not related to new products and therefore not reflected in the activities of the FDA. Perhaps nowhere in the biomedical research arena is innovation more rapid than in genetics and genomics, though good indicators of this are hard to come by. Again, let me just show you two pictures.

This chart shows the number of genetic screening articles indexed in PubMed by year of publication. Note that there's been quite a dramatic increase over the past decade and a half or so. Similarly, if we look at genomic patents issued by the United States Patent and Trademark Office, you see very similar trends.

So a related factor inherent to technological change which makes managing innovation difficult is that even after introduction of new technologies into practice, the medical profession shapes and expands their application. So there are several ways in which this happens, but one is via expansion of the target population within a given disease category.

So again, if we return to CABG or coronary bypass surgery, only 4 percent of patients who were treated with such surgery today would have met the eligibility criteria of the trials that determined its initial value. In particular, these trials excluded the elderly, women, patients with a range of comorbidities, all of whom do receive CABG today.

Another example is screening for prostate cancer using PSA. While its role in managing patients with established prostate cancer is quite clear, its role as a general population screening tests remains controversial, but its use has been expanding quite rapidly.

Comparable expansion patterns can be found in minimally invasive surgery, laparoscopic techniques for gall bladder removal, for example, and reduced the per-patient cost for surgery by about 25 percent. Yet, to the surprise of many, total expenditures for gall bladder surgery rose by 18 percent after introduction of the innovative techniques. Why? Well, again here, there was expansion of the market. The number of gall bladder removals increased by 60 percent. So here again we had expansion of use. While the much less invasive procedure enabled physicians to remove the gall bladders of sicker patients, less sick patients also opted for the surgery after the innovation was introduced.

Similarly — I won't provide too many more examples of this — the introduction of laparoscopic techniques for bariatric surgery were an important contributing factor to expanded use of that surgery for the treatment of morbid obesity. An analysis of New York State discharge data suggests that there's been nearly a 700 percent increase in the use of this technique over the past five years.

So what does this all mean? In economists' terms, the fact that the target populations often expand after introduction of a new innovation or technique suggests a greater demand for medical services than often is anticipated. As a result, even cost-saving technologies can lead to more aggregate expenditures if they expand the size of the relevant market.

In addition to expansion of the target population within a particular disease category, we also often see the discovery of totally new and often unexpected indications of use. So the history of pharmaceutical innovation is replete with such discoveries, as this slide depicts. One case in point are alpha blockers, which were first introduced for hypertension and only 20 years later found to be an important agent in the treatment of benign prostate hyperplasia. Another example which some of you may be more familiar with, TMS, here too we have an example of an innovation which was developed for one thing and turned out to have a range of unexpected uses, developed in the 1940s as a tool to analyze compounds, initially used primarily, as I understand it, by organic chemists to electronically weigh molecules, but of course by the late 1990s it's been widely used in neonatal genetic screening to screen for metabolic disorders.

So the discovery of new and often unexpected indications of use is an important public health and economic phenomenon, and pharmaceuticals, when we do have some data, new and unexpected uses accounted for 40 percent of revenues. We don't have as good data for medical devices, but we believe that a similar pattern holds there.

One interesting fact to note is that widespread use is often itself a precondition for identification of new uses, and thus clinical practice itself a central source of medical innovation. One implication of this is that there are difficulties in making choices about technologies early in their lives, since we may not know all of their uses at the point.

So to conclude this part of the discussion, high rates of innovation and new, often unexpected applications and uses make evidence-based medicine difficult. Policymakers often watch evidence-based answers change before their eyes into fresh new questions.

So this leads us to our second theme, the range of challenges in the analytic realm. We think it's clear that the dynamics of technological change I just discussed argue for ongoing assessment throughout the life cycle of technologies. These assessments can utilize a spectrum of research designs ranging from randomized trials to case studies. Over time, premarketing studies have become more heavily reliant on randomized or other well controlled studies for both drugs and therapeutic devices, but for diagnostic technologies to detect rare genetic disorders, the low frequency of disease is a major constraining factor for conducting large-scale prospective premarketing studies.

For the therapeutic technologies to treat genetic diseases, sponsors and patients and physicians want to establish the benefits of new technologies and introduce them rapidly following regulatory approval, and as a result randomized trials are often conducted in specialized centers with well defined populations to facilitate efficient hypothesis testing. But even for the most rigorously conducted randomized trials, the gold standard for evaluation, a range of challenges remain.

Such trials in general have limited time frames and seldom mention long-term effectiveness or safety, often are underpowered for secondary outcomes like adverse events or costs. Because they limit patient heterogeneity and are often conducted in centers of excellence, they also raise questions about generalizability. Also, in the case of diagnostic tests, when they're introduced into clinical practice, the test characteristics — for example, sensitivity and specificity — may evolve. Of course, these studies are costly. As a result of all of these factors, regulatory and coverage decisions on rare diseases are therefore typically made in contexts of real uncertainty.

So what can we do about this? Most importantly, diminishing these uncertainties argues for postmarketing studies. However, overall funding for evaluative research is quite limited, especially for postmarketing studies in clinical procedure trials. Again, it's difficult to get good data on this, but we estimate that private and public funding for these trials is less than 1 percent of the overall health care budget. If these inadequacies in funding persist, considerable uncertainty will remain about the value of many evolving technologies in this arena, which will constrain policy in clinical decisions.

So far we've discussed difficulties in getting good evidence because of either the nature of technical change or the nature of the analytical enterprise. But even when we can get good quantitative evidence from a scientific perspective, there are often challenges incorporating growing body of evidence into existing policy mechanisms. Most industrialized nations use supply-side mechanisms — for example, public planning and regulatory tools — to distribute or limit the supply of medical technologies. On the demand side, some countries, like the United Kingdom, use global or regional budgets, whereas countries like the United States and Germany employ instead coverage and reimbursement decisions made by insurers to control the uses of technology.

But ultimately, both mechanisms need to integrate qualitative considerations, including considerations of the preferences and values of stakeholders with the body of quantitative evidence that's out there at a given point in time.

So consider, for example, regulatory decisions. As mentioned, premarketing decisions rely increasingly on quantitative data provided by randomized trials to determine a technology's efficacy and safety. However, the ultimate determination of the acceptability of tradeoffs and risks and benefits depends on value judgments. A case in point is Flosequinan. This heart failure drug was approved because it improved functional status and quality of life. Subsequently, it was found to reduce survival, and the drug was withdrawn. Yet, when the issue was presented to heart failure patients who have a very debilitating disease, 40 percent responded that they would accept a slightly higher risk of death to achieve a better quality of life. This suggests that value judgments are pivotal in decision-making and that the outcome of the process of drug approval, or disapproval in this case, depended heavily on which stakeholder groups were represented on the decision-making panels.

Similar issues arise in budgetary and reimbursement decisions where payers and advisory bodies, such as the advisory committees for Medicare and Medicaid, struggle with making tradeoffs between costs and benefits. These decisions increasingly are grounded in what's known as cost-effectiveness analysis, roughly speaking a technique for comparing the relative value of various clinical strategies typically in terms of qualities or the cost of an intervention per quality-adjusted life year saved.

Cost-effectiveness evidence can encourage the purchase of good value for money. But there's great variation in how such evidence is operationalized and debate about whether cost-effectiveness ratios should be used, for example, as strict thresholds in decision-makings or just an input to the decision-making process.

Let me just skip over this slide.

There are a range of other issues with cost-effectiveness analysis as well, including that it's difficult to take into account whether a technology is static or evolving in cost-effectiveness analysis, getting back to the first theme that I touched on. Cost-effectiveness analyses may also be insensitive to such important qualitative considerations, such as equity and distributive justice. So as an example of this, the use of QALYs, quality-adjusted life years, as a measure of effectiveness may encourage political divisiveness by juxtaposing the interests of the young versus those of the old, with the latter having inherently less capacity in terms of life expectancy to benefit from interventions.

So in response to these types of concerns, the Dutch have developed what they call a social utility function to ensure equity in allocation of funding to the elderly, who on the basis of cost-effectiveness ratios alone might be deprived of needed services. But the general point here is that even if we have enough evidence to do cost-effectiveness analyses, ultimately policymaking must wrestle with conflicts of values and interests, which raises important questions such as how to integrate stakeholders into priority-setting. So once again, scientific evidence is not a panacea.

So in conclusion, the challenges that industrialized nations face right now arise from remarkable medical progress over the past 50 years or so. Throughout that time period, technological change has brought new forms of medical care that have extended human life, reduced pain, risk and disability, and often, though not always, proved to be very costly. As health services research has grown, the hope that rigorous evidence may inform policy and depoliticize difficult decisions has also grown.

However, it's clear that while better empirical evidence about the costs and consequences of medical technologies can make policy decisions sharper and better grounded, translating analysis into policy is itself a highly difficult process. These difficulties manifest themselves in a range of ways, including in the evolving applications of technologies, questions about the interpretation and extrapolation of evidence, and a wide variety of value judgments. We believe that these uncertainties and questions

about the evidence base argue for a continued evaluation of technologies both in the pre- and postmarketing settings, and also that the existence of a variety of value judgments also raises the question of institutional innovation, in particular the question of how we, as policymakers, as a society, should integrate myriad stakeholders into priority-setting.

While new medical technologies get a lot of attention, the design of new institutional innovations receive much less attention. However, many nations now experiment with a range of institutional innovations that do, in fact, try to blend evidence with politics, and we believe these deserve careful scrutiny and cross-national case studies. Deeper digging into these institutional innovations, how analysis gets used in these cross-national efforts, is needed as a foundation for sharper thinking about how quantitative and qualitative information should best be integrated into managing technological change.

I think that's it.

DR. HOWELL: Thank you very much, Dr. Sampat.

Are there questions or comments for Dr. Sampat at this point?

(No response.)

DR. HOWELL: No comments at all?

I think one of the many interesting points that you made is that in the discussions of screening for the rare diseases that have been on the table for a long time, one of the issues that has surfaced is, number one, they are rare by definition, but once they are defined and once a treatment is available, all persons who appear with that are immediately treated. So the need for developing a system for following all these children as a "postmarketing" type survey is going to be a very critical issue, because you're going to be learning more about the conditions long-term than you might have known at the beginning. So that's a very interesting thought.

Any further comments?

(No response.)

DR. HOWELL: Thank you very much.

We'll move on, then.

(Applause.)

DR. HOWELL: I'll ask Dr. Atkins to join us here. Dr. Atkins will be speaking about making policy when evidence is meager and in dispute. Dr. Atkins is from the Agency for Healthcare Research and Quality. He's the chief medical officer for the Center for Outcomes and Evidence.

Dr. Atkins, welcome.

DR. ATKINS: I'm going to use this since I realize it's after lunch and I need to stand up to get my blood flowing, and I figure if you can see me, you might think twice before you decide to close your eyes and listen to me with your eyes closed.

I'm here to talk about one of the challenges about decision-making in the face of less than ideal evidence. If you had perfect evidence, you wouldn't all be here, or your meeting would be a lot shorter. So I'm just going to give a perspective from someone who has grappled with these issues. My background is I'm an internist, a clinical epidemiologist and have spent about 10 years working with the U.S. Preventive Services Task Force, which wrestled with a lot of difficult screening questions and often got right in the middle of some heated political controversies.

What I've taken away from that, and this picks up a lot on Dr. Sampat's point, is that often it's debates that sound like they're about evidence but they're really debates about values, about political issues, about resources. What I'm going to propose is that taking a systematic approach can help you separate those issues and separate the things about evidence where there often is a greater consensus than the debate would imply from those issues about values and resources, where people will have different opinions depending on where they sit in the decision-making process. Hopefully that will if not lead to greater consensus, at least you can understand why you're disagreeing, rather than having, as we've had, debates about mammography doesn't work in women under 50, yes it does, no it doesn't, yes it does.

So I'm going to walk you through some examples of just what do we mean by a systematic evidence-based process. I'm not going to belabor that, but I'll illustrate it with some concrete examples. I'll use an example which people are probably less passionate about in this room, prostate cancer screening, or at least half of you are less passionate about.

(Laughter.)

DR. ATKINS: Then I'll take an example that's probably more familiar to you and you'll probably have a hard time separating from completely, which is newborn hearing screening, but it's at least distinct from what you're wrestling with.

I have no vested interest in the outcome of this group, but I hope I can help you think about some of the issues that contribute to some of these controversies.

So again, these are observations that are in the article that's in your briefing book, and I think it's a given that policymakers never have the evidence they'd like to have when they have to make a decision, and they don't have the luxury of saying come back in five years when the randomized trial is done.

It's very confusing not just to the public but to clinicians to have what look like esteemed scientists sitting there testifying, whether it's before Congress or at a panel, arguing about what the scientific evidence shows. But as I said, often if you tease apart those arguments, you can find that there's a general agreement about some basic facts about the evidence, and what they disagree upon is where do you go from that evidence to making decisions, and that thinking about that can help at least clarify what the actual fundamental issues are.

Now, these are the requirements for an effective screening test which are in the background paper that you've already seen, so I won't belabor them, because in general most of these are met by the issues you're debating. Obviously, you're here because these conditions have important health consequences, we now have technologies that can detect them, we have technologies that in general you think have adequate test performance, like sensitivity and specificity. There is maybe some debate about how effective the treatments are for all the conditions you're considering, but presumably the things that you're considering have some treatment.

But the real debate is how much benefit would there be, and are there any downside consequences of a screening policy, and how would you weigh those benefits and the downstream consequences to say is this worth doing on a universal basis.

Now, often, having worked in evidence-based policy for 10 years, there are criticisms about, well, evidence-based policy, that sounds nice but it's just not practical. I will show that these are misperceptions. One is that it's only good if you have randomized trials. What I hope you'll take away from this is that taking a systematic approach is just as useful, or maybe even more useful, when you have evidence that's more variable and not as high quality, because when you have good randomized trials like in cardiology, it's pretty simple to get people together and say the trials of statins are all pretty consistent and they prevent heart disease, reduce heart attacks and improve mortality in certain populations.

But often it's perceived as oh, well, you just want an approach that's setting a standard of evidence that's not attainable. So I want to disabuse you of that concern, that it can still be useful in dealing with whatever evidence you have. On the Preventive Services Task Force, which sets an admittedly high bar for evidence, we did make recommendations that were based on other types of evidence. You just have to scrutinize that evidence a little more closely.

Obviously, one of the concerns is the reason insurance companies love it is because it's a way to set the bar higher and pay for fewer things. Now, I'm not here to defend insurance companies, but obviously the point is that's a separate issue, how people apply it. It's still a useful issue to say how sure are we about what we know and what we don't know, and what should we do given our state of current ignorance.

Obviously, there are other issues that go into decision-making other than evidence, and I think that point has already been made in terms of realities of practice. There are issues of liability, reimbursement, patient expectations. So this is not an attempt to incorporate all those. Those are separate issues. It's an attempt to walk you through at least what the evidence says.

Then lastly, it's not useful when the evidence is poor. Actually, I'll say it's especially useful when the evidence is poor because it gets you through saying, okay, what do we really know?

This is a diagram that Muir Gray, who is the head of the U.K. screening program and also a very prominent health policy person, uses that I find a useful sort of schematic. What it points out is that evidence is just one piece of the decision-making, and I think this is exactly the point that Dr. Sampat was making. It's one piece of it, and then you have to think about the values and you have to think about questions of resources, and you're working in that intersection of them all and trying to come up with the right decision. What I'm going to walk you through is a process to get as clear about what's in that circle of evidence. Then you have to think about what we know about those other issues.

So what are the things you need to do in terms of setting policy? Well, this is just a proposed set of six questions to walk through. The first thing is what's the outcome I really care about? How good is the evidence about that outcome? The third step, which I think is often underemphasized in this process, is how well is it going to work in the real world? So we have evidence about how it's going to work in one setting. What's going to happen when I make a recommendation and this is implemented in 50 states? How is it really going to play out in the real world? Because I think it's a rule that it's not going to play out exactly as you would hope it would play out, and you have to think about what's going to be different.

How do these benefits in the real world relate to the potential costs, adverse effects, other effects? Then what I think the critical one is is what's good enough evidence? If you have any one take-home point, really when people are debating about policy issues when the evidence is poor, they're really just saying they have different thresholds for that term "good enough." For some people, depending on the things that are most important to them, they're going to set that threshold a little bit lower because they don't want to wait for better evidence and they'd rather take the chance of acting a little too soon. Other people are going to set that threshold higher and say I really don't want to act until I'm sure what's going to happen, and if that means I wait five years more for better evidence, or two years more or

whatever, that's a price I'm willing to pay because I'm more concerned about jumping too soon. So understanding that dynamic I think can help sort through some of these issues.

Then lastly, there are other considerations. It's not just about evidence. There are other considerations that may not be captured in the evidence. Dr. Sampat talked about some of those.

So this is just a graphic example of how one thinks about it in terms of prostate cancer screening. As many of you may know, although prostate cancer screening has been widely adopted, there's still debate about really how effective it is. So if one says what are we really trying to accomplish with prostate cancer screening, what this schematic points out is what we're really trying to do is not just detect prostate cancer, although people may think that's a good in itself. We're really trying to reduce deaths from prostate cancer or the morbidity from advanced prostate cancer.

What the top arrow represents is that would be the ideal evidence, if we had a trial, and such trials are under way but not yet completed, a trial that actually studied the link between screening and prostate cancer mortality, a randomized controlled trial. Now, that's something that we rarely have with adult screening tests, and you never have with newborn screening tests.

So in the absence of that, one can try to say, all right, what do we know about how screening would work, and what's the evidence we have to piece together what we know in the absence of that perfect evidence? Well, we screen because we think we can detect prostate cancer earlier, and we assume that if we detect it earlier, our treatments of early prostate cancer will be more effective than treating it when it presents clinically. So that's arrows 2 and 3.

But what it also illustrates is that along the way, there are other outcomes other than the thing we care most about that we have to consider. So there are the outcomes of the screening test itself. Those are false-positive tests, the consequences of false-positive tests, meaning subsequent biopsies or work-up. Then there are consequences of the treatment itself. That's especially important if you think that maybe you're going to be treating some people who you never would have treated otherwise. I think this is probably an important part of the debate in newborn screening, the issue that you're going to find cases that may not have needed to be treated, and you're going to subject them to some treatments which may be harmful.

If we knew we were only going to find people who needed to be treated and there was no debate about that, then the harms of treatment wouldn't be such an issue. But prostate cancer is a classic example where we now know that there's quite a variety of prostate cancers out there, and there's probably in this wide spectrum a group of cancers that would have sat along quietly, especially in older men, never have come to attention. Now we're good at finding them. Once it's found, it's very hard not to treat them, and the treatments have their own morbidity.

So this is just a way of pointing out to think about the most important outcome, think about the other outcomes that are inevitable that you can't ignore, and realize you're going to have to somewhere at the end piece together how those play out.

So how good is the evidence that the intervention will improve the outcome? That's the second issue, and again as an internist, I plead ignorance about the scientific details of newborn screening, but I understand that that's part of the debate about some of these issues, how sure are we that our treatments are good. The systematic review is meant to — often it's conceived that systematic review means looking for 2,000 articles, and we can't look at 2,000 articles. I think the most important thing about a systematic review is just being explicit about what you did.

So it doesn't depend on how many articles you look at or how much time you spend doing that. You just have to be explicit to say this is the evidence we think is relevant, this is how we found it, these are the outcomes that we care about, whether it's the clinical outcome or whether it's an intermediate

outcome, such as finding it. This is how we looked at the individual studies to weed out studies that were good and bad, and all of you who have spent time with the medical literature know that just being published in a peer reviewed journal doesn't guarantee that a study is high quality or relevant.

Again, the goal of it is to be transparent. So the idea is not simply that it will always give you the same answer, but at least someone looking at it can understand how you got to the conclusions. So I think the most important thing about being systematic is not exactly what your literature search strategy is or how you rate individual studies. It's just being clear about what you did so that people can look at it and say that sounds reasonable.

Again, the aim of the systematic process of looking at how good is the evidence that we have is being clear about what you know and what you're not quite sure about so that decision-makers can make that decision more easily, not to obscure the things that you think but aren't sure about.

Again, I think I just made these points. These are misperceptions about we don't have the resources to do a systematic review. Again, it's being explicit rather than being exhaustive that's the most useful thing. Again, it doesn't require having large numbers of RCTs. The systematic process is most helpful when you have studies that are all over the board in terms of their study methods, because within those variety of studies there are some that are more likely to be biased and some that are less likely, and you want to separate those out.

It doesn't require quantitative synthesis. So again, we often think of systematic reviews as meta-analyses where we've got 12 trials and we want to pool them together and come up with one estimate. The point I've been belaboring today is it doesn't require that. You can do it with whatever kind of studies, and it's most useful when you've got weaker quality evidence.

So a step in the systematic review is looking at quality of evidence, and I'm going to not spend too much time on this because I think there are whole books written about it and I don't think it's the important point I want to get across. But just to say that when we talk about what's a high quality study, that's basically one way of defining it. It's one where the study's design, how it was conducted and analyzed has minimized selection measurement and confounding bias. That's a lot of epidemiological gobbledygook. Basically what it means is how sure are we that it's given us the correct answer. So the grad group, which I've been a part of, says it's the extent to which we can be confident that an estimate of effect is correct.

So given that there's a body of published literature, that not all of it is good, the highest quality literature within that are those studies we're most confident are giving us a correct and not a biased answer.

So the goal of doing that is, again, to identify those ones which are least likely to be biased, and epidemiologists talk about internal validity. Is it even giving a right answer for that study? That's a function of the study design. We don't have the luxury of having RCTs in the areas you're considering. It's also a function of how it's carried out. So if you're talking about a case series, how good is the follow-up? If you've lost 50 percent of the kids to follow-up, that's going to be a less reliable study than a study that's got 80 percent follow-up.

So there are issues about how studies are executed, whether you're talking about case series or cohort studies or randomized trials, and there's no one formula for what makes a good study. It's going to vary with the topic.

So this is the one that, again, I think is maybe most important because it's often overlooked in the debates. How is it going to work in the real world? Again, it's an unfortunate truth that carefully controlled research studies often overstate the benefits of the intervention as it works out in real practice, and that's what epidemiologists would call external validity. How applicable are the findings in this carefully

controlled study to the question I really want to know, which is should we be doing this in the general population?

The reason they overstate the benefits is that the harms may be minimized because you have a carefully controlled setting where you can be sure that all the patients are getting the best tests. So to take the newborn screening example, you have a carefully controlled setting where you have the best laboratory methods, careful quality controls, you're sure that the diagnostic tests are all properly performed, the follow-up is adequate, the enrolled subjects may be prescreened so they're more likely to comply with the interventions, there's careful follow-up.

So the treatment is likely to work better than it's going to work in the typical setting with an over-worked state screening program or an over-worked pediatrician, and any harms may be minimized. To take the specific example of newborn screening, issues that are going to dilute the benefits in the real world are problems of loss to follow-up of kids that have gotten the initial screening test, whether the diagnostic tests they get after screening are done properly and appropriately, whether the interventions that are then offered to them are appropriate, and whether the patients are able to adhere to them.

Then the biggest challenge is saying we've got some evidence about how it can work under ideal settings, some guesses about how well it's likely to work in the real world, and is that benefit big enough to justify the downsides? Those downsides would be possible harms and costs. I'm not really going to talk about economic costs or cost-effectiveness here, but you can think of costs as non-economic costs, which are things like opportunity costs or diversion of resources. The reality is if there were no cost issues, we also wouldn't be here.

So somewhere one has to make a judgment about what's the implication not necessarily setting some threshold of does this reach some acceptable level of cost-effectiveness, but what's the real-world implication of telling every state they have to do this? Is it going to have any adverse effect on what they're able to do for other conditions? So it's something that has to be at least on the table.

So to assess this balance of benefits and costs, you need to come with some estimate of how big are the benefits and what are the harms. Are there harms of false-positive screening tests? The diagnostic tests may be relatively simple, so you may say there's not much harm. Are there psychological harms? That's a difficult issue. If you can confirm the diagnosis easily, the psychological harms are probably short-lived and not important. But you need to at least think about what are the consequences that I want to think about, and do I have any evidence on them? Then you need to figure out how to present those tradeoffs and look at opportunity costs.

I think I'd better move through more quickly here.

So this is just if you take the prostate cancer example that we talked about — I'll skip over that.

The fifth thing is what constitutes good enough evidence. Again, I think I've already made this point, it depends on your perspective. It depends on the values you place on different outcomes and this judgment about what's the risk of acting too soon or acting too late.

Then what other considerations are relevant? Dr. Sampat already touched on those. They are concerns of equity, cost, and feasibility.

So let me move through the newborn hearing screening. What are the particular challenges for newborn screening? Well, these have already been touched on. A variety of factors make research on newborn conditions more difficult. They're not only rare but they involve children. Research can be more difficult. As we've heard, the technology is evolving. It's an emotionally charged issue. It's hard to argue with the evidence provided by that missed child who has had a terrible outcome. Yet, the other thing that's difficult is you're not making decisions for individual patients. You're really making decisions for a

population. So you can't really leave this to the clinician and the patient to figure out what's best. You're making a policy decision which is going to affect a whole population.

Let me walk you quickly through newborn hearing screening just to illustrate how some of these things play out. This was a very controversial and difficult issue for the task force. I don't want to belabor whether they got it right or wrong. But if you think about it, the aim is not to find kids, at least as a task force. The argument for it is you can improve speech outcomes in an important way, and you can measure that at 2 to 3 years, but presumably that's going to have long and lasting benefits. There are adverse effects that you need to think about along the way.

So it's pretty clear from the evidence that you can detect it earlier. You can quantify how many kids you're going to detect earlier. As a result of detecting earlier, kids get into treatment earlier. If they didn't get into treatment earlier, it wouldn't make any difference. You can again sort of quantitate that. It's important to think in comparison to what. So the benefits don't look quite as large if you compare it to a strategy of testing high-risk infants, which was sort of the norm at the time the task force looked at it. There are false-positive tests. Kids have to come back for more testing as a result of that. As a result, because the condition is relatively common but rare compared to false-positives, you have to evaluate a lot of kids to find the one kid who you're really looking for who has the moderate to severe language disorder.

The real problem for the task force — and again, I'll state up front that the task force sets the bar pretty high. The evidence that this early detection leads to better speech at the time the task force looked at it was relatively weak. There were sort of case studies, lots of loss to follow-up. So although it's certainly logical, and to a lot of pediatricians and hearing specialists it seems to make intuitive sense that kids are going to talk better if you find them, it was hard to quantitate how much of that benefit there was.

So just to sort of think through, this was the evidence wasn't too controversial, but the conclusions were very controversial. So one was this issue of what's the right comparison, and again, the reason the task force thought the benefits were smaller than often portrayed is because of concerns about the real world, how is it going to work in the real world, and then this concern that just doing screening isn't going to solve the problem unless you have the resources to do the follow-up. In all screening tests, especially with kids, that's a critical issue, and that's often a big cost of the screening is all that follow-up.

What benefits are important? Well, obviously, what benefits are important vary a lot. The task force sort of said we only care about speech, but for a lot of people that's sort of crazy. If you're a parent and you have a kid, you don't want to go a year knowing that they're deaf. So just finding the kid, even if their speech isn't affected by it, is an important outcome. That's a perfectly valid value judgment, but it needs to be up front.

There are all sorts of other things, regret over missed diagnoses. All these things are relevant to your sort of discussions. Information itself is valuable, and even if you can't treat the underlying condition, you can get kids in for social interventions. That can help the family out. All perfectly valid value judgments.

The other considerations that are relevant. Well, there are two arguments. One is you shouldn't recommend screening unless you have the resources to do the rest of the screening program in terms of the follow-up. Other people will say, well, the only way to get those resources is to start with the screening to show how big the problem is, and the resources will follow. I think that's a difficult political decision, but it's important to be there.

But again, the resources decisions are made at the state level, and I think it's a reality that states are strapped these days. So thinking about how these recommendations are going to play out in the real world, are extra resources going to flow into this or are you going to do lots of screening and then

everything is going to fall apart after the screening step, I think is an important issue, and how to help them work through that.

The equity concern is another issue, and it's obviously part of the reason you're here. There's something fundamentally troubling about the fact that what state you're born in seems to affect what you're screened for. So the evidence isn't going to get at that issue. It's something you need to think about. I also often mention that an approach that you can take in prostate cancer, where you say we're not sure, there are tradeoffs, let's discuss it, do you want to get screened, and you can have that decision, that's not really feasible to do when you're talking about newborn screening testing on a heel spot specimen.

It looks like I have two minutes left.

So when is the evidence good enough? We talked about that. So what's the risk of waiting for better evidence? The first question is, is it likely we're going to get better evidence? If you're never going to get better evidence, then it's not likely. But the likelihood is some of the things you'd like to know you might be able to find out. But if you wait for that, you're clearly going to miss opportunities, so that's a problem.

What's the risk of acting too soon? Well, you're going to divert resources. If there's a concern that you may actually be treating kids who don't need to be treated, you may harm some otherwise healthy kids. Again, that decision, different people are going to reach different answers to that decision. But again, it's conditioned on if we're going to wait five years and we're still not going to know anything more, waiting isn't very useful.

So what's the kind of better information we might like to get? Whether or not we're likely to get it is for people who know this issue better. Do we know enough about how well these tests perform in the real-world setting, or is the research mostly from specialized laboratories? Are all states going to have access to that quality of laboratory? Are the interventions safe? How effective are they? Again, specifically this issue of are we sure enough about the natural history that every kid we identify when we do these tests in the real world is going to need that intervention.

I think our experience — prostate cancer is the classic example. But the more I've looked at screening tests, the more I've come to believe that every disease has a spectrum of disease, and as you start to get better at screening for it, you inevitably pick up a broader spectrum for whom the benefits of treatment are really much more variable. We would think that every woman with breast cancer needs to be treated, but as we do mammography and find ductal carcinoma in situ, we're clearly picking up people for whom the benefits of treatment are smaller. So we need to always be thinking about that.

So let me close with two slides.

What can you do when decisions are uncertain? I already talked about shared decision-making, which may work fine for prostate cancer but it doesn't really work for newborn screening. When you're dealing from the position of Medicare or a payer, you can have conditional coverage. Lung volume reduction surgery for asthma, Medicare said we're not sure it works. People are doing it, the public wants it. We'll do it, but only if you enroll in a clinical study so we can get more information as we go. That study showed that it worked for some people and probably killed other people. So that was an important way of getting better information and refining it.

You could let states make their own policies. Again, that's a challenge to why you're here and this idea of equity. Or you could think about staged implementation. So you have a group where there's clear consensus on everything and we'll do those all now. There's another tier where we're not sure and we'll start to do it in a way that we can get the information we need, whether it's through pilot testing or other kinds of experiments.

I did finally get to my conclusions. The point I want you to take away is this explicit process is useful when it's imperfect. What you really want to do is clarify what you know and what you don't know to separate this issue of are we arguing about the evidence or are we really arguing about fundamental differences in what we value or whether we think we can afford it or whether we think it's fair to kids. Those kinds of disputes are perfectly legitimate. There's no reason why everyone has to come to a certain issue. But if you obscure them by saying we're arguing about whether the test works or not, you'll never get anywhere.

Again, thinking about acting too soon or acting too late.

Thanks. I think that's all I had to say.

DR. HOWELL: Thank you very much, Dr. Atkins.

(Applause.)

DR. HOWELL: Are there questions or comments of Dr. Atkins? He certainly hit on a lot of hot-button issues for this committee, to say the least. Any comments or questions?

(No response.)

DR. HOWELL: I'd like to have you spend just a few more minutes talking about the systematic review of evidence. Let's assume for the sake of argument that one does a Medline search on one of our rare diseases which we do, and we get out 100 articles, which would be a large number for some of these conditions. Those articles are reviewed by experts in the area and so forth. How do you get around the question of, well, he reviewed it, but he's very biased because he's invested in this area and so forth. In other words, if you have experts reviewing the evidence, by definition they will have a position ordinarily, because they've either worked in it or they know about it, and I think that's one of the things that has surfaced in our deliberations here.

Some of the groups have had reviews of the literature, and then the people who have commented on it tend to be people who have worked in the area. It's a small group. How do you get around saying we've had a systematic review and so forth?

DR. ATKINS: Well, I think the first way of getting around it is being explicit about what goes into that. So if you're saying we're going to look at a bunch of what's really case series literature, then you can set up ahead of time what are the things we'd want to know about a case series to decide whether it was a good one? So the first one would be how did they identify their cases? Did they use a method that everyone would agree is reliable? What was the length of follow-up? What was the proportion who were lost to follow-up? Did they define the outcome?

So there are better criteria for randomized trials than there are for these other types of studies about what factors make a good or a bad study. But you can spell those out ahead of time and so prod a person who may not be the most objective person to say, okay, when you say this is a good study, please document these steps. It's an inevitable tension. With our evidence-based practice centers, we tend to lean towards people with more general methodological expertise, and we get experts to consult to avoid that bias, but I think we get criticism sometimes that if we had someone who has more expert about it, they would have identified other important issues.

So I think you need both. Ideally you have both, someone who understands the methods issues and may not be as invested in the outcome, and people who really understand the nuts and bolts of the science and can identify things. Sometimes it's overt bias, but sometimes it's just — we're all biased. We just have different biases. So you need some sort of protection against that, and that's usually at least

being explicit about what are the characteristics we're going to consider in deciding whether these are good quality or lower quality studies, and you can usually come to some agreement ahead of time and extract that information, or you can come up with — often we do it just with inclusion/exclusion criteria.

We can say, look, there's no way that kind of study is going to tell us anything reliable because there are just important biases. So if it doesn't meet this criteria, we're not even going to look at it. But you need to spell those out. When I say explicit, I mean spelling that out ahead of time so someone can understand why you didn't look at Robinson's study from 1993. Oh, I see, it didn't use mass spec as a way of identifying; it used some other biochemical test, and that's not really what we're considering.

DR. HOWELL: That's helpful. The subcommittee and working groups are clearly going to be looking at considering additional conditions that will be added to the panel, and I think one of the first things that will be on that list will be how does this group examine evidence, what's the mechanism that we have in place. So we'll need to be thinking about that.

Bill, you had a comment?

DR. BECKER: Yes, thanks.

Dr. Atkins, in expanding on this topic of — I guess what we're talking about is external review, a methodological review, at this point we have a report. The methodology that was utilized was clearly heavy with scientific input. There wasn't a formal external methodologic epidemiologic review of the quality of the study. The report is out there. It's released for the public. It's been commented on, and now we're trying to respond to those issues and move forward.

Is there any usefulness at all in us doing a methodological external review at this point, or is it better or a more efficient use of our resources committee-wise and otherwise to move forward and just get past that and say, okay, that's just a limitation. We didn't do it, acknowledge it, accept it, accept the criticisms of that, and go on and keep that in mind, as I think Rod just said, for the future as we consider the process for adding or modifying panels or programs in the future? Is there any point in going back and doing a retrospective look at the — an external review retrospectively?

DR. ATKINS: That's a difficult sort of value decision. I mean, one possible approach would be to say, well, there are a limited number of areas that seem most problematic. There are comments or what else we know from the literature that suggest that the controversy is over a subset of these conditions. So one could say we'd better go back and take a closer and perhaps more systematic look at those conditions. The danger of sort of putting your head down and moving ahead is that if, I understand it, you're moving ahead to making a policy decision which is going to get out there, that the ability to modify those things is often difficult.

So once you make a recommendation for 29 conditions, five years from now it's hard to drop five of those. Maybe that's a little too glib to say that, but I think it's harder to pull things back than it is to move them out.

The other recommendation would be, if you decide to go ahead, to set some clear parameters for what you would like to learn in going ahead about the conditions that seem controversial. So if there are six conditions where there's debate in the international literature about whether you should do it, and say at this point, given all the considerations, we think it's better to go ahead, we acknowledge that we don't know everything we'd like to know, and specifically we would like to better define these four characteristics. You can't require states to maybe — well, maybe you can.

So number one, could you get that information from all the states, or if it requires more detailed information than they might get in the course of their routine screening programs, say we're going to try to fund a couple of states to really collect detailed information about how accurate — so some information

you can get, follow-up rates, diagnostic rates, et cetera, but the clinical course of the disease, compliance with therapy, any adverse effects of therapy, things like that, you might want to require some more information.

So you could lay out some parameters, and than that information, if it went against what you had hoped, may make it possible to change course.

DR. HOWELL: Coleen?

DR. BOYLE: Thank you very much for the talk. I really appreciate both of them, actually, really helping us think through the process.

A question. In the beginning you laid out a framework of helping us sort of lay out the dichotomy of what's evidence versus what's values and resources. I was looking at your seventh slide where you laid out the questions for setting the policies or a systematic process, and I was having a little bit of a difficult time deciding which was the guidance for laying out the evidence versus how — because I think that's very helpful for us as a committee, because I think a lot of our challenges have been separating the evidence from the values and the resources aspects of it.

So I'm hoping you can help me a little bit with that slide in saying which is the evidence part of it and how do we separate out what's the values and the resource aspects.

DR. ATKINS: The evidence would be sort of how many kids have a positive test, what proportion of the kids with a positive test actually have the underlying disease versus false-positives. So it's sort of quantitating how many people with the disease get treatment, maybe evidence on how many of them adhere to treatment. The values issue is how big an issue is it that we have false-positives. Some people would say false-positive? Eh.

DR. BOYLE: It's almost like for each one of those questions there, there's the evidence piece of it, and then how much do we care about that in some way.

DR. ATKINS: Right. So the evidence is what do we know about how likely these different outcomes are. The values is how important those outcomes are. If you put all your weight on an outcome of the kid who you find early and you can get into treatment and they do better, that's going to lead you to a different decision than if you say, well, we also have to put some weight on these other aspects, like false-positive tests or the possibility of over-treatment, et cetera. That's the hard part, because there's no answer to that. How many unnecessary biopsies is too many to find one woman with breast cancer?

DR. HOWELL: This is a marvelous discussion. I hope that you're going to be able to stay around to come back into our discussion, because there are so many things — I mean, when we talk about false-positives, Professor Rinaldo down here will be very interested in that subject. But it's interesting, having sat through the deliberations of the folks that put through the ACMG report, it clearly was implicit throughout that there would be a possibility of removing conditions if they were shown through further study — so that has always been on the table.

We need to move ahead, and we'll now have Dr. McCormick, who is going to talk about incorporating evidence-based expert opinion into the decision-making process. Dr. McCormick is the deputy director of the Office of Orphan Products Development at the FDA.

Dr. McCormick, welcome.

DR. McCORMICK: One of the things I've always had a bit of trouble with, not knowing quite how to handle in my life, have been left-handed compliments. I got a call from Dr. Puryear, who said, "We would like you to come and talk about making decisions when you don't have very much evidence. The people at the FDA have told me you make more decisions without evidence than anybody I know."

(Laughter.)

DR. McCORMICK: And then the story continues because about a month after I got that first call, I got an agenda, and on the agenda it said I was going to be talking about evidence-based expert opinion. So I called her up and I said, "What is evidence-based expert opinion?" And she said, "I'm not really sure, but it's a term your boss uses." And I said, "Oh, that evidence-based expert opinion."

(Laughter.)

DR. McCORMICK: So here we are. I thought about evidence-based expert opinion, and a couple of examples that I could come up with is, for example, how the FDA reviews its data. What you get is large clinical trials that are usually done fairly well, and they have a lot of information which is shipped to the agency, and then a person who knows the disease goes through all this information, tries to interpret what could be attributed to the disease, what can be attributed to the therapy, and to come up with some sort of recommendation whether to approve the drug and allow it to go out for sale or not to.

To me, that sort of fits the definition of evidence-based expert opinion. But that's not what we're talking about here, and it doesn't happen in the real world very often. The only other example I could think of is, for instance, for proprietary databases where you can go and buy information, something based on actual data, they will give you information. Again, that's not what we're really talking about here.

What we're talking about here is basically using experts in lieu of data, and how do we do that, and at what point do we give up on data and go to experts. The watchword at the FDA always is that data always trumps opinion, and I think that's not a bad sort of philosophy to have. The only difficulty with that is where do you get the data and how do you get the data?

Well, there are reasons we don't have data, and these have been talked about in both previous talks. Some of it is time. We could do a nice study over 40 years and come up with a reasonable answer. Are we really benefitting this group of patients by detecting them early, or after 40 years is there any difference between any of them? But that's just not done in the real world. The second one, obviously, is money. So instead of doing it for 40 years, what we could do is put a million and a half people in that study and we could do it over five years, and we could probably have a similar event rate, and we could come up with pretty much the same information. But who in the world is ever going to put a million and a half people in a study? It's almost impossible to do.

So those are very real limitations that we have to live with in the real world. Here's the one you want to be very careful about. Is the perfect the enemy of the good? Because one of the things that we have a real tendency to do, especially people associated with academics and academics and government, is we're always trying to make it just right when we do it, and we spend so much time trying to make it just perfect, just right, that we never get around to doing it.

I see that happen time and time again, and that is, I think, the area where there's real room for intervention. You need to be critical about this. I mean, I would love, as was pointed out earlier, to have perfect data done in a double-blind randomized controlled trial. But if that's not a doable trial, am I better off with the next best thing? I think that's one of the areas that we really need to be very careful about.

Now, as I mentioned earlier, I think going to expert opinion as opposed to gathering data is a decision. It's a decision to give up on one form and go after another. I think that 99.9 percent of the

decisions in medicine need to be and are done on a risk/benefit analysis. What do I expect to get out of this, and what anticipated consequences/problems can I foresee if I do it?

Now, one of the things I think that we all do automatically, human beings, is what would the result be of a bad decision? Most of us are pretty good at listing those. We can probably think of a couple of hundred for just about anything that we do, and that certainly influences our decision to move ahead or not move ahead. But I think the one question that we all tend to not ask or need to ask a lot more is what are the consequences of no decision? Oftentimes, the consequences of no decision aren't a whole lot different than the consequences of a bad decision, when you sit down and you just make up your list. So that's something I think that we all need to keep in mind.

Now, when you decide to go to an expert, the problem always becomes what expert? Our office actually uses experts to some degree because what we do at the office is we try to determine the size of a population, because our law, the eligibility for the orphan benefits for a drug company is determined by the size of the disease or condition that the therapy is intended to treat. Now, for most diseases, there's pretty good references out there in the literature. Somebody has done a decent epidemiological study along the way, or there are wonderful things like SEERs database where you can find all this information.

But for some of the rarer ones, it's very difficult. So what we've said is we will accept the opinion of three experts telling us what this population is. The criteria is that they can have no financial stake in the company, and the other thing is they need to tell us how they came to their decision.

Now, one thing that you find out about experts is that some people are experts because you have a problem, they have worked long and hard in an area that is very similar to the place where you have the problem. Their data that they've been looking at for a long time probably is going to have significant carryover to what you intend to do.

Now, what was brought up before is that other people out there are experts because sometimes on very, very limited data they develop very strong beliefs about things, and they will fight to the death over those. Therefore they get their name in the literature everywhere, it's all over the place, and they become almost a spokesman for the condition, disease, whatever. Those you really have to weed out because they aren't going to bring too much other than controversy into your discussion.

So I think everybody in this room I'm sure has hired somebody at one time or another. You've got to remember, when you're getting an expert, you're hiring somebody. You use the same criteria to pick your expert as you would a good employee. What does he know? That's your job to evaluate it. Does what he knows fit into where I want to go with this? That's another thing that a good employer needs to do. And is this the kind of person that is intellectually honest enough that he will say I'm wrong? Those are the criteria, I think, that you're really looking for.

I just sort of threw this one in because whenever I hear somebody start off with "I believe," I think there are numerous things in life where that is very important, to believe, but I think when you're getting into a discussion about scientific topics or health policy and that sort of thing, then you have to be pretty careful about that and you really need to limit it as much as possible.

Another thing when you're picking the expert is — we talked about does he have knowledge in an area that's similar to the problem you're dealing in. The other question is how generalizable is the information that he has? For instance, I'm sure if the world's expert on cell growth did all of his work in fungi, and you want to study mammalian cells, then maybe that's not going to be a real good person to go get. You may want to get somebody with a little less fame than the world's expert in fungus growth. So that's another consideration to think about.

The big thing which I talked about a little bit earlier is that any time you get an expert opinion, have them tell you exactly how they came to their conclusion. I talked earlier about getting the size of the

population. Well, we get a number of various responses. One would be a letter that the company wrote, sent out to the experts to sign, and they mailed it in to us, and they are identical. Obviously, that's of no value whatsoever. As opposed to finding someone who said, well, I have a very typical practice, I have three people in my practice with this particular disease, there are another 800 people in the country who treat this disease besides me, and it's the sort of disease that almost always gets referred to an expert somewhere. Therefore, based on these pieces of information, I have determined that there are so many people out there with this disease.

The ability to follow that thought train is very important. While you may not have the knowledge that you're hiring that expert for, because if you did you wouldn't be hiring him, but if you don't have the knowledge the expert has, you can still look at how he goes through his evaluation of the data, his recognition of your problems, and how he comes to the conclusion that he does. So I would never take an expert opinion without a detailed analysis on how they came to their conclusions or recommendations. I just would never, ever do it.

If that's the answer that he tells you how he did it —

(Coin flip shown on slide.)

DR. McCORMICK: — then you don't need him. You can do that just as well yourself.

Now, the one thing to remember, too, when you're using experts is it's his opinion, but it's your decision. One of the things we tend to do is to feel sort of obligated to use an expert's opinion once we ask for it. Well, I think you have a little bit of a need to ensure that you're treating the expert fairly, but your analysis of how he came to his conclusions is every bit as important as how he came to his conclusions.

So if you don't like the way he came up with the information that he's given to you, remember it's your decision, not his, so feel free to just pass on by it.

Here's where we'll differ. Very few decisions are irreversible, and certainly when you make a decision that's troubling you, then the reasonable thing to do, as was pointed out earlier, is to — let's say that anybody who is going to be treated for this particular disease which we don't have good information on needs to go into a study. That's a very reasonable approach to take. Or just to put some sort of follow-up on the patients that go into this group somehow or other, let's see what's happening to them. Or for you to see what the rate is of people with various genetic diseases that you're turning up with these screens. Is it really worth it?

If you're worried about pulling it back, there are things you can do. You can sunset it. I mean, when I look at, for instance, the vaccine recommendations, they change them every five years. One year you're going to have to have three shots, the next time around when they evaluate you're getting two shots. One time it's going for 15 years between shots, the next time it's down to five years between shots.

That's okay, because what they're doing is they're adjusting based on the evidence that's presented to them at the time, and I think that's the important thing to remember here. Actually, I have a huge advantage. I make a lot of mistakes, so I don't have a hard time admitting them anymore, and that's the approach I think you need to take, that I'm making a decision here based on an imperfect set of data. There is a much higher probability that I will make the wrong decision than if I had perfect data, and you just understand that, you accept it, and you're willing to say at some point, when the evidence becomes clearer, that you've done the wrong thing, I have done the wrong thing, and therefore we will try something else, hopefully with a better set of data this time because it's been going on longer.

I think with that I should shut up and thank you very much.

(Applause.)

DR. HOWELL: Thank you very much, Dr. McCormick.

Are there comments or questions for Dr. McCormick?

(No response.)

DR. HOWELL: I hope you will stay. I think we're going to take a break right now, but then we're going to come back and have the committee discuss decision-making for the committee as we move ahead. So if you all would stay, all three of you, that would be very good. Thank you very much.

Let's take a break and be back at 2:45. I might point out, remember that we're going to come back, hopefully toward the end of this period, and talk about the committee assignments, because we did not do that earlier.

(Recess.)

DR. HOWELL: As you know, this morning we decided that we would defer the discussion of the subcommittees until after we had heard the decision-making, and we need to really now think about the decision-making process for this committee as we go forth. The thing is that I have a few notes here about the kinds of things that we should at least discuss and so forth, and one is how we will examine the evidence. Our speakers have talked about that somewhat. The basis for decision-making, evidence only, cost/benefit analysis, other considerations that we've heard here, what constitutes evidence, what kind of evidence will we do.

One of the things that clearly we will need to consider is the process for bringing tests and technologies before this committee as we're going along. Those will flow likely through the subcommittees and so forth. We should talk a little bit about the subcommittee and work group structure and how they will be constituted to review evidence. We talked a little bit about that with regard to the subcommittee, but that's obviously an interesting thing.

We will need to continue to think about expertise that we need to add, either as standing members of the subcommittees, and the subcommittees have really been working on that, or on an ad hoc basis. But we really will need to think about that, because we would anticipate that the subcommittees we have, and working groups, will be bringing a variety of materials through the committee and back to the whole committee.

The other thing that we can continue to think about is incorporation of representatives from other organizations that we talked about a little bit this morning with regard to the folks from the public health community and so forth.

So let's hear your thoughts about developing a plan for how we will handle evidence as we go forth. We're not talking about the ACMG report. We're talking about how this committee will review things that come before us as we move forward, because there are a considerable number of conditions out there at the current time that have had recently defined or recently published or recently updated information about therapies that have been either very effective or partially effective, and at the same time many of these conditions have tests that are in pilot phases that are being tested either in small pilot groups in states and so forth, and we really need to think about that we have this sort of information here and we have this material coming forth, and how do we constitute a recommendation based on those that would perhaps add additional conditions to the panel in the future.

Let's have your wisdom on how we move off ground zero here.

Amy?

DR. BROWER: Well, I think what we heard that was really important is to define our parameters for assessing evidence ahead of time. So it's not only important for the expansion of the panel but as well as evaluating follow-up data for the continued inclusion of the 29 and the secondary tests on the current panel. So I think as a subcommittee, the Laboratory Subcommittee and the Follow-Up Subcommittee could maybe draft their parameters for how they're going to evaluate evidence and have that for consideration for the whole committee.

So it sounds like transparency through the process, and to what factors go into evaluating the evidence seems to be most important.

DR. HOWELL: Coleen, you chair one of the committees that was referred to. What are your thoughts about that?

DR. BOYLE: Well, in thinking through, I hadn't really thought about the Follow-Up Committee having an explicit role, but what I had been thinking of when I was listening to the talks earlier, and one of the suggestions from one of the reviewers from the public comments — maybe it was more than one reviewer — was that one approach in going forward with the 29 conditions was to do it in more of a pilot phase aspect. I think David may actually have suggested that in some of his concluding remarks. So I guess in expanding on what Amy just said, I think it really would behoove us to have very explicit recommendations about continued evaluation as we move forward with the expansion of newborn screening.

So I guess I'm sort of seconding her ideas there, that we be very explicit about how state programs and follow-up be conducted, particularly maybe for some of the more questionable conditions. I don't know if we want to get into the details of separating that out, but to sort of have a way of objectively evaluating the impact of the expanded technologies.

DR. HOWELL: Well, you know, although newborn screening has been around for many years and so forth, we really have not had a systematic mechanism. I mean, the very well known studies that were funded by Duane's institute on phenylketonuria are the only really major studies, and everything else has been very, very marginal. So although one might make a point for screening for some of the conditions that we clearly don't know a lot about, you can make a very strong point for following up on some of the conditions that have been around a long time that we still don't really understand why there's such variability in outcomes of therapies and so forth.

We want to come back and discuss this, but one of the things that's important is that there's been a lot of discussion about the importance of following up on these kids. It's almost a postmarketing survey program, because you're introducing screening for a condition that you don't know all the parameters and you really need to follow up to see what's happening. One of the issues that follows right on top of that is that this will be a fairly big deal, and to have a system in place that would follow all these children, although they're not large numbers, they're going to be scattered around the country, and resources to do that is going to be a real issue.

So one of the things that Denise was speaking to me — she can speak for herself — but just as we were breaking is the fact that we really do need to talk about the fact that for these things to be accomplished, there will have to be a recommendation that funding be made available, because to simply say to all the states you need to do this, it's not going to happen readily. The funds just won't be there, and the institutes and the NCH and everybody else don't have the funds to do that.

So you're making a specific recommendation as we go forward that the Laboratory and the Follow-Up Committees specifically would develop parameters for the laboratory diagnosis and the follow-up of these patients and so forth.

DR. BROWER: Really getting at the issues of implementation of this current panel and adoption, and seeing how well adoption is going through the follow-up.

DR. EDWARDS: First, I would like to thank the panelists and Denise for suggesting this, as I recall, at the last meeting, because I think that this has been very helpful in assessing what has been a very sticky issue as far as many of us are concerned.

I think there were a number of things said, and I think one of the things that really hit home with me was the consequences of no decision, which we really haven't talked about in this group, but there are consequences, and I think many of the people sitting here in the audience would echo that strongly.

In the agenda book, there's a letter from Jennifer Howse, a member of this committee who all of you know who couldn't be here today. It was sent from the perspective of the March of Dimes. I can't speak from that perspective, but I can tell you that it started from the telephone conference call which the Education and Training Subcommittee had had. I'm kind of jumping about the agenda here, but at least in my own mind it all fits together.

The question that was raised is whether it was the Laboratory Committee that had the responsibility for follow-up on here, and when Education and Training was looking at this, we thought this is a huge, huge responsibility. You'll remember many of the comments that came from the respondents, the comments that we reviewed this morning, one of the things that they referred to was that this be a dynamic process, one that kind of constantly evaluates and reevaluates and looks not just at new conditions that might be considered, but evaluates all conditions, the 29 basic conditions that we're looking at, so that the whole thing becomes a dynamic process.

Well, as we were looking at the charges to the different committees, subcommittees actually, looking at those charges, we were thinking this is such a huge piece, and I think this to me is what Jennifer's letter addresses, and that is this is such a huge piece that this probably cannot be done by one of the subcommittees. It needs expertise. We didn't have a recommendation about who should do it, but it seemed like that the subcommittee, the Subcommittee on Laboratory and so forth, that even if you take that out, the subcommittee has a full plate.

So some group, if we're going to make this a truly dynamic process and evaluate and reevaluate, some group probably beyond the subcommittee — maybe the subcommittee could take responsibility for overseeing it, but this is going to be a huge responsibility if somebody is going to scientifically evaluate the responses that we're getting and look at new tests. So I don't want to speak for Jennifer because Jennifer speaks very articulately for herself, but I think this is what she's driving at, that if we're going to do this, this is a huge process in and of itself. But I think she's also saying — and if she doesn't, I would — it needs to be done.

DR. HOWELL: Let me comment about that. The members of the committee have Jennifer's letter in the book, and fundamentally she has a variety of thoughtful comments. But the core thing that she has pointed out is the fact that she was concerned about the breadth of the charge to the Laboratory Committee that would be the addition, or potentially subtraction, of additional things and so forth. I think this is one of the things that Amy had commented earlier about. Although we were going to talk about the subcommittee charges a little bit later, maybe you could comment a little bit on that, and we'll come back and have you present your charges.

Do you want to comment some more on that, Amy, before we go?

DR. BROWER: Sure. We definitely agree, it's a big role and the scope is very broad. But we also think that having the Laboratory Subcommittee start to make a working group that has the expertise that's needed to really look at these new panels in an approach that's agreed on by the full committee, because this is really a charge of the full committee as a whole. The committee owns the expansion of

the panel and the evaluation of the current panel. The Laboratory Subcommittee, in our minds, was going to provide the structure and provide a draft agenda and proposal for moving forward that the larger committee could evaluate.

That's what we discussed in our subcommittee today. So we weren't, as a small subcommittee, going to be able to complete the whole charge. We were going to provide the structure and the organization for a working group to do that.

DR. HOWELL: But basically, I think there's general agreement, Steve, that there needs to be a broader group that would be much more broadly focused than just the Laboratory Committee.

DR. EDWARDS: I don't have a problem with the broadness of the group. I just think that the amount of work that this group is going to need to do is just going to be tremendous, and that we may need to have financial resources in order to do this. It may be beyond the scope of the people who are sitting at the table now.

DR. HOWELL: Well, I think it clearly will be beyond the group that's sitting at the table, and that's why I think other expertise will have to be brought to bear on the subject.

Piero, and then Denise.

DR. RINALDO: Go ahead.

DR. DOUGHERTY: Well, I was just wondering if we could break this into two parts. One is some kind of group to develop the criteria, working with the experts. Then once that's done, it seems that it will be a lot of work to apply the criteria to evaluate suggested new conditions, but there needs to be that —

DR. RINALDO: Not just new.

DR. DOUGHERTY: Not just new, but there needs to be a format to do that that the committee has to approve first. So that's the first task, without getting into how enormous it's going to be, to actually apply those criteria to old and new conditions. So I'm wondering if you're suggesting that the Lab Committee come up with the criteria or oversee a group that comes up with those criteria, or that the full committee do that. I think that's the first step, even though I know you all want to move quickly to considering new conditions. But we really need a process first.

DR. HOWELL: Piero?

DR. RINALDO: If you look at the executive summary, I believe you can find this algorithm, which also considering that we have three preeminent experts, we certainly can use it as a starting point. Remember, early this morning was the discussion about that the report did not really address newborn screening as a system. Yet if you really review or perhaps modify, we have 19 defined criteria that I believe were used, and it seems that they were able or sufficient to generate a product. Now we have those 19 criteria built here as a first step of an algorithm that basically determines if things should be considered and evaluated.

So I beg to differ. There is a starting point defined. I believe the starting point is what could benefit from the feedback that we received through the public comments and the expertise that now we have sort of made available to us. I believe that, at least in my mind, the structure that Amy was mentioning before, it's perhaps not to do all the work but rather to define, if you will, the rules of engagement. I think we really need to have advocates for additional conditions. Perhaps they are experts, so perhaps they are people with vested interests, but perhaps it could be just members of the

public, non-professional support groups that should be told in a clear way that this committee as a whole, the subcommittees, the working groups, whatever, are different layers.

There is a sort of an application process almost. We can say that if you believe you can make a case for certain conditions to be considered for addition to the panel, these are the things that we'll ask you to provide. We'll ask them to come. Basically, I presume there would be a review process to see if it's really the right time or the information is still not adequate, but if the review process says that there seems to be an opportunity here to discuss a particular condition. We have already mentioned many times today severe combined immunodeficiency, lysosomal disorders, SMA, you name it, Wilson.

So there are a number of things that I think are at the stage where they deserve a hearing and an assessment. I don't know if we really have to restart from scratch. I believe we can take what was done in terms of the criteria, perfecting them, perhaps modifying the weight of the scores. There are a lot of things that we can do in retrospect, but I wouldn't restart from scratch. I would use it.

DR. HOWELL: Bill?

DR. BECKER: I totally agree with Piero. The template — maybe you could argue that the template could be modified, and hopefully we'll learn about the evaluation process as we move forward. But the template for the criteria for evaluations of conditions was part of the product in the ACMG report. Let's test it. I think at the last meeting Piero suggested, and I agree, that we should test-drive it on a couple of conditions, maybe not more than that. Perhaps at the next meeting of this committee, the October meeting, we could agree on a couple of conditions that we want to run through the algorithm, bring it back to the full committee to see how the process works.

I think it would speak to Steve's and Jennifer's message about allowing the process to be vetted through the full committee through a couple of these disorders, and obviously offer the comments that the committee feels appropriate. But I do agree with Piero completely that at least the algorithm is a good starting point for us to have this iterative process sort of continue.

Now, the committee is, of course, completely free to modify the process as we see fit going forward, but I would support at least a trial run, picking a couple of conditions that we can talk about the next time.

DR. HOWELL: The algorithm that's being discussed is in the executive summary. It's under Tab 6. This is the thing that Bill and Piero and others are talking about.

DR. DOUGHERTY: Could I just say that if you compare this to the fact sheets and what was used to come up with those scores, there's a lot more in those fact sheets that the experts voted on beyond these kinds of questions. So there really is a different algorithm that was used in the decision-making process.

DR. RINALDO: I'm sorry. I have to point you to the fact that all the criteria are right there, the first step in the survey score, because those that were determined — it's how you weight all those 19 criteria that defines which path you use. So I don't think it's an accurate statement that they are not included here. They are. They are the very first level.

DR. DOUGHERTY: I'm sorry, we shouldn't get into a debate about this report again. But there were questions about how much does the test cost and how much does the treatment cost, and is the treatment effective, that were in the survey but are not reflected in here. That's my only point.

DR. LLOYD-PURYEAR: That were in the survey and not what?

DR. DOUGHERTY: That were in the survey but are not in this algorithm that's here in the executive summary.

DR. LLOYD-PURYEAR: How are they not there?

DR. DOUGHERTY: Well, there were questions about the cost of the test, the cost of the treatment, whether the treatment that's available is effective, and I think there were some others that I don't have in front of me.

DR. HOWELL: Those are all in the score.

DR. LLOYD-PURYEAR: They're part of the score.

DR. RINALDO: They're all built into the score.

DR. HOWELL: That's what those numbers are.

Derek has been very patient over on the end here.

MR. ROBERTSON: I guess one concern I have is if we just keep moving with this, then are we — I guess it gets back to what we spoke about this morning — are we going to ignore some of the criticisms of the approach that this had? I think that that's what we really haven't addressed. I mean, I think your question, Rodney, is how should we approach reviewing and how should we treat evidence, and we got from the speakers kind of a blueprint for that. I particularly like Dr. McCormick's thing where you start with are there data, because data always trumps opinion, and go from there.

So we have that, coupled with some of the other presenters as well, Dr. Atkins, and see how we can follow that as we apply it to what was done. I think some of the commenters had an issue with the survey and how it was applied, and I don't think we've even addressed that. Are there legitimate criticisms of how the survey was applied?

So until we review that and really get a sense that, yes, we need to improve the survey, or maybe we don't need a survey, we shouldn't have done a survey, we should have done something else — that's not to take from the report, because the report is the report. We keep getting back to that. But in terms of moving forward, the only way to do that effectively is to look at the criticisms and see how that weighs, and couple that with what we heard this afternoon. Did we do everything that we could have done in the ACMG report, and now moving forward?

If you have an opportunity, if you're going to look at a new condition that you want to see should it be included, or should one be removed, if you just do the same thing that we did before, you have the possibility of the same criticism, which we just haven't addressed. We haven't looked at that. I don't know what the committee's feeling is about the survey tool. I mean, one commenter had some serious concerns about how the survey was applied, and we haven't talked about that. We haven't really talked about was there enough data looked at. We haven't done any of that before we can say — we have to see how do we apply that to what we heard this afternoon.

DR. HOWELL: Any comments about Derek's commentary?

DR. BECKER: Well, I think that we're not as far apart as it may initially sound. I think that, based on the information that's been provided to the advisory committee about how to assimilate policy decisions when perhaps the evidence isn't randomized controlled trials, as we heard in our presentations, and apply that information with the tool that was developed in the ACMG report, could get us to the place that Derek suggests.

I think he makes a good point in the sense that maybe we need to be very clear that we are going to apply the algorithm with the information that we just picked up this afternoon and apply certain, for lack of a better descriptive term, philosophical tests of the evidence. I think that's what we're really talking about here, that now as we move forward, and we do need to move forward with candidate conditions, can we apply these tests or criteria or guidelines that have been provided to us this afternoon in evaluating the evidence and the information that would come through the survey tool for candidate conditions? In other words, are we learning as we go?

DR. HOWELL: I think that one of the questions that has been addressed here is how one assesses data. For example, if you would look at one of these boxes, it says is treatment available and necessary? That would be a literature review and you could review it, as has been suggested here, which I think was largely done, I might point out, by the College Committee. It did exactly what these speakers have suggested, basically. Unlike the large studies of prostate cancer and so forth, it's quite possible to review everything that's been published in many of these conditions because the numbers have been so few. So it was not a matter of selecting the articles that were reviewed, and they were reviewed by experts.

I think the one thing that was not there, there were not criteria for assessing the articles that were done prospectively, and obviously that's a very good thing.

DR. LLOYD-PURYEAR: They were assessed retrospectively.

DR. HOWELL: That's correct.

DR. EDWARDS: I think that's true of what's bee done, and I have no criticism whatsoever of what's been done. But for some of these processes, where there are very few cases, maybe more information may come from the studies that are being done than exist now. That's what I'm talking about as far as a dynamic process is concerned, reassessing information about old or already included conditions, and in addition I don't think we should just look at new conditions. I think we should reassess the data that comes, especially when the data is about very rare conditions where there's not much in the literature to go by.

DR. HOWELL: I think everyone would agree 100 percent with that, and that's the issue of being certain that we try to have a comment about asset allocations to accomplish that.

DR. DOUGHERTY: Rod?

DR. HOWELL: Denise, go ahead.

DR. DOUGHERTY: Well, I'd like to make a suggestion. We deliberately did not give the full report for evaluation to the experts we brought here today, but I'm wondering if a next step might be to look at this algorithm, the survey and the literature review fact sheet to them — I know David is already really busy — or some experts to say how can we take the questions that were in this algorithm and then modify the process of getting to the answers somehow so that it would be more explicit and more evidence based, rather than an either/or approach of starting from scratch, which probably should not be done because I think the right questions were actually asked in the ACMG report. It's just that the way they were rated, the way they were asked, perhaps, the format is not really reproducible and very explicit.

So somebody could compare and contrast and give us a best-case scenario where the questions would be the same but the process of getting to the answers might be more along the lines of what we heard today.

DR. HOWELL: Piero?

DR. RINALDO: That makes perfect sense. We have criteria, we have an algorithm as a starting point, and now, based on the lessons learned, we see how they can be modified to give us a better product.

DR. HOWELL: Any comments about that?

DR. BECKER: Well, we were just commenting over here. Remember, I asked the question about an external review, a methodologic review, and I think that was the question that was sort of on the table. Philosophically, I think that's —

DR. HOWELL: It seems to me that it would be foolish to disregard the huge amount of effort that's been put into this algorithm. But everyone I think would also agree that there probably are opportunities to improve that, and as we go forth — this algorithm is not mysterious. It's been in the literature for 40 years, basically, about how you do screening. It's frequently quoted as newborn screening, and the Wilson and Jungner thing had nothing to do with newborn screening for those who never read it. It had to do with screening of adults in populations. But anyway, the bottom line is the criteria for doing that have been around for a long time, and they've just been formatted for this particular algorithm and a little bit refined.

But I think it would be a good idea to have someone look at it and give us some wisdom.

DR. RINALDO: But the one thing I hope we would be doing, then — I'm wondering, when you say a method review, I wouldn't do it asking the question if they found validity in the way it was used. I'd rather move forward. I really am concerned when I see anything that intentionally or unintentionally can lead to revisit the work that was done. Earlier was made a statement about the questionable conditions in the 29. Honestly, I would like to know which ones. Which ones have a question? Because I just went to it and looked at it, and I cannot think of any. So I would like to know which are the questionable conditions.

DR. HOWELL: I think that perhaps the issue is the conditions on the list about which we need more information. That I think is an issue, and I think you would agree that many on the list are conditions that we would like to have a lot of data about and so forth. But I would agree, I would not question their presence on the list. But I would say that we need a lot of information about them, long-term follow-up, retrospective follow-up.

What I believe I hear percolating around the table is that we're not talking about the past now. The past is past. It's history. But to have some of our esteemed scholars to my right look at this document or certain documents and make comments about how they might suggest we use this and the modified this to look at conditions that we would think would be nearing prime time for addition. Is that what I hear?

DR. RINALDO: I certainly support that. What I would like to emphasize is that this would make it actually easier for us to not only evaluate whatever evidence or material is brought to us but also for the people who want to advocate a particular condition, because they will know exactly what questions we're asking. So it would be their job to really define or provide the evidence and certainly participate in rating the evidence, because that was really one of the big questions, as we have said a number of times. It's very easy to find disagreement. So, quite frankly, how do you go with that? You can have Nobel Prizes to disagree on things, and then which one do you believe? So there must be a way to rate it.

DR. HOWELL: Duane?

DR. ALEXANDER: I think we're nearing agreement that there needs to be clearly a process related to this committee that taps into some additional outside expertise that reviews proposed new tests to be added to the screening armamentarium, as well as providing some oversight over existing tests

where there are any questions, where there are recommendations for gathering additional information about a condition, particularly when genetic heterogeneity may influence treatments and so forth.

I've mentioned before that there is a parallel kind of a process in the government that I think has a lot of similarities to what we're talking about here, and that's the Advisory Committee on Immunization Practices that the CDC does, where they have regularly scheduled meetings with outside experts. They have an agenda that provides an opportunity for reexamining the timing of current immunizations, provides a mechanism for consideration of addition of new vaccines into the armamentarium, gathering additional data on existing ones, et cetera.

This is a system that's been in place for several years now, and it seems to work pretty well. I think we could stand to learn something from this, and I would suggest, Mr. Chairman, that we might try to request a presentation at our next meeting from the Advisory Committee on Immunization Practices about just what they do, what their procedures are, how they decide what they're going to look at, what their criteria are for consideration of new vaccines, revisiting old ones, whatever. We can provide some specific questions to them that we would like to have addressed that are particularly relevant to our situation, and they may provide some useful information to us as we go about setting up some sort of a subcommittee of the subcommittee, if you will, to guide us on providing advice on newborn screening practices.

So I would suggest, Mr. Chairman, that if people agree to it we might get a presentation from that group at our next meeting just as information to provide some parallel to what we're talking about doing that might be useful guidance to us as we set up a process for newborn screening consideration.

DR. HOWELL: Steve?

DR. EDWARDS: I think this is exactly what I had in mind. I'm somewhat familiar with the ACIP and feel like this is pretty much what I had in mind. I think it speaks to the dynamic process that some of the critics have put into this, and I think it's exactly what we need. I think it's a part of our response to the Secretary as we review the critiques of this. I think that we can say that this is the model that we have in mind.

DR. HOWELL: Any other comments about that?

MR. ROBERTSON: I hate to keep going back, but are we not going to comment on the public comment?

(Laughter.)

MR. ROBERTSON: I'm looking at one that caught my eye which was from the lead-off. It was Jeffrey Botkin from, I think, the University of Utah. They have some very specific criticisms about the survey tool, about the report, and I'm not doing it one way or another, but if we are going to move forward, if we're going to do another survey, are these criticisms ones that we want to take into consideration? For example, I'm just paraphrasing this, but they said it was skewed toward a certain set of providers, for example.

So I think it is moving forward, but I don't think we've addressed any of the criticisms. We're talking about, okay, we're going to do this, but if I looked at this report, my question to the committee would still be what do you think of Dr. Botkin's comments, or what do you think of somebody else who criticized the report? I mean, we haven't looked at that, and that will help us to then move forward.

DR. HOWELL: Would anyone like to make a comment before I make a comment?

DR. EDWARDS: I would start with some comment. The first is I think we have addressed this. If you'll read the minutes of the meeting last time — well, you were here for it — it covers it in significant detail. It doesn't answer every question, but I think that we have spent a good bit of time addressing some of the concerns that came up on the questions about methodology. One of the questions raised today which I think was very pertinent is is this a perfect survey, and I would say no. But I would say that the statement made today, is the perfect the enemy of the good, I think that what I heard our discussion last time say is that this is probably not a perfect instrument, but it's very good and it's an appropriate place to start action.

Another one of the questions that came up today is what are the consequences of inaction? Are we going to sit around for another 10 years trying to come up with the perfect instrument before we act? My own implication is that we can't do that, that a considerable period of time and considerable thought has gone into developing a good product. I would not say that this is a perfect product, but a good product, and a lot of the discussion of that is in the minutes of the last meeting, a lot of the reasons for that. We did discuss it significantly.

So I don't know that there is an answer to this, but I feel like that we have at least addressed the problem, and I personally am comfortable that we have done a good job and that this is a good report, and that there are consequences to inaction, and that we need to move forward from here.

One of the points that I hear you saying is that we should discuss this in our report to the Secretary, and I totally agree with that. But I think that we can include some of the discussion that we've already had, and I don't think that we can give a perfect answer to it.

DR. HOWELL: Let me make a comment.

Oh, go ahead.

MR. ROBERTSON: Well, I just wanted to say that, to me, that's exactly the type of dialogue I think we need to be having, because that addresses right on point exactly what, to me, the agenda item is. So that's what I was trying to pull out the whole time. I don't know if we had that type of dialogue last time, because we didn't have the comments last time, at the last meeting. But that's exactly what I'm looking to hear, because I want to hear this committee say just that, that it's not perfect but it's good, because I know some others on the committee had a major problem with the methodology. Having heard what we heard this afternoon, that they are still willing to endorse the report because it's not perfect, but then, as you said, moving forward, is there anything we can do to get it a little bit closer to being perfect, because that's a different responsibility.

DR. HOWELL: Let me make a comment, and it will come back to this. Tomorrow we're going to go back to our famous letter to the Secretary and basically the points that I teased out of that today were generated by issues that were raised in the thoughtful documents that came, and it was certainly not our intention to respond to everything in Jeff Botkin's letter but to look at the thing.

So we'll come back to that tomorrow in our letter. But on the other hand, let me go back to the vaccine issue that was discussed, and that is that we will indeed invite an expert to the next panel meeting to discuss the vaccine program. As a matter of fact, we have one of the leaders of that program who is sitting right back here.

PARTICIPANT: Used to be.

DR. HOWELL: Okay, used to be. But we have an expert on the program. Actually, I was told that when this committee was structured, the thoughts were there was a lot of looking at the vaccine program, the way it worked, with an idea that subcommittees and working groups of this committee would try to work in a similar way. So I think we can have some clarification of that for next time.

DR. BOYLE: Just going back to — not to beat a dead horse, but to go back to the framework that Piero talked about and I guess David Atkins' talk, I'm having a hard time in my mind trying to resolve the differences between those two. Maybe Denise's suggestion of asking the experts in evaluation research to take a look at the framework that was used in the ACMG report will help me. But I guess our whole ideas was trying to move this into a more systematic process, a more transparent process, and maybe that will do it.

But I have a hard time thinking through actually what we would do taking that framework. I'm not arguing about the criteria. I'm arguing more about how it was done, the survey approach, a survey of experts. I thought what we were going to do was start with the evidence, and yes, evidence based on what's available, and then evolve from there and try to use the evidence around the criteria, but in a very systematic and transparent way, starting with the first thing, is there available tests. What does that mean? Define what that means. Maybe that's part of a nomination process that people have to go through to actually nominate new conditions for the panel.

I guess I'm having a hard time resolving those two issues for me in my mind.

DR. DOUGHERTY: Well, I guess what I was suggesting is that we have the experts provide sort of a how-to, how you could address those criteria in a more systematic and explicit and rigorous way, and then we could use that. I'm not sure about the timing now, if we're hearing from the ACIP, whether we want to wait to hear how they do it before trying to go ahead and getting some specific advice, or we could do the two things in parallel.

DR. HOWELL: We don't want to stagger things. I think we would like to get as much stuff on the table as possible, frankly, and I think we should try to get them to come, and we could get this at the same time.

Duane?

DR. ALEXANDER: I think the survey methodology that was used has served its purpose. It basically tapped into a scientific consensus among the experts in the community. I don't think that's the methodology we would plan to use in the future. We will use some of the same criteria, we will ask some of the same questions, but doing a survey of the community to decide whether you add a new test to the armamentarium I don't think will be appropriate at all. I think we can do much better than that for new things coming on board, and I think that the ACIP model might serve us well as we try to set up a mechanism to do that.

The survey was the best we probably could do under the circumstances to test expert opinion. I personally think that they did a good job. I can't quibble with the results. I would not want to revisit it. I am made comfortable by the concept that I think that the mechanism we are talking about putting in place has the opportunity not only to look at proposed additions to the screening armamentarium but to revisit periodically the existing ones as well, get data, ask for more data to be collected, make sure that there are no problems cropping up that need to be addressed.

So I'm comfortable with us proceeding with a recommendation for implementation of that with the understanding that there's going to be an ongoing oversight mechanism to look at it.

DR. DOUGHERTY: Can I say —

DR. HOWELL: As long as you're brief, Denise.

DR. DOUGHERTY: Yes. I wasn't proposing that the survey be reconfigured because, if you recall, the survey questions were the same questions given to the experts who were supposed to bring the evidence to us. So it would be that approach addressing the evidence, not doing a survey.

DR. HOWELL: We'll look at that.

I think the other thing that's important that we need to keep in mind is that we will need to have a mechanism for continuing input of the public and parents and so forth about these tests, because their positions and ideas on this are very important, and such things as burden of disease and so forth is very, very dramatically different if you're dealing with the child at home as opposed to sitting in a ninth floor office building and seeing them every month. So the mechanism of including that will be important.

Piero?

DR. RINALDO: I think one thing to keep in mind is that the process there was really driven by the fact that we had 84 conditions to consider at once. So somewhat it was preventing the opportunity to give undivided attention to any given one. So I completely agree. In fact, I think that because some of the conditions that we are likely to revisit in the next round were already included, I think it would be a good opportunity to compare the outcome of what happened the first time with what happened the next time when we do it with a modified and likely to be improved process. So I really don't see a problem with that. I think it's absolutely the right way to go.

DR. HOWELL: I think we have a plan. We will get expert opinion about this document and move ahead.

Let me do two things. Since Jennifer isn't here and she has passionate feelings about this, I want to comment about two things before we move on. Her letter has some greetings at the beginning that I won't go through, but she points out that, "The proposed charge for the Laboratory Standards and Procedures Subcommittee seems too wide a domain for one subcommittee."

DR. RINALDO: Rod, can you tell us where this is? Sorry. I'm trying to find it.

DR. HOWELL: Yes. It's in Tab 6 at the very, very back of Tab 6. I'm reading this predominantly for the audience that doesn't have it. "However, I prefer leaving the various elements of the charge with the Laboratory Committee that's directly related to the laboratory, and I suggest reassigning the responsibility of defining the uniform panel, which is much broader in scope, either to be handled by a working group of the full advisory committee or a subcommittee." That's the situation that Amy is talking about, et cetera.

"Defining and implementing mechanisms for the periodic review and assessment of the infrastructure services and laboratory procedures are clearly a high priority and need to be undertaken immediately to support the effective implementation of the current uniform panel."

She then continues to talk about "Defining and implementing a mechanism for the periodic review and assessment of the conditions" — I think Dr. Alexander helped in writing this — "to accommodate new data and capabilities is a huge undertaking and more appropriately might be handled by a separate or additional group." Again, I think we would all agree that those are important areas, and that can again be a subcommittee or an ad hoc working group.

Dr. Alan Hinman is here, and I'm going to get out of the agenda completely and ask if he would like to make a few comments about the vaccine program, since that's an area in which you, to say the least, have great expertise.

DR. HINMAN: Thank you very much, Dr. Howell. My name is Alan Hinman. I've worked with the Centers for Disease Control and Prevention for many years and for 10 years was in charge of the immunization program. I was at one time executive secretary of the ACIP. The ACIP has been in existence for about 40 years. It started as a committee of 15 members who did all the work themselves. They reviewed all the evidence, they wrote all the recommendations.

As life got a little more complicated, they began to depend more and more on staff, and currently the ACIP, its work, a lot of the content work is done by staff, predominantly staff from CDC, but also people from NIH, from Dr. Alexander's institute and from other places. So it is somewhat a different situation. Its charter, as I understand it, is also somewhat different. The ACIP has about five, I believe, ex officio voting members from the government, from the various government agencies involved, as well as having about I think between 15 and 20 liaison members representing agencies such as the Academy of Pediatrics, the Academy of Family Physicians, American College of Obstetrics and Gynecology, nurse practitioners, a variety of other groups that are interested, the AMA, and the National Medical Association.

These add a lot of expertise to the discussion. These are non-voting members. The way the meetings are set up is there's sort of an inner circle, like this one, of members and ex officio members. Then there's an outer circle of the liaison members, and then there are the rest of us, who are invited for public comment. But the ACIP has been developing recommendations, as I say, for about 40 years. They have recently become more and more interested in explicit evidence-based approaches, as we've been talking about here.

You're a newer committee than they are, but you are coming into a situation which is already very complex, whereas with the ACIP things started out a lot simpler. There were a limited number of vaccines, evidence was really pretty good even though the studies maybe weren't as nice as one might like. So I think the situations are not identical, but there are some nice parallels.

This is the first meeting of this committee I've attended, but one of the differences I think is the amount of staff work that goes into researching the issues, drafting statements with members of the committee who form subcommittees or work groups around a particular topics. There was one recently on meningococcal conjugate vaccine, which included members of the committee, other people who had expertise, representatives of the manufacturers, as well as CDC staff, and they drafted the statement that then was reviewed and approved by the committee.

You're in a situation where at the moment I don't think you have quite that level of staff support, but you're describing problems which are going to be, from my perspective, very difficult for you to resolve as a committee that meets four times a year. It's going to take subcommittees, work groups and other people to help resolve a lot of these issues, both methodological and content.

So I'd be happy to answer any other questions about the ACIP. I would, since I'm at the microphone, with your permission I'll make a slightly separate comment. That is that I think Dr. Dougherty's suggestion to in essence have a review of the approach used in the ACMG review basically to determine whether there are any fatal flaws in the approach — I don't think they're there, but I believe that would help some of the discussion and some of the criticisms that were raised, and also could suggest ways in which, as you go forward, to assess other conditions. There might be some ways of improving on, because this was clearly a massive undertaking.

I'd be happy to try to answer any questions.

DR. HOWELL: Thank you very much. It's very helpful to have an expert on hand when we were talking about the vaccine area and so forth.

We were, not too long ago, talking about the decision-making process and so forth, and I wonder where we are with this and what you would like to do as far as moving forward about decision-making of

this committee. We're going to come back and talk about the subcommittees later, so let's not talk about that right now.

DR. TELFAIR: Just a comment. I'm not quite sure where we're at either, or left off, but it was a comment that I wanted to make when we were on that track about evidence, because we were talking about the scope. I think in terms of considering the scope of evidence, that considering that there are going to be decisions being made, that we need to make sure we broaden the evidence in the areas by which decisions are going to be influenced.

What I mean by that is that clearly the type of evidence we need to look at is data related to programmatic implementation and issues, as well as any kind of consumer data, particularly for our group, which is follow-up and treatment. We have to look and see what studies have been done in those areas in terms of that, because if we're going to make recommendations, or if we're going to move in the direction that we're charged to do, we have to consider what else has been done, how successful has it been, does it make sense to go in the same direction, what are the strings that we can assist, et cetera, as we do this evidence review. So I'm just suggesting that we keep that in mind as part of what we do when we consider what kind of evidence to be looking at and scope of evidence. We need to be a little bit more diverse in it as well.

DR. HOWELL: Do you want to continue our discussion on decision-making? Do you have additional wisdom on the subject?

DR. BOYLE: I think I'm a little lost.

DR. DOUGHERTY: Yes. What kind of decision are you trying to get to?

DR. BOYLE: I feel like we're bouncing around a number of different issues, and I'm not the only one.

DR. HOWELL: I think the thing is that we've discussed how we would examine evidence. I think that we have some general ideas on that. We would look at it in a systematic way. We will have experts with preplanned areas that will be examined in those decision-making processes. That was the one thing that certainly was not in the ACMG report. In other words, there was not a series of questions that were to be asked prospectively about each of the articles. I think we discussed that we were going to be doing that. I think that's the main subject.

We touched briefly on cost/benefit, and that was touched very lightly in the previous studies. Is anyone interested in pursuing that at great length at this point in time? The question is are you interested in pursuing issues related to cost/benefit in any depth as far as looking at adding additional tests and so forth to the panel? We're talking about going forward at this point in time.

DR. DOUGHERTY: Well, I think if this process happens where we have some experts review the current or previous criteria and suggest some improvements, are you suggesting we ask that they may think about cost effectiveness? Because have we decided on moving forward with that kind of approach, where some group of experts is going to review the current — the ACMG criteria suggests some improvements in how to do it and bring it back to the committee. Should we vote on that?

DR. HOWELL: I thought we had agreed on that, but maybe we should formally vote on it. I thought we had agreed that we would ask the group of experts on my right here to review the algorithm that we've had, if they would be willing to do that, and Michele can talk them into doing that.

DR. LLOYD-PURYEAR: David is going to kill me.

MR. ROBERTSON: Don't ask. They may say no.

(Laughter.)

DR. ATKINS: What timeline are you talking about?

DR. HOWELL: Soon, but I don't know that we have some concrete date that's going to fall out of the sky.

PARTICIPANT: Before the next meeting. By the next meeting for sure.

DR. LLOYD-PURYEAR: So, David, you're going to do that? Jack, do you want to take a look at it too?

DR. DOUGHERTY: We can go back and ask for some further assistance from the agency.

DR. LLOYD-PURYEAR: So you're asking him to review the algorithm?

DR. HOWELL: That's in the executive summary of the ACMG report.

DR. DOUGHERTY: And the fact sheet criteria.

DR. RINALDO: Not the fact sheet. The criteria, and how the criteria are weighted. That's really it. The criteria really are the first step in the algorithm.

DR. LLOYD-PURYEAR: Review the criteria, review the weight of the criteria. What else?

DR. RINALDO: And the algorithm.

DR. HOWELL: The algorithm is, I think, the most important thing.

DR. LLOYD-PURYEAR: Are you asking him to apply it to a disease?

DR. HOWELL: No.

DR. DOUGHERTY: No. I think we're asking them to review the process, including the criteria, the weights, the method for collecting data, and give some advice about how that could be improved for the future.

David, does that sound like a charge that someone on your staff could do?

Of course, I'm kidding. David doesn't have staff.

DR. ATKINS: Yes.

DR. HOWELL: Is everyone in agreement with that? Any concern about that? Any further questions or anything?

I think that we're moving on.

DR. EDWARDS: The only concern that I have about it — I mean, I'm all in favor of it, but I don't think it should stop our process. I would like to see us today, as Derek had suggested, go ahead and respond as best we can to the Secretary, respond to the criticisms, and we acknowledge up front that there are people who have been concerned about the process by which it was done, that we have evaluated this and we discussed it at our meeting in April, and that we discussed it again at our meeting today. We feel comfortable that although it is not perfect data, it was a very difficult study to do and that we feel that a good job has been done with it, but that we are asking as a further confirmation of this an expert group to look at it again just to be as sure as we can, and that we believe that this should be assessed in terms of a dynamic process with the model of the ACIP being before us, so that we're not just looking at this once. We will have a continuous method for evaluating and reevaluating.

But what I'm trying to say is a long way of saying that I think we should start answering the question, that we shouldn't delay anything further by waiting for this report, but that we should move ahead. But as Derek has suggested, and I think this is very important, we should confront this question that's been raised and the criticisms head on, as I think we're doing, and that these are ways that we're doing it, but that we should move on, that we shouldn't wait three months until somebody reassesses this, but we should recommend that we move forward.

DR. HOWELL: Well, I think the reassessment is for the future as we move forward, in looking at the future and not at the past. We can comment that we're aware that there are some areas that can be perhaps enhanced for the future, but that the report — I think you put that very well. That would certainly be my sense, and again, we're going to go back at the end of the day tomorrow. We're going to leave promptly at 3 o'clock tomorrow, I might point out, for a variety of reasons, but we will come back to this, but the first thing on the letter, the first thing, confronted the issues, as you recall, and we'll look at those again tomorrow that have been raised.

Does anyone else want to say anything about the decision-making process?

MR. ROBERTSON: I guess one thing that wasn't clear is that it's still going to stay in the Lab Subcommittee, because I don't have a problem with that. I mean, I think they could look at it if they're going to be making decisions. They, in other words, would be bringing back a decision. If they were to look at the new conditions and then bring it back to the full committee after they have looked at it, I think that was a question that Jennifer had raised in her letter, and I don't know if we've actually resolved that.

DR. HOWELL: That's been discussed on the conference calls a good bit, and that's what Amy discussed earlier today.

MR. ROBERTSON: So are we going to leave it there?

DR. HOWELL: Well, we're going to discuss the subcommittee charges, and we can talk about that a little bit more, but again, the vaccine program I think has relevance to this as we go forth as far as adding expertise to the future.

DR. BECKER: But the review of the algorithm process has application to this discussion as well. There are two issues. Both of those issues tie into some conversation of the subcommittee's charge, which is actually how we got started on this whole thing to begin with.

DR. HOWELL: Yes.

DR. BECKER: So I think there are a couple of issues. I mean, not to finalize things, but Derek, for your response, we may not come to a final conclusion on this until after some more information is in.

DR. HOWELL: But there's general agreement that the adding or deletion of conditions is of broad interest to the committee and the decision will not reside in any subcommittee, but that work may start in a subcommittee and expand and having an additional work group, et cetera. I think that's clear.

Greg, you had a comment?

DR. HAWKINS: I just had a quick question. Have we thought about the process of how someone would request whether a new test be evaluated or comes in to the committee to be evaluated? Who will make that request? Does that come from us? Does it come from an individual? Does it come from a group?

DR. HOWELL: It hasn't been discussed. What's your wisdom? Because we hopefully will soon start having, like real soon, some things to think about and talk about.

DR. RINALDO: I think it probably should come from HRSA and HRSA should inform the public and the various professional organizations that have all sort of connections and affiliations. It's almost a call for applications. I mean, if you have a condition that you think needs to be evaluated or should be considered, there should really be a process. You'd say, "We would like this condition to be considered."

Then at that point, once we have those, rather than having us going around the table and saying, well, SCID or whatever, I would rather keep the committee separate from the process and see what comes up. I'm pretty sure that, even in the audience behind us today, there are probably people who are just waiting for that opportunity. I think it would be more important than to see how we're going to consider.

So again, in trying to not delay things too much, it would be great to have already this happening between now and October, and so that could be part of the meeting in October. Just see by what level of interest and what level of specific proposals might come forward, and then decide, because it's one thing if we got two. Obviously, it's a totally different story if we have 50, but that also is a way to really have a sense of what kind of work we have ahead of us.

DR. HOWELL: Peter, can you provide us insight?

DR. van DYCK: Well, I don't know if I can provide insight. I can provide the thought that to me this is a committee process, not a HRSA process, and I think however the committee decides issues should be raised to them — from the public, from a government agency, from a member of the committee — I see it as arising from multiple areas, and then be a committee decision on what gets reviewed according to these forms, and then a recommendation made to the Secretary. I mean, that is the way the committee works.

DR. HOWELL: Right. Now, how would you suggest that we acquire recommendations? I guess that's the question. You know, from the public or from professional groups?

DR. van DYCK: Well, you have a couple of methods already. One is you get letters. You have a public comment period where people could formally raise that issue. I mean, I think you have several mechanisms. You might want to create a mechanism for doing it.

DR. HOWELL: Coleen?

DR. BOYLE: I actually sit on another committee at NIEHS. It's not a federal advisory committee. It's an NIEHS committee that evaluates reproductive hazards, and anyone can nominate a particular chemical, drug, whatever exposure they consider might be a potential reproductive hazard, and then there is an informal evaluation process that goes on. Obviously, there's a work group that takes that on

and they do a review, a preliminary review, and that's submitted to the committee. Then they decide whether there's enough evidence there to justify a more formal review. So that's just a way to try to standardize that approach.

DR. HOWELL: I'm concerned about having a mechanism that's fair, that everybody is aware of or potentially aware of how to get a recommendation in.

DR. BOYLE: Well, that's part of our public comment. We have a public record.

DR. HOWELL: Do you advertise it in the public or anything? Do you have to come to Washington and testify?

DR. BOYLE: No, no. You can nominate a particular hazard via email and just bring up that you're concerned about X, Y, and Z, and then the committee does a preliminary evaluation of the evidence and then a more formal evaluation if it's deemed necessary.

DR. HOWELL: Piero?

DR. RINALDO: Well, I'm wondering, also considering the timing and looking at the October meeting, hopefully we'll have a sense of the potential improvements we can make to the criteria and to the algorithm. At the same time, when the notice of the next advisory committee meeting is posted — I believe it's published in the Federal Register — there could be there something that specifically informs the public that in one of the public comment periods, there will be an opportunity to sort of nominate conditions for, again, the next level of review.

So at that point, we'll have possibly a vastly improved process and we'll have a time to discuss it, and then at the same time, we can say, okay, now we have a better process, and so we can discuss the list. That would be certainly that you really clearly define that people have no more than five minutes, but that would be interesting to also to see — we cast the net and we see what we catch or what comes up.

DR. HOWELL: Peter?

DR. COGGINS: Yes, I don't know what process we'll ultimately adopt, but I think it's going to be important to — because if you look at some of the decision points in the algorithm, I mean, one is is a test available? Is there treatment available? That changes all the time. So I think as a sort of standing agenda, maybe a starting point is to rereview some of the 86 tests which were not adopted in the 29 and just go through that, because if a test is now available or if a treatment is now available, that would change the ranking.

So I think you need another mechanism to identify other opportunities that come over and above that, but I think as a standing agenda, take a look at what's already been identified, but discarded for whatever reason.

DR. HOWELL: I think your point is well made. Obviously, on that original group, there's a considerable number of over 20 conditions that are "no test available," and I would assume that many of those are going to be high-priority items. Some of them I'm aware have had tests developed since this report has been published or put together.

Well, it seems to me that the sense of the committee I hear is that we should take information from anybody that sends it to anywhere before the committee with no restrictions. Is that fair?

DR. LLOYD-PURYEAR: Yes.

DR. HOWELL: And you can put it in the Federal Register?

DR. LLOYD-PURYEAR: Yes.

DR. BOYLE: I just feel like we need to have our process together before we actually do that.

DR. van DYCK: Right. Yes, I would agree. That's what I was going to jump in and say.

DR. LLOYD-PURYEAR: I was going to say, I think we need to —

DR. van DYCK: I think there needs to be a process. It needs to be approved and voted on, we all need to agree on it, and then that can be available to the public and announced in the Federal Register that that kind of process is available. It gives people at least an idea, so that everything in the world isn't proposed. There is something against which an individual can judge their sense of success for the committee before they submit. We might even want to say that they should submit a form as a draft. I mean, I think there's some discussion that needs to occur before we open it.

DR. RINALDO: I agree, and I'm fully aware that we might end up with about 15,000 entities.

Yes, I think there should be a form and perhaps it should be focused again on what Peter said. You know, very much as a first pass, the test and the treatment, and it's fairly easy to evaluate if a test is available because you really need, beside the description and methodology, to have data, biosensitivity, specificity, positive predictive value, detection rate.

So again, you can tell there. Really, you can, and obviously, if people just say "not available, not available, not available," it would be quite conclusive in what you're going to do. You say, well, come back when you have it.

So if we can define a relatively simple form with key questions about the test and the treatment, then I think we really will have enough, and this could be done ahead, I think. We can sort of somehow find a mechanism to collect these applications and then evaluate them electronically to have something here already that made the first pass by the time we meet in October.

Or, I realize, you could say let's talk about all this in October and then do it in January. Again, I would personally like to keep the pace somewhat going, but it could very well be that that's a discussion of this criteria that could happen in October. It's entirely up to you and how fast you want to move.

DR. BECKER: Rodney?

DR. HOWELL: I would like some more time, but on the other hand, I hate to wait months for something that's fairly straightforward if we can accomplish something.

Bill?

DR. BECKER: At the risk of developing an idea on the fly, indulge me for a half a second here, because I like Piero's idea and I think it speaks to what Peter suggested as a format or some standardization of how these requests are made.

At the risk of maybe oversimplifying the process, but if we take a subset of the criteria tool itself and create an entry point, an application or a nomination — yes, that's probably the correct word — a nomination form, and Piero, I'd be willing to work on it with you, if we could have some subset of those key elements like Piero suggested — availability of a test, a treatment, and maybe some other fraction of those criteria that we have already actually kind of looked at or thought about — that might form the basis

of an application or nomination form format that we could utilize as a process for bringing candidate conditions up to the level of the committee's consideration for discussion then at a subsequent meeting, whenever that could be.

The question really, and Piero sort of alluded to it, is can we create that form in the intervening time between now and October and get it vetted through the committee to be utilized or is it going to take a little bit longer than that? I guess that's really the question that could be there, but I think we could come up with a short form — a nomination form, for lack of a better term — that might be acceptable for use in bringing candidate conditions before the committee.

DR. RINALDO: It's really driven by the timeline because, on the other hand, one could make the argument that it would perhaps give greater confidence if we were using criteria that had been through the experts or the external review that we were talking about before, rather than having somewhat a risk or a chance that we use them now and then we find out that perhaps there was some major change that could improve them.

So I don't know. Either way, I think it's a reasonable process. It's more about if we try to do it between now and October or we should be sort of planning to have the first round of these evaluations next year. That's really what it is.

DR. HOWELL: Denise, you want to comment?

DR. DOUGHERTY: Yes, I would just like to clarify I think something I've heard Piero say before, and the difference between that and an ACIP or some other process is that I think I heard you suggest that it should be the responsibility of somebody who is proposing the condition be included to actually fill out the entire form, whatever the decision-making process is. You have said that.

I really think that's really putting a burden on families or others, and I think there should be an independent process of the committee that would not be so burdensome. The nomination form could be clearly really less of a burden, but then it would really be an independent process of the committee, whatever it is we decide to do, that would actually judge whether the condition really meets the criteria.

DR. RINALDO: Sure. I mean, it could happen that a lay person decides to nominate a condition, but let's say if we talk about SCID, although I'm sure Amy could do a great job, I would expect Rebecca Buckley or Jennifer Puck to be the person that takes that role. Again, you can think of lysosomal conditions. I don't think it would be the parent of a child with a disease, but rather it would be recognized professionals that know what is presented.

But again, I don't know why we have to be so strict. But I really think there should be professional involvement in this. It could be organized parent support groups or it could be professional organizations. You know, we really don't know what could show up.

DR. HOWELL: Amy?

DR. BROWER: What's the breakdown, Coleen, on the requests you get on the environmental or the toxins? Do parents or consumers nominate?

DR. BOYLE: Yes, consumers do nominate. I mean, it's not the same volume. It was initially a big volume, but it's not the same volume. Each quarter we meet, and there are probably seven or eight nominations, but this committee actually has money and staffing to do a preliminary evaluation of any nomination, which is something we don't have.

DR. DOUGHERTY: But I think my point is still that going through a systematic process the way it might be suggested, even what you did with the ACMG report, would be very onerous for an individual or even a group of parents or even a set of professionals.

I'll use as an example, and David can weigh in here, we have this evidence-based practice center program, and the way we get nominations for conditions or topics for them to review is to ask professional societies for the questions that they need help with. For example, we've got one on toilet training. What's the evidence behind the kind of advice you can give for toilet training? And it's even very hard for these professional organizations to come up with a question, a set of questions, that corresponds to what the evidence-based practice center can actually look for.

So it's a two-step process. One, getting the topic, and then having a group of experts look at what the preliminary evidence is, and then actually the third step is doing a full-fledged evidence review if there's enough there.

DR. HOWELL: My thought on the process is simplistic, and that is I think there are really two questions you would have at the onset. Number one, we would assume the condition would be substantive and of major concern, and you would want to know is there a reliable laboratory test available? That would, of necessity, have a reference. Is there a treatment available? That would have a reference.

Those are the two key things I think that would permit it to get out of the gate, and I don't think that either of those would require further study by our experts because those are two very basic things, a test and is there a treatment.

DR. RINALDO: It sounds to me like it's writing an abstract. You provide a succinct set of information, in this case facilitated by the fact that you had to respond to specific questions.

DR. HOWELL: Right.

DR. RINALDO: Now, obviously it would require some thinking, but to say it's a huge undertaking, I don't see that. Perhaps I'm missing something.

DR. HOWELL: Anybody else have any comments about this document?

(No response.)

DR. HOWELL: Is it something you think could be developed promptly, so that we could get some input before the October meeting?

DR. BECKER: I volunteered Piero, and I don't know if he is willing to work on it.

The other thing I would say, if this helps you, Denise, for the ACMG report we had parents complete the entire survey tool. So even a small subset of that I think is achievable.

DR. HOWELL: Well, can we work with these two to come up a document?

DR. LLOYD-PURYEAR: Yes.

DR. HOWELL: Michele will work with you two, and we can try to get some input before the next committee.

DR. LLOYD-PURYEAR: That's fine.

DR. HOWELL: We don't have a process currently in place for vetting these, but we can see what we can do.

DR. LLOYD-PURYEAR: Send it out by email.

DR. HOWELL: Send it out by email, but then we also don't have time today to discuss how we're going to handle these when they come in.

DR. RINALDO: So the conclusion is that in October we'll review the first attempt to define the questions or we want to handle that sort of remotely and then see some examples coming from the system?

DR. HOWELL: Is that the sense of the committee?

DR. BECKER: I think it would be possible to have some candidate conditions nominated by October.

DR. BROWER: And I think as a committee as a whole, as we get rolling on some of these issues, we're going to have to start working remotely because four times a year isn't enough to get accomplished what we need to. Several issues need the committee's buy-in and advice as a whole, not just the subcommittees.

DR. van DYCK: I think it's important the committee not raise expectations that we can't meet, and I think it would be wonderful to get the nomination form developed, basically the draft approved by email, and then when we come face to face, we have a document in front of us that we can use as the basis for a discussion of what process then we can implement and where that fits in the implementation. I just think we need to have a process down before we invite from the public input.

DR. HOWELL: That's a sound conclusion. I hear nodding of heads, and I don't know whether it's because it's 5 o'clock or whether you agree.

(Laughter.)

DR. HOWELL: But why don't we then go ahead, Piero, and you and Bill can work on a document, we can look at it by email, and you will have it then for the next report. By that time, we will also have a little clearer plan of how we're going to move these through the subcommittees.

We urgently need to move ahead to discuss the subcommittee charges. We're going to review the subcommittee charges, and I doubt that this should be terribly lengthy or onerous. The only interest seems to be in Amy's committee. There may be others. I'm just joking.

But the thing is that the committees are going to be meeting in the morning, and let me remind the folks in the audience that they're open to everyone here, and I hope that you will go to your favorite committee and comment.

Can we start with the first committee on the agenda here, which happens to be Steve Edwards' committee. Actually, it's Jennifer's committee that Steve Edwards is reporting since Jennifer was unable to be with us today.

DR. EDWARDS: Did you want me to read the material here? I think, unless people have questions, that we don't need to read it.

DR. HOWELL: I would agree.

And where are the charges? What tab are they in?

DR. EDWARDS: It's on Tab 7.

DR. HOWELL: So the Education and Training Subcommittee is there.

DR. DOUGHERTY: Could I just make a suggestion that we let the people in the public know or have a sign up tomorrow about where these subcommittees are meeting? Because that's not on the agenda.

DR. HOWELL: Right.

DR. DOUGHERTY: We're not doing it at 9:00, so there's time. No, we are doing it at 9:00.

DR. HOWELL: It's the first thing out of the barrel. I don't know where they're meeting, so maybe we can find out in the meantime and announce that.

DR. EDWARDS: We need to also let the committee members know.

DR. HOWELL: That will be helpful.

(Laughter.)

DR. EDWARDS: It's not the first thing in the morning.

DR. HOWELL: ACOG is first.

DR. EDWARDS: ACOG is first. So we'll all be here.

DR. HOWELL: So if we fail to have those information bits today, we'll have them in the morning.

DR. DOUGHERTY: Thank you.

DR. HOWELL: Now, you've got the presentation here for the committee. Is there any comment about the Education and Training Subcommittee?

DR. DOUGHERTY: We might say what they are for the public.

DR. HOWELL: They're here, but you want to read that?

DR. EDWARDS: If you want me to.

DR. HOWELL: Well, it's just one page.

DR. EDWARDS: But some of them are a lot longer.

DR. HOWELL: Well, I know, and we won't read them.

DR. EDWARDS: It says, "Review existing educational and training resources for heath professionals, parents, screening program staff, hospital birthing facility staff, and the public, and then identify gaps and make recommendations for action regarding the five groups."

DR. HOWELL: And we will hear a report from your committee tomorrow after you've met about what you're doing in this area.

It's been interesting to me how much interest there is in the education area, which has been gratifying, and people have talked to me about interest that they have in educational aspects of newborn screening. So I think there will be a lot of support for the work of this committee from other groups that can come and help your committee that are not members of the committee.

Well, that was quick. Now we'll move on to the Follow-Up and Treatment Subcommittee.

DR. BOYLE: Before we leave this, I guess last time during the education presentations, we had that fine presentation from the woman from Louisiana, who's name I don't remember.

DR. LLOYD-PURYEAR: Terry Davis.

DR. BOYLE: Yes, but she obviously made the point very well that there are a lot of materials there, but in terms of literacy level and just from a health communication and education standpoint, they were lacking. Is that what you were thinking about in terms of gaps?

DR. EDWARDS: Yes. Actually, some of this is already being done. We're going to hear from ACOG and from the American Academy of Pediatrics and others. Actually, these things are already being field tested, but one of the gaps, too, is the question about literacy and understanding.

DR. HAWKINS: I was just going to suggest maybe we change the word from "gaps" to "deficiencies"?

DR. HOWELL: Okay. "Identify deficiencies." Are you agreed to that?

DR. EDWARDS: Yes.

DR. HOWELL: Excellent.

Coleen, we'll do your committee.

DR. BOYLE: Sure. I'll read our charge. "The charge for the Follow-Up and Treatment Subcommittee is to engage in a multi-step process that identifies barriers to both short- and long-term follow-up of newborn screening results. Specific to the challenge is integration of health care systems, financing of services, and information technology." That's the first bullet.

"Develop recommendations for overcoming identified barriers in order to improve these results, and then to make recommendations for mechanisms for establishing accountability for newborn screening follow-up guidelines."

DR. HOWELL: Amy?

DR. BROWER: Well, I just have a question. Because this current panel is based on the literature and we looked at the literature to tell us whether or not there are treatments and do these treatments work, the Follow-Up Subcommittee is going to be finding out this information sooner than things are

published. So is there an opportunity to capitalize on information systems that you guys might recommend being set up, so that we find out earlier is this current panel working and are treatments working?

And was there any plan in the subcommittee to start to foster clinical research in head-to-head trials of different treatments? Because this is follow-up and treatment. So I was just wondering in the treatment area.

DR. BOYLE: I can be honest with you. The committee hasn't really thought a lot about the treatment-related issues, and in reading the public comments, I guess that was one of the issues that was sort of glaring for me. So that's clearly one of the issues that we need to discuss tomorrow, and also obviously all the implications from the conversations we've had so far in the committee. I appreciate that.

DR. BROWER: Yes, maybe access, because I know for the Laboratory Committee and the committee as a whole, how this panel is implemented and how treatment and follow-up is going with the implementation of this expanded panel is important in deciding whether to retain these tests on the panel for the future. So I just wanted to know if there's an opportunity to build that data into the committee's deliberations as a whole as you guys find out early about follow-up.

DR. HOWELL: How strong is our data on follow-up programs in the states? Do we have a lot of data about it? You know, I know that this is being done and that's being done, but is there a systematic effort to say that 31 states have well-organized follow-up programs and so forth? Do we know that? Do we have that? Does that come through HRSA?

DR. THERRELL: It does.

DR. HOWELL: It does.

DR. THERRELL: We have some of that data.

DR. HOWELL: So you think that you will have an opportunity to provide really good data about the follow-up?

DR. THERRELL: We collect some of that data and we're going to collect more, and there are a couple of research projects that we're funding right now. Those people are going to report at the request of the subcommittee on follow-up issues. So yes, there's a lot of information that we have.

DR. HOWELL: Well, I'm sure we'll have more information about that.

Any further comments about Coleen's committee?

DR. BOYLE: Actually, I have a comment after we're finished talking about the charges of the committee, just a more general comment about the charges of the subcommittee versus the sort of larger charge of the main committee. Maybe we can discuss that after.

DR. HOWELL: Okay. We'll hear from Dr. Brower, and then we'll go back. She's going to need about an hour.

(Laughter.)

DR. BROWER: No, I'm not.

We just included some background slides to remind ourselves, mostly, as a subcommittee of what the charter of the larger committee is. So that's what the first slide just goes through and I won't read that, and then the Laboratory subcommittee members.

We have three proposed charges of our subcommittee. We want to define and implement a mechanism for the periodic review and assessment of the conditions included in the uniform panel, the infrastructure services needed for effective and efficient screening of the conditions included in the uniform panel, and the laboratory procedures utilized for effective and efficient testing of the conditions included in the uniform panel. So we're really all about definition, implementation, and some information from the follow-up group on adoption and how that impacts the current panel and future panels.

That was just a quick overview.

DR. HOWELL: Let's have some further discussion about organizational aspects before we come to the thing tomorrow about how your committee — let's refocus on the discussion of earlier today — would deal with the addition of new conditions, which has been one of the main areas of discussion in Jennifer's letter and so forth.

DR. BROWER: And we've had a lot of discussion in our subcommittee about how to organize this and had come up with the idea of ad hoc working groups, where we would invite experts to participate in the working groups and the working groups would work outside of the subcommittee, but would work on an agenda that's drafted by the subcommittee, but approved by the committee as a whole. So the committee as a whole will have visibility into what these ad hoc working groups are working on as well as the process that they're using in their determinations, and that we'll be sort of a facilitator of that information being presented to the committee as a whole.

DR. HOWELL: Comments or questions of Amy about that?

DR. DOUGHERTY: I guess I would defer accepting that charge until we have this review and hear from the ACIP in October about what the best mechanism is to proceed with considering new conditions.

DR. HOWELL: It's my impression, and again, I'm not an expert on the vaccine program, but the vaccine program I think indeed uses working groups that are established. Is that not correct?

DR. HINMAN: Yes.

DR. HOWELL: Yes. So that establishing working groups that would have broad expertise that's related to a specific issue is exactly — we'll hear about that in detail, but I think that is how that works.

DR. HINMAN: Yes. The working groups are ad hoc around a particular topic. They include both members of the committee and others, including industry representatives, you name it, to discuss a particular issue and bring something back to the overall committee for the committee decision.

DR. DOUGHERTY: Well, I guess the question is are they working groups, ad hoc working groups, to a subcommittee or to the entire committee?

DR. HINMAN: Typically speaking, for the ACIP, they're to the entire committee, but in a different advisory committee that I'm a member of, the National Vaccine Advisory Committee, sometimes committees have work groups also.

DR. HOWELL: Or subcommittees have work groups, right?

DR. EDWARDS: This was one of the concerns that I had, and I think that this is a concern that Jennifer Howse was raising in her letter to you about wondering about the volume of work that was being accepted by the Laboratory Committee.

So I think that if this model, the ACIP model, were to be adopted and responsive to the whole group, I think that clearly that would alleviate my concerns, and I think it would alleviate Jennifer's. If it were organized around the Laboratory Committee, then I think that my concerns would still be that this is a big plate for this one particular committee.

DR. LLOYD-PURYEAR: I just want to make sure. I'm writing this down. But you're comfortable with the way Amy described it, that it's only there providing the infrastructure, but it's answerable to —

DR. EDWARDS: Yes, but I would like it to be answerable to the whole committee.

DR. van DYCK: I wonder if this is an issue that we could have fuller discussion on tomorrow during the presentation from the subcommittee. I mean, it's just kind of hit us cold here.

DR. HOWELL: If you have working groups of the whole committee, you kind of end up then with subcommittees and working groups and so forth, and I think we'll need to think about how that will work out.

DR. RINALDO: Well, I thought it was stated pretty clearly that whatever these subcommittees do, any sort of decisions about recommendations are made by the full committee. So really the subcommittees are sort of the proponent for things that come here to the whole committee for discussion. So there are no decisions made by any of the subcommittees. I thought that was already well established, so I don't know what the concern about this is. Nothing is going to happen at the subcommittee level.

DR. EDWARDS: My concern is not you're making the decisions. My concern is the volume of work that is there for the group to do. I mean, I trust you to make — I mean, it's not that I don't trust Amy. I just felt like you take that out and you've still got a really, really full agenda.

DR. RINALDO: But I'm wondering here if perhaps, you know, clearly you look here at the presentation by the three subcommittees, and two have elected to have basically just a one-page summary of very simple bullets that themselves, you can make the argument, are as large and perhaps even larger than the task that we have in the Laboratory Subcommittee.

I don't really know if what this subcommittee has to do is in any way greater than what the other two have. It's just that there is a little bit more elaboration about the details. So we went to a greater level of detail in expressing the things we have to do, because you can go a few pages back, and I can tell you when you start looking at the amount of work the Education Committee is supposed to have —

DR. EDWARDS: We only have one page's worth.

DR. RINALDO: Well, but that again, I really think it's —

DR. BROWER: I could rewrite it.

(Laughter.)

DR. RINALDO: You know, you're talking about education and training resources for five groups. That's a humongous amount of work. So if only you were going to a set of bullets from each of them, I

guarantee you that we could make the same argument about the other subcommittee. You have an equal or certainly comparable amount of work to do.

DR. EDWARDS: I have nothing against your working as hard as you want to work. I'm just saying that I pull this out as being an absolutely essential part of the work of this group, and I think that it is a large volume of work and that you've got enough work to do without that, and that this ACIP group should be responsive to our committee as a whole.

Now, I am not speaking for our committee. I'm speaking for me. I think I can speak for Jennifer. It is my impression that that's her feeling, too.

DR. HOWELL: Bill?

DR. BECKER: Yes, if I could make a suggestion, I think there's consensus about the second and third bulleted proposed charges to the Laboratory Subcommittee, and I think that we could accept those. From a procedural perspective, go ahead and accept those, and it seems like, and I think Denise suggested this as well, that the first bulleted item, where there's been some conversation recently and actually sort of continuing since we started the day with this, needs more consideration. There doesn't seem to be as much consensus.

Perhaps we might want to wait on approving that particular charge to that particular subcommittee until we have a more complete discussion, and it might need the information to be provided at the next meeting before we can make some resolution on it. I'm not saying that we can't agree to the some of the charges that have been proposed, but that we're not quite ready for consensus on that one particular item.

DR. HOWELL: With regard to the documents that Amy has provided, what part would you hold off on?

DR. BECKER: The first bulleted item.

PARTICIPANT: No, the second one.

DR. HOWELL: Well, people are talking about 1 and others are talking about 3. What page are you on?

DR. BECKER: I'm on the proposed charge of the subcommittee for Amy's subcommittee.

DR. HOWELL: And you are on —

DR. DOUGHERTY: Page 3, the first dash, and then it's expanded on page 4.

DR. BECKER: Right. It's the first dash.

DR. HOWELL: You would like to hold at a later discussion the conditions included in the uniform panel. Is that what you would like to hold for later discussion?

DR. BECKER: Steve, is that the one?

DR. EDWARDS: No, I was really more concerned about the third bullet, the one that says, "Establish ad hoc working groups comprised of people with the necessary expertise to evaluate tests,

technologies, and benefits to the individual and to society." That's what I saw as the component of the ACIP model.

DR. HOWELL: Well, the tests and technologies are the core part of their program, and Bill is talking about the first dash that talks about the conditions to be included in the uniform panel, which is the broader issue.

DR. RINALDO: This is actually an issue about the conditions already in the panel. So I'm a little surprised by the fact that suddenly this again resurfaces as an issue.

Perhaps you can rephrase. I understand that now suddenly we have concerns about two out of three. Why? Why now?

DR. BECKER: Well, I can speak to mine. I thought there was some consideration that was needed to determine exactly at what level or what process, I guess, is the better word, the committee was going to utilize for the assessment, the continuous assessment, and then either the addition or modification to the uniform condition panel.

By that, I specifically mean the process we were trying to determine whether that was going to be a charge of one of the subcommittees or whether that was going to be a work group if the subcommittee was going to provide structure to it, because that's what I understood, or could that be some other process, like the ACIP model or any other model that is more centered around the full Secretary's Advisory Committee itself?

That's kind of what I understood from some of the conversations today. Maybe I missed something.

DR. RINALDO: I really wonder if we're having here an issue of semantics because we could have exactly the same conversations about the other two subcommittees if there was perhaps somewhat a greater effort to outline the things that you're going to do. I have a feeling that if we had a one-page summary of the things with absolutely generic language, we wouldn't be having this conversation.

I think, again, because nothing really happens and is carved in stone at the subcommittee level, I think that the rest of the committee should at least just give an opportunity to this subcommittee to get their thing in order and come back with something. Then, rather than arguing about it in advance what we're going to do, but actually argue or discuss the outcome of the work of the subcommittee. Nothing will happen and nothing will be decided, so why don't you wait and see what gets done to really see if something is wrong or right?

I feel a lack of trust, really, here that I don't know where it's coming from, and if that's the case, I think you should just say it clearly.

DR. HOWELL: Five o'clock is approaching.

Are you going to talk about lack of trust?

DR. EDWARDS: Yes, I want to talk about that, because I think that I have communicated very poorly if that's your thought. I don't see this as a lack of trust at all. I see this as a huge responsibility. I love the idea of using the ACIP model for that. I just don't see that part to be a part of the laboratory group. I see that to be separate from the laboratory group.

I don't want to stand in the road and block this. I want us to go forward, and I trust Piero implicitly, and Amy. I don't know who everybody on their committee is, but I trust you all, I promise you.

But I just see this as being a huge issue related to the dynamics of the whole program and related to a model that Duane has explained to us, which I think would work very well. I think the only question is should this model, should this program, be under the auspices of the Laboratory Committee or should it be under the committee as a whole? I would prefer the committee as a whole, but if this implied that I don't trust the Laboratory Committee, I would be happy for the Laboratory Committee to do it.

DR. RINALDO: One comment I want to make is you might remember that when we were discussing the subcommittees, the process really went from quite a large number of different areas and topics when we had a sort of reality check and said we had to really condense it, and that's when the decision was to identify the three utmost priorities and develop subcommittees for those three things. They were education and training, follow-up and treatment, and laboratory issues.

So all I'm saying is now suddenly we are revisiting that thing and saying but now we have to add one other one. I'm wondering, because the day that we get a more detailed bulleted list of the things the other subcommittees will do, the same discussion may come up. "Oh, that's huge. That's a lot of work." But I think the committee should be the one who really tried and in good faith come back and say, wait, way too much or we're just not able to do it.

Again, it goes back to the point. Do you really want to have a fourth subcommittee, a fifth subcommittee? Remember, at one point the list was six or seven.

I'm looking at Michele and Peter and really would like to hear from them.

But I thought the reason why we went with those three was because the perception was that otherwise we will be spread too thin and we will really require the involvement of a rather large number of additional people. It could very well be that things have changed now that we've given it some more thought, but I see this as a reversal of a pretty extensive discussion that we had the last time we were here.

DR. HOWELL: Dr. Alexander has a comment.

DR. ALEXANDER: Mr. Chairman, I'd like to just suggest a way we might proceed. I think part of the problem is some discomfort with the concept of putting the most visible of all the activities of this committee, which is the content of the screening panel, under a committee that's called Laboratory Standards and Procedures, where it sounds like there might not be a total fit just from the name, from the nomenclature that we're talking about.

However, I'm not sure we're ready to decide yet whether we need a fourth subcommittee or whether we might incorporate it or change the name or whatever, but as a practical matter, we do need I think to start down the road of some discussion in the subcommittees and report back tomorrow to the full committee about both laboratory standards and procedures and how we might proceed, even though we await some additional information on the ACIP, with the process for consideration of addition of new tests to the screening panel.

So I would suggest that we allow the Laboratory Standards and Procedures Subcommittee, for their meeting tomorrow and their report to the full group, to continue to consider this component of their charge, while withholding final judgement as to whether that would eventually be part of a separate fourth subcommittee or incorporate it within the Laboratory Standards and Procedures, just so that we have an opportunity to get some work done on that particular topic tomorrow and report it back to the committee.

DR. HOWELL: That suggestion has already come from my right.

(Laughter.)

DR. HOWELL: So it's coming from both directions, the left and the right.

(Laughter.)

DR. HOWELL: It seems to me that that's a prudent solution. We'll go ahead and meet tomorrow, and then when the reports come back, we can readdress this issue and see where that might be.

Does that seem sensible with everybody? Let's then proceed with Dr. Alexander's suggestion, which seemed a very sound one.

I think we're done. I think Michele had a list of where we're meeting in the morning.

DR. LLOYD-PURYEAR: We're meeting here.

DR. HOWELL: No. Well, we are meeting here, but there was somewhere circulating a list of where the rooms where.

DR. LLOYD-PURYEAR: That can be given tomorrow. That's for the subcommittee meetings.

But I do have a reminder. Dinner is at 6:30. It's at the same restaurant we've been eating at. So you all can meet at the hotel between 6:00 and 6:15 and come over.

DR. HOWELL: We will see you all bright and early in the morning, and we'll look for you to be filled with wisdom.

Thank you very much for all your hard work today. I think that a lot of things were accomplished. Thank you very much.

(Whereupon, at 5:05 p.m., the meeting was recessed, to reconvene at 8:30 a.m. on July 22, 2005.)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
ADVISORY COMMITTEE ON HERITABLE DISORDERS AND GENETIC DISEASES IN NEWBORNS AND CHILDREN

Fifth Meeting

Friday, July 22, 2005

Rotunda Room, 8th Floor
Ronald Reagan Building and International Trade Center
1300 Pennsylvania Avenue, N.W.
Washington, D.C.

IN ATTENDANCE:

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C O N T E N T S

P R O C E E D I N G S (8:35 a.m.)

DR. HOWELL: Ladies and gentlemen, we are a few minutes late, but the committee has considered this. Let me welcome you to the second and final day of our fifth meeting of the advisory committee. I think we had a lot of very fruitful discussion yesterday that should lead us further along in our work here.

We're going to start off this morning with a presentation by Dr. Anthony Gregg, representing the American College of Obstetrics and Gynecology Committee on Genetics. Dr. Gregg is from Charleston, South Carolina, where he heads the Maternal and Fetal Medicine Program. He is Medical Director of the program there.

Dr. Gregg, welcome to the committee. Thank you very much for coming.

DR. GREGG: Thanks very much, Dr. Howell.

I just want to correct you. I'm from Columbia, South Carolina. Many people don't recognize that there are two medical schools in South Carolina. It is the American College of Obstetricians and Gynecologists, not the American College of Obstetrics and Gynecology.

I just want to make that point right off the bat and introduce you to the American College of Obstetricians and Gynecologists. We're a unified group, and we're unified by a commitment to the health care of women.

This group consists of fellows, both national and international, and there are physicians that have attained board certification in the field of obstetrics and/or gynecology. The college also consists of junior fellows. Junior fellows are ABOG, American Board of Obstetrics and Gynecology, in approved residency training programs in obstetrics and gynecology.

There are associate members. These are physicians typically that are recognized for their provision of valuable services in OB/GYN. Because they have not gone through an ABOG approved residency training, they are not eligible to be fellows. This consists of national and international members as well.

There are these educational affiliates, they hold non-M.D. degrees. They are active in some facet of OB/GYN, again both national and international. Then there are medical students that are also considered in part the membership of ACOG.

In total, there is somewhere between 40,000 and 50,000 members in the American College of Obstetrics and Gynecology. ACOG's missions are primarily four. One is to serve as a strong advocate for quality health care for women, and to maintain the highest standards of clinical practice and continuing education for its members. We exist to promote patient education and stimulate patient understanding of and involvement in medical care.

Our focus is to increase the awareness among the members of the college and the public on the changing issues that face women's health care.

There are numerous committees within the American College of Obstetrics and Gynecology, in fact too numerous to even put on one slide. So I'll cut to the chase. The ACOG Committee on Genetics does exist, it has existed for quite a number of years. The Committee on Genetics considers all aspects of genetics as it relates to reproduction, and develops appropriate recommendations regarding clinical management, education, and research issues.

It has a formal liaison with other groups such as the American Academy of Pediatrics, the American College of Medical Genetics, and the Teratology Society. It interacts with the Center for Disease Control and Prevention and the National Institutes of Health, as well as other federal agencies as needed.

The committee develops written opinions on newly emerging or rapidly changing issues in the field, and responds to matters referred by other College committees and groups.

To give you an idea of the scope of the Committee on Genetics, you will notice that we deal with various aspects of reproduction and genetic issues. I won't show you examples of the types of documents that are put into place to try and educate the members as it relates to things like cancer, but those also exist. This is an example of one. You'll notice also on the right that we from time to time revise these documents, or in this case, committee opinions.

We have written documents on prenatal and preconceptional carrier screening for genetic disease in focus groups in an effort to educate the membership. Even in cases of rare diseases, we've tried to educate the membership as to their existence and how to approach screening.

We do as well approach our membership and try to educate them regarding various metabolic diseases. The first committee opinion put forth by the Committee on Genetics is in your notebook. It was issued in October, 2003. This committee opinion was very germane to this group here today.

What is a committee opinion? An ACOG committee opinion, they represent an ACOG committee assessment of emerging issues in obstetric and gynecologic practice. As I said earlier, they are reviewed regularly for accuracy, and when needed, or when the committee views they're needed, changes are made.

I want to make the statement that ACOG as a general rule, and in fact you can even take it to the bank, makes no policy statements. That's why I put as the title, "policy" in quotes. These are strictly guidelines. ACOG does not seek to establish the standard of care either.

So in that document, I'll summarize what some of the comments are. ACOG recognizes that technology drives change. Newborn screening dates to the '60s with technology such as tandem mass spec, and expansion of newborn screening programs must be considered.

ACOG recognizes the importance of statistical considerations in adopting national and statewide newborn screening policies. In particular, maximum sensitivity and specificity should be sought after. There is a tradeoff between the false negative and false positive rates, so confirmatory testing is required.

This committee opinion goes on to recognize that there is an absence of constitutional or federal mandate for newborn screening, and therefore that state autonomy does exist. State statutes or regulations determine specifics related to newborn screening. Consent is required in two states.

This document goes on to describe that tests are specific depending on the state. The fees vary across states, and the source for the fees in these cases also vary across states. The document recognizes that systems must be in place for adequate communication and treatment, and that these things do cost money.

ACOG recognizes that technology is driving the change, and that costs may prevent families from universal access to technologic advances being considered. ACOG is concerned that tandem mass spec may result in identification of diseases for which there are no effective treatments, that there is identification then of more disease entities, and that this will result in a need for greater follow up. In sum, the potential exists for added cost without benefit, and there is also the issue of what happens to the stored blood spots after their predetermined use.

This document states that the obstetrician may have a role in prenatal education about newborn screening. Prenatal education about newborn screening not only provides parents with an understanding of the reasons for obtaining their newborn's blood specimen, but also informs them that an initial positive test result does not necessarily mean that their child will be affected.

Many patients will turn to their obstetrician for additional information regarding newborn testing.

What about this education? Clearly ACOG is in the business then of providing education to care providers and women. Women are pregnant or non-pregnant, there is no in between. The information then must flow from care providers to women, and ACOG of course believes that there should be considerable attention in educating the care providers.

There is another group, and that's Families with Affected Children, or Families with Positive Screening Results. Care providers provide education to these people as well. But once the education is set into motion, clearly pregnant women talk to other women, non-pregnant women, and non-pregnant women talk to pregnant women. There is an education loop here. We see this day to day in our practices. Also families with affected children help to educate other families and other women.

When should education take place? There are specific time points in a woman's life where this can take place. One is during the gynecologic care. This is a great opportunity, because women come in for recurrent gynecologic care, pap smears, and well woman exams. This starts at an early age. The education process can certainly begin here.

The detraction is that this is remote in the case of newborn screening from the time that this information might be necessary. Preconception counseling visits are a great opportunity to discuss newborn screening. Patients are motivated at this time, they're attentive. The downside is that many patients never present for preconception counseling.

Education can take place during the pregnancy, either early in pregnancy or late in pregnancy. Patients again are motivated and attentive during these time periods, but there can be multiple distractions.

In the postpartum period, again, patients are I think generally motivated and attentive. The downside is that they may be considered a vulnerable population for things like consent, and there are also from time to time other distractions.

With regard to the ACMG report, there is an important omission. That is the failure to include an obstetrician representation on the expert panel. It is uncertain that obstetrician representation was integral in the survey of health care providers and consumers related to the importance of various features of the data collection instrument.

ACOG notes that five major areas were to be considered by the ACMG. However, one of these was discussed extensively, a uniform condition panel. The remaining four areas were discussed with much less focus and vigor. However, I will point out that the uniform condition panel in our opinion was very well thought out and extremely well done.

In fact, the fact sheets could be used to provide a rapid resource for obstetricians faced with specific questions posed by patients. Despite the fact that this wasn't specifically the charge in that first focus of the ACMG report, I think they do already feed into the education resources for care providers.

This will look like it's a little bit of a digression, but I think that it's helpful to understand that the American Board of Medical Genetics requires specific areas of education for people to receive certification in clinical genetics. I've highlighted in yellow a few of those. They clearly relate to the aspects of this committee.

The American Board of Obstetricians and Gynecologists I said in 2002, anyway, has over 33,000 Active Diplomats. That means people who are board certified. Of those, about 4 percent were maternal/fetal medicine subspecialists.

The American Board of Medical Genetics in 2002 had a little over 1,000 clinical genetics certificates. Ten percent of those were people who were also obstetrician/gynecologists. So the point is there is significant overlap in these two groups. The current president of the American College of Obstetricians and Gynecologists is a board-certified geneticist. The current president of the American College of Medical Genetics is a board-certified obstetrician. So again, highlighting the overlap.

The reason to show you the maternal/fetal medicine aspect is because it might be appropriate since all obstetricians, typically the generalist obstetrician, has some referral base when there are complicated pregnancies or genetic issues. It may be relevant to begin some of that training in the maternal/fetal medicine area.

There is already a prototype for education. This monograph that was distributed in October of 2001 was jointly put together and distributed by the American College of Obstetricians and Gynecologists, as well as the American College of Medical Genetics. This monograph I think can serve as a template. This is the table of contents in that monograph, to begin to reach out and educate care providers. You can almost in some cases swap out some of the language here word for word and begin to educate care providers in this format. It's also a format that has already been well accepted by obstetricians in the community.

I'm going to stop there. I'd be happy to answer any questions.

DR. HOWELL: Thank you very much, Dr. Gregg.

I think that those of us in the genetic community have enjoyed a very fruitful and rich relationship with the American College of Obstetricians and Gynecologists. I appreciate your highlighting that.

I think that some of you will recognize that my accent is from North Carolina. In view of that, I'm very aware of the fact that there are two medical schools in South Carolina. But I must also apologize to Dr. Gregg, because I had a long discussion with him before the meeting this morning about Charleston, which is the other medical school.

But anyway, thank you very much. Are there questions of Dr. Gregg? Can I lead off with the first question? I'm keenly interested in what the current policy and practice is in the obstetrics community about educating mothers about newborn screening specifically.

DR. GREGG: I think it's reasonably fair to say that most obstetricians don't take an active role at this point in educating mothers about newborn screening. I think that's probably not incorrect of me to say that.

On the other hand, this committee opinion is reasonably young in its distribution, 2003, and if you'll read through it, I think that there's certainly room for change once this committee establishes that we need to change it.

It is a fact, I think, that as busy as obstetricians are in day to day practice, to spend lots of time in educating about newborn screening, it simply just doesn't happen, I don't believe.

DR. HOWELL: Piero has a question.

DR. RINALDO: Dr. Gregg, I have a couple of questions.

In one of your slides, actually the third one, there is a statement that I completely agree with. That is the importance of statistical consideration. There is a sentence about the tradeoff between the false negative rate and the false positive rate.

I was wondering if your committee gave any consideration of actual targets that will define what is an acceptable performance.

I have another question. I don't know if you want both together.

DR. GREGG: Well, let me try to take the first one first.

DR. RINALDO: Yes.

DR. GREGG: I can tell you that I wasn't on the committee at the time this was drafted. I have thought about your question, and it occurred to me that as I think about the conditions that are included in the panel, clearly the statistical measures are not defined in the report, as best I can tell.

It's interesting, because we look at screening as obstetricians from the standpoint of second trimester serum analyte screening, and we try to look at these and level the playing field by setting a 5 percent false positive rate as the baseline, and then we see what the detection rate is from there when we set that.

DR. RINALDO: So do you realize that if we had a 5 percent false positive rate in numerous screenings, we would have riots in the streets?

DR. GREGG: I can tell you I'm not at all suggesting that you have a 5 percent false positive rate. I am suggesting that probably you should let us know what it might be for each one of these. This is what patients will ask.

DR. RINALDO: Absolutely.

DR. GREGG: And patients will want to know how likely is it if I've got this.

DR. RINALDO: My other question is, and believe me, this is not new territory in the discussion about newborn screening, but I really would like to argue with you a little about this concept of identification of more disease entities will result in the need for greater follow up. That's a fair statement.

The next one, however, the added cost without benefit. I would like you to comment on a hypothetical scenario. Let's agree that we stay away from the definition of effective treatment.

If you have a child with a metabolic disorder and you know the diagnosis, and at the first signs of decompensation, they start throwing up or are lethargic, you can sort of give them 24 hours of IV fluids and send them home versus a catastrophic event if you let things go beyond a certain point and require 2 or 3 weeks of stay in intensive care at the cost of tens of thousands of dollars.

Considering a scenario of that kind, would you still say that was added cost without benefit?

DR. GREGG: I don't have the numbers, and I don't know that it's published, but maybe you can direct me to a specific reference from an epidemiologic perspective on the cost of screening nationwide, and what the return is on the dollar for that, for each one of the disorders. I don't have that reference. I didn't think I saw it in the ACMG report.

DR. RINALDO: Again, this is part of the discussion. That report was supposed to cover everything under the sun, so there are obviously areas that are for further discussion.

DR. GREGG: Can I ask you, is there a reference out there?

DR. RINALDO: Well, yes, I believe there are references out there.

DR. GREGG: Okay.

DR. RINALDO: Actually, we're one of them. But it's more of an anecdotal example of exactly the situation that I described to you where a child that wasn't recognized to have a metabolic disease spent two months in intensive care at the documented cost of $400,000.

Once it was diagnosed, it was out of there in less than 48 hours. There was an analysis of the regional newborn screening card to show that even after months of storage, it was still clearly informative.

DR. GREGG: What were the projected costs of the follow up for 29 conditions added to a panel, and what did you project in your publication then?

DR. RINALDO: It wasn't the purpose of that publication. But I believe that there is a body of literature, and that really overall there seems to be a recurrent conclusion that you might make a distinction between cost savings and cost benefits, but overall I think there is a quite substantial body of evidence. Even when you limit to a few diseases, you see that there is enough of a return that really can easily justify. Jim Filiano of Dartmouth published one a year or two ago, but I'd be happy to send you those references.

Finally, there is another aspect where I think your committee, and it is unrelated to newborn screening, could actually help a lot when it comes to education. To really recognize the critical relationship or connection between maternal complication of pregnancy like acute fatty liver, HELLP

syndrome, and certain metabolic disorders that by the way, are covered by the expanded newborn screening panel.

So to me, unfortunately it's not an uncommon event. I've had a conversation with an obstetrician that never heard of LCHAD.

DR. GREGG: They never heard of LCHAD?

DR. RINALDO: LCHAD deficiency. The fact is that probably between 15 and 20 percent of cases of acute fatty liver in pregnancy are caused by the fact the fetus has this particular disease.

I hope that could be in your list of things to do for your committee, to do one opinion about that.

DR. HOWELL: Bill?

DR. BECKER: Thanks for your comments. I appreciate the perspective of your committee. My question is how can we best engage your organization to I guess join in a partnership to accomplish what your opinion document suggests, that OBs need to be more involved, actively involved in the newborn screening and education process with pregnant women. What would your opinion be of how we can engage your organization to the betterment of what we all seek here?

DR. GREGG: I think a letter of invitation to ACOG to have a liaison person. I think this was discussed maybe briefly yesterday.

DR. BECKER: Yes.

DR. GREGG: But that's how I would address it.

DR. BECKER: Would you see your committee and your organization as being receptive at this time?

DR. GREGG: I would guess very much that they would be receptive.

DR. BECKER: Okay.

DR. HOWELL: Are there other questions?

Dr. Alexander?

DR. ALEXANDER: Tony, as you indicated, obstetrics is developing its own screening activities in a more active way than they ever have in the past, with both first trimester and second trimester analyte screening.

The question I have, is there an opportunity here to try and utilize this intervention in a screening context to educate or at least begin mentioning to women the newborn screening? Not so much when the initial screening is done, but perhaps when the results are delivered saying this is a screening we do during pregnancy for a small number of disorders. There will be another screening done after your baby is born for a variety of other disorders.

Has your committee considered that at all as a recommendation to practice?

DR. GREGG: I think that what you're suggesting is exactly what has to happen. That at the time that we are discussing the nature of serum analyte screening, the nature of first trimester screening using ultrasound markers, first or second trimester anatomy ultrasounds, these are exactly the opportune times to bring up newborn screening. I completely agree with you. That's what I should envision should take place.

DR. HOWELL: Dr. Puryear has a question.

DR. LLOYD-PURYEAR: I know ACOG is pilot testing newborn screening parent brochures and educational materials for discussing newborn screening with parents. Can you tell me how that has gone?

DR. GREGG: Well, they've been distributed, and the Committee on Genetics I know has looked at them. There have been no substantive changes to my knowledge made as it relates to those pamphlets. We've all seen them.

I think they're in executive committee at this point waiting for final approval to be disseminated.

DR. HOWELL: I would like to underline what I think is the importance of the education of the pregnant woman on the newborn screening. I think that's particularly relevant in some of our states that still have very meager screening programs, and informed parents will want a complete panel. If they don't know about that prospectively, it is very hard to pull that off.

In other words, if you have not planned ahead and purchased the materials and are all ready to roll and you are only in the hospital for 24 hours, it is very difficult to get that done. So hopefully that will soon pass off into the sunset, but it is still with us for awhile.

Derek?

MR. ROBERTSON: I remember one of the things that my wife was told by her OB was kind of what to expect in the birthing process. When we were going through the ultrasound and that type of thing, there is an excitement about the baby. I don't know if we would have remembered much about what is going to happen after the baby is born and the newborn screening process. You're caught up in what is going on there.

But I know when she explained what to kind of expect, what is going to happen and all of that stuff, then maybe adding on and saying once the baby is born they're going to be tested for a variety of diseases and disorders as a routine process in the hospital. That's kind of the process once the baby is born.

DR. GREGG: You know, the only thing that I would say is that women in pregnancy, there is a wide spectrum quite frankly of what their interest level is, yet even those that are disinterested and are very interested are still going to have, in most cases, newborn screening.

So there are multiple time points. I don't think one specific time point is going to be right for every patient. I think obstetricians can pretty much get a feel for what the targeted time points are. There are certainly times when we try to disseminate information that is both relevant to screening during pregnancy, and as you point out, the intrapartum care, the birth plan, and then I think we need to tack onto that what happens after the baby is born routinely.

I mean, some patients don't recognize that there is a shot of Vitamin K given, or that there is any care provided to the baby right in the delivery room. So I think that we probably need to tack a little education piece onto what happens after the baby is born.

Pick your time. It's not going to be one time for every single patient.

DR. HOWELL: Peter?

DR. van DYCK: Is there any thought in publications that ACOG does related to content of prenatal care? Having a prompt about doing prenatal discussion of newborn screening at some point throughout the pregnancy as part of the written content of prenatal care?

DR. GREGG: So again, unfortunately there is a wide range of let's just say what we call our ACOG OB forms. Some use those, some use their own form. But there are prompts typically that can be easily incorporated into electronic medical records, into handwritten records, to prompt them at certain times to do things.

Those prompts already exist for let's say drawing a type and screen, doing glucose screening at certain time points, and ultrasound at certain time points. These prompts already exist, and adding another prompt is a reasonable way to make sure people are doing what they need to do.

DR. van DYCK: Is that something that would be fostered by the ACOG Committee on Genetics? Or would it come from another committee? What would be the mechanism for that recommendation to come?

DR. GREGG: I'm guessing that multiple committees would have to be involved in the exact track. I couldn't tell you, but certainly there are people that could.

DR. HOWELL: Thank you very much, Dr. Gregg.

I think we'd better move onto our subcommittee meetings. We have a block of time for the subcommittees to meet, as you know, this morning. The committee locations are as follows. The Education Subcommittee is meeting in Continental A, which is on the concourse level. The Laboratory Subcommittee is also on the concourse level, and that's in Meridian B. Finally, the Follow-Up Subcommittee is meeting in the Rotunda break room, which is downstairs kind of under this room. It's right past the registration desk.

For those of you journeying to the concourse level, as you know, the elevators are quite eclectic here. They go to certain floors, and certain floors they don't. But anyway, if you get in the elevators on the left, I believe all of them, certainly the majority of them, go to the concourse level.

DR. EDWARDS: (Inaudible.)

DR. HOWELL: Well, I was statistically correct and so forth. But anyway, I know that the one that has padding goes down. I don't know why it's padded.

Then at the conclusion of these meetings, we'll have a break from 11:00 to 11:15, and we'll return here and hear from the committees between 11:15 and noon.

So let's go off to do great and wonderful things. Thank you very much.

(Recess.)

DR. HOWELL: Ladies and gentlemen, let's please find your seat and we will begin. I think that the committees have had very busy, and I hope successful, meetings.

We will start first with the Education and Training Subcommittee. Dr. Edwards, the co-chair of that committee, will be reporting in Dr. Howse's absence.

DR. EDWARDS: Thank you, Mr. Chair.

We had a very productive session. We had, in addition to our presenters, maybe 20 people attending our session who are from the various other disciplines, not committee members. Everybody participated and contributed to our discussion, which we appreciated.

Our primary agenda related to, first of all, reviewing some of the screening programs that are already occurring. We know that Terry Davis talked to us at the last meeting here. There are materials that are now available to ACOG, to AAP, and to Family Medicine that are now actually getting out, and will be getting out into the field.

These are materials that explain the newborn screening program. We had a lot of very good discussion about what it constitutes, and how do you educate people, how do you motivate people once they have received materials, how do you know that they're incorporating the materials that you're sending them? So there are some unanswered questions on this.

Family Medicine with Dr. Kahn will be doing focus groups on the people who received their materials so that hopefully we can get feedback on the impact of the program. I think probably the discussion as much as anything focused on some of the potential problems.

It is pretty clear from the discussions that it will take a good while to accomplish what we're hoping to do, and that it will take multiple iterations to get it imprinted on physicians. In fact, the most discouraging thing that I heard was that the estimates are that it takes 10 to 12 years to really get physicians really incorporating new material such as this into their practices.

I think as I started, I didn't mention all the people who presented. Dr. Tony Gregg from ACOG and Beth Steele presented for them, Amy Brin presented from the American Academy of Pediatrics, and Dr. Norman Kahn presented from family practice.

So we had an excellent discussion with many appropriate points raised by the participating audience. After that discussion, the next item was in reviewing some of the materials that are already out there from the standpoint of the state screening programs. Dr. Bill Becker from our committee made this presentation.

Every state does have literature. There may be one that doesn't, but almost every state has literature. Again it was pointed out, and this kept coming up. You just can't do it with a single presentation. It is going to take multiple opportunities. It is pretty clear that for optimum communication, the obstetrical community will have to be definitely involved in it.

As Dr. Gregg was saying, there are several opportunities during interactions with pregnant patients. One of the problems that he also mentioned, and I may be misquoting him, but I think my recollection is he said the average patient comes in at 22 weeks of pregnancy. So then that takes away all of the first trimester. In fact, you're almost into the third trimester by the time the average patient makes contact with the OB office.

One of Dr. Becker's suggestions, which I hadn't thought of, and we hadn't discussed before, but it's so obvious that you don't know why we hadn't, is developing slide sets to put on the website of the different medical organizations to further the education of our physicians as far as our program is concerned.

There is a real feeling that unless physicians really can buy into this, think that it's important as far as their practice and their service to their patients is concerned and see the necessity for it, it's going to be very hard to have this incorporated into practices on a regular basis.

So there was a good bit of discussion of this. Then we had our presentation from Ms. Engelson, who represented health and human services agencies. They had a meeting and will continue to have meetings with the different organizations represented in health and human services in putting together the materials that they already have, what they're doing, and they will be communicating with our committee. We see that as a very important resource for our committee, and the necessity for continued communication. This is a resource that we had not been dealing with.

Then finally we discussed membership of the subcommittee. At the present time, we have four members on our subcommittee, the same four that are on the larger board. We had discussed this in a telephone conference call on July 1st when Dr. Howse was leading the discussion.

So we actually had limited it to seven. We were not discussing people, we were discussing organizations that need representation. I had hoped that we had limited it to seven earlier, but what we ended up with today was actually adding more people to the list rather than honing it down. We were not trying to make a decision today. We were trying to get suggestions from the people who were attending our meeting about their ideas, about who should be on it.

I have talked with Dr. Howse about this. She feels that this is something that would lend itself well to a telephone conference call. So I think that we will be making a decision on this. But we did expand the groups that we're looking at. They are ACOG, Family Medicine, the Nurses Association, parents, and the public.

One of the points raised in our discussion was that underserved public should be represented here. Birthing centers, screening program staff, health educators, a specialist in the field of dealing with metabolic problems, International Society of Nurses, and the National Conference of State Legislators.

Now, we haven't really discussed how many people we can have on our committee. I didn't even count these, but it is probably ten or more, which is probably more than we can accommodate on the committee. But this is the group that we'll be looking at in making our decisions about recommendations to this body about other representatives on the subcommittee.

DR. HOWELL: Thank you very much, Dr. Edwards.

Are there questions or comments for Dr. Edwards?

DR. EDWARDS: Well, maybe I first should ask the other members of the committee if they have anything to add to that.

(No response.)

DR. HOWELL: Hearing no comments, I think it would be very important to proceed with the discussions of persons you would add to your committee. You've got a lot of work to do.

Did you talk about education of non-English speaking people? I'm particularly interested in the Hispanic population, which is so large and growing. Did you discuss that?

DR. EDWARDS: It didn't come up today. It has been discussed among our group.

DR. HOWELL: That would be an area that you will really need to think about as far as education is concerned, culturally and language-wise.

Are there any other comments? It sounds like you had a productive meeting today. It seems to me that adding folks to your committee will be an important thing, and you're going to discuss that soon in a conference call. Are you on the conference call?

DR. EDWARDS: It's not scheduled yet. We just discussed the possibility of it.

DR. HOWELL: Excellent. Well, thank you very much. If that's the end of your report, we'll go over to Dr. Boyle and the Follow-Up and Treatment Subcommittee that met earlier.

DR. BOYLE: Yes, well, I think since we met back in April, our committee has gotten its rhythm. Although I have to say it has only gotten its rhythm in the last six weeks. I do feel like we are meeting regularly and starting to move forward.

From this morning's discussion and from some input from folks yesterday, I actually want to modify our charge slightly and make it very explicit. In the first bullet, for those of you who don't have it right in front of you, it says our first charge is to identify barriers to follow up. We're going to insert "and treatment" to make it explicit that we are not just covering the issue of the actual event of follow up, but we're going to be talking later on. The charge of our subcommittee is to think about specific treatment-related recommendations.

Modification, which I think is a very good recommendation, came from a participant in our subcommittee this morning, was that rather than refer to or focusing on three areas, specific barriers, one is the integration of health care systems, the other one is financing of services, and the third one was information technology. We're going to refer to that instead as information systems rather than information technology to enlarge it beyond just IT-related issues.

In our phone conversations, we have had a lot of discussion around additional expertise that our committee needs. We have extended invitations to six individuals to be full members of our subcommittee. Four of those invitations were accepted. We have two members that were actually able to join us today. Jill Fisch is the Director of Educational Awareness at the Save Babies Through Screening Foundation. Many of you know Jill. We're delighted to have her working with us.

The second person is also very familiar to us. He gives us the state of the states every meeting, Brad Therrell. We are delighted to have Brad working with us, given the sort of direct line he has to all of the state newborn screening programs.

The other two members, they are two invitees that have been accepted are Javier Aceves, who is a primary care physician I think familiar to some of you around the table. He is in New Mexico. He is really representing the medical home perspective on our committee. And Carol Green, who was here yesterday and was not able to attend today because of a prior obligation. She is from the University of Maryland School of Medicine. She is a metabolic specialist and really represents that perspective.

We do have invitations to two other individuals, both from state newborn screening programs. Julie Miller, who oversees the newborn screening program, and George Cunningham, who is the chief of the Genetic Diseases Branch in California, who a lot of you know about.

So I feel like we've made significant progress. We have a number of other consultants that have been identified that hopefully we will bring in as needed. During our discussion today, a number of additional consultants or essentially expertises were identified, particularly we have been approached by the child neurology group specialty to have a representative on our subcommittee.

From those attending our subcommittee, there was a suggestion made that MCH directors also be represented on our subcommittee. So we'll obviously be taking into consideration all of these other types of expertise that we could perhaps draw from different points in time in our deliberations.

What we've decided to do as a committee is really try to address our first charge. Obviously, these are sequential charges, so we're starting from the beginning, and we've had numerous discussions around trying to kind of get a sense of the state of knowledge around identifying barriers in health care systems, financing, and information systems.

We have been made aware by Brad Therrell of some ongoing work by a gentleman, Tim Hoff, who is at SUNY in Albany. He has several publications in the works, some of which were shared with us, as well as a survey done of newborn screening programs that specifically address the issues and challenges in regard to long-term follow-up.

We're going to be drawing from his work, as well as hopefully extending some of his work in a subsequent survey that Brad, Tim, and some other person who I can't remember his name right at this minute, who is going to be doing. So we're going to hopefully be able to pull states in a much more explicit way regarding barriers around those three issues.

The other thing we were thinking of doing is have an informal or maybe a more formalized session at the APHL meeting in October. Apparently in the presessions at the conference, there is actually a session on follow up. What we are hoping to do is actually have some type of qualitative research done that we conduct as our own subcommittee around those issues and take advantage of the clustering or congregation of the people who we want to get information from. So between now and October, I will be working with Brad on that.

The other thing we did, we did a live discussion around the specific areas that we were trying to focus on, and made assignments during our subcommittee meeting in terms of those people who would take at least the initial group, like workgroups of our subcommittee.

So for health care systems, Denise has agreed to sort of take the charge in trying to identify sort of the state of knowledge there and perhaps move us as a subcommittee further towards coming up with some kind of statement and guidelines around what we see as the barriers and how to overcome those barriers.

Financing. Peter and Brad have agreed to take a look at financing-related issues. We had a big discussion about financing. Lots of good ideas, many suggestions about perhaps bringing a number of speakers in for our October meeting, particularly around the issues of financing and Medicaid, as well as private insurers. There were a number of suggestions made during the committee as to who might be able to make those presentations and what perspective those presentations should come from. Whether it be an example of sort of best case scenario at a state level where they have been successful in terms of negotiating and managing the Medicaid perspective, same thing from the private insurance perspective, as well as perhaps have a higher level perspective on those issues as well. So we're going to hopefully flesh that out a little bit more and get back to Michele on specific suggestions.

In terms of information systems, I'm going to hopefully take the lead on that. We had several folks from the audience who were very insightful in terms of providing guidance as to where to start with that, particularly Alan Hinman. He is going to send me some documents and hopefully jump start that activity.

The other issue we also talked about is really what we considered an extremely important perspective in thinking about these barriers. That's really the parent and advocacy perspective. We sort of clustered all of the other perspectives in terms of the state newborn screening perspective and the primary care perspective of the medical home into the work of the larger subcommittee, but we really wanted to highlight or spotlight the parent advocacy perspective.

So both Jill and Derek, Jill Fisch and Derek Robertson, are going to be working together over the next I guess next few weeks to try to understand what has already been done by some of the parent groups. Jill mentioned that the Genetic Alliance has done a number of surveys of their parent clientele in terms of looking at specific barriers.

One other thing I didn't mention that we are going to do, and again, Jill, who is very ambitious, actually said that she would take responsibility for this. We were all delighted with that. She was actually going to go through the public comments and actually take a look at what comments might be specifically related to our subcommittee's charge, and how those might be integrated into what we're doing.

I felt like there were a lot of stories that were told from the parent perspective, maybe getting a better handle on it and trying to characterize some of the barriers that were identified through that aspect as well. That's where we stand.

DR. HOWELL: Thank you very much.

DR. BOYLE: I should ask my fellow subcommittee members if they have anything to add to that. Peter? Denise? Jill? Brad?

(No response.)

DR. HOWELL: Thank you. Very good.

DR. TELFAIR: We did just get into a discussion related to the issue of reimbursement and payment as well. Insurance, the insurance issue. There is more work to be done. Several members agreed to begin to look at that issue from different perspectives, talking to state level persons, and also persons who are involved in that work. So that's something that the committee will also be working on.

DR. HOWELL: Very good job. Your committee obviously has a lot to do.

DR. BOYLE: Well, I mean, that was one of the things we were trying to narrow our focus on, but I think maybe at this point it is —

DR. HOWELL: But it sounds like you have defined a variety of situations, and a number of people are moving ahead, which I think is very good. I congratulate your committee on that.

Any further comments on the committee before we move onto the final of the three reports? Dr. Brower chairs the Laboratory Subcommittee, and she's going to report on that committee.

DR. BROWER: Thank you, Rod.

We had a great meeting on the Laboratory Subcommittee. We had nine additional participants, a wide representation, as well as we were joined by two consultants that are reporting to or working with the Laboratory Subcommittee. Jana Monaco, who is a parent and a board member of the OA Association, as well as Dr. Harry Hannon. So we welcomed their participation in this subcommittee meeting.

We had a great discussion about our charge. We wanted to first clarify as a group the discussions yesterday of the evaluation of the expansion of the panel and the current panel. We want to clarify some of the issues in our charge. I want to note two of our charges that we listed out, one is the laboratory procedures, and the other is the infrastructure services.

We really think about those two charges in the context of what we call the 2005 uniform panel. So we're going to be looking at the implementation of the current panel, as well as all of the issues that go along with that.

We discussed several things, such as clarifying any questions about the current panel, whether it is the 29 primary targets or the 24 secondary targets. We want to identify whether there is confirmatory testing available for that current uniform panel. We want to look at the core infrastructure that's available for the implementation of this panel and define those elements that are important in the core infrastructure.

We are going to be looking at metrics in the preanalytical, analytical, and postanalytical phases. So we had some good discussions, as well as good discussions from the participants in the committee about what those metrics should be, and how we can evaluate those.

We also had a big focus on how we can take advantage of and capitalize on efforts that are already ongoing, whether at APHL, through the regional collaboratives, or other groups. We really want to utilize efforts that are already ongoing across the nation and build those into the goals that we have as a subcommittee.

We spent a lot of time thinking about really the second proposed charge of the subcommittee, which is really evaluation of new candidates to the expansion of the panel, as well as looking at the existing panel. We came up with a proposal that we'd like to present to the committee as a whole for discussion.

So this is kind of an idea that came up in our working group. This is really designed to look at the current panel, as well as look at new candidates. I want to walk you through it. Up here we really thought about nomination of the conditions based on a questionnaire, or based on HRSA's work with outside groups. So this is a structure where questions start, or things get nominated to be added to the panel.

Those nomination forms would go to HRSA staff, where HRSA staff would do a preliminary evaluation of the information. If the HRSA staff feels like it needs a certain level of evidence and criteria, that condition would be presented to the full advisory committee.

The full advisory committee would review the information from HRSA, and make a decision whether to proceed or defer. Deferments would be where there is not enough information available. We would ask the full advisory committee to identify not only that there is not enough information added, but what information is needed.

So if there are tests or conditions that don't yet meet the level of evidence to proceed, we would ask that we would define those so that they can circle back through as the body of knowledge accumulates. The full advisory committee, if it has decided to approve and proceed, then we would go to the Laboratory Subcommittee to evaluate the test. So this is a test that's new, proposed to be new for a disease. So the Laboratory Subcommittee would evaluate the data and whether a test is available.

We propose that the Follow-Up and Treatment Subcommittee would evaluate whether a treatment is available. Really these are the two gatekeeping items. Is a test available, and is a treatment available. If it passes these two subcommittee evaluations, it would go to the full advisory committee for evaluation. If it's approved, then the chair of the full advisory committee could assign it to an ad hoc working group.

We would envision and propose that there is a liaison from the Laboratory Subcommittee and from the Follow-Up and Treatment Subcommittee in this ad hoc working group. This is just a rough draft that we put together based on our discussions and input from the committee as a whole. We really want to emphasize that things start with HRSA, where HRSA is really going to be collating the information,

digesting it, and providing it to the full advisory committee, and that the full advisory committee has a critical role throughout this process.

Are there any questions or thoughts about this proposal?

DR. HOWELL: Is the group clear about what Amy has suggested here with the diagram that has been presented and so forth? I think that the sense of the committee, and I sat in on these discussions, was to figure a way to evaluate the test, which is critical, the benefit or treatment, which is critical, and then vet it through the committee and have an ad hoc working group.

That ad hoc working group, as I understand it, would have a broad variety of expertise not only from the laboratory and the treatment groups, but other groups that would be looking at it, and come back with a final recommendation. That would be a working group from the full advisory committee.

DR. EDWARDS: Now, this ad hoc working group, is this comparable to what Dr. Alexander was talking about as an ACIP equivalent? Or ACIP-like organization?

DR. HOWELL: I believe the answer is yes, but he is here and can say yes or no.

DR. ALEXANDER: Yes.

(Laughter.)

DR. HOWELL: Well, thank you.

DR. EDWARDS: Thank you.

You know, this looks like something very much like what I support. But knowing how smart Dr. Rinaldo is, I'm sure he has outsmarted me somewhere on this. I really like it. I think this is very good.

DR. HOWELL: Now you are paranoid.

(Laughter.)

DR. EDWARDS: No, I'm not paranoid. They really are out to get me.

(Laughter.)

DR. HOWELL: I sat in on the committee. I think the committee was trying to respond to the concerns that were expressed at the table. The thing about the working groups, you need the expertise of the follow-up group and the laboratory group before it goes there. Then when it goes to the working group, you need a very broad constituency, some of whom will be clearly ad hoc. Some of the conditions that will come up will have very specific expertise that are required. So you'll have some consistent expertise in epidemiology, test evaluation, whatever it might be, but you'll have an ad hoc group there.

DR. DOUGHERTY: This seems like a lot of steps around identifying whether there is a test and treatment. I thought one of the nominations of the conditions would be that somebody would say there is a test and a treatment.

I'm not sure what HRSA would be doing, except assessing the validity of those claims in the nomination. So that could go to the full advisory committee, and then it could go directly to this ACIP ad

hoc working group. I'm not sure what the Lab Subcommittee and the Follow-Up and Treatment Subcommittees would be doing.

DR. HOWELL: Let me speak to that. I think that HRSA will be looking at the things generically, but not making decisions about it. In other words, I think the thought would be that everything would come to the committee.

Since the lab test and the treatment are so critical to their getting it in, I think that the Lab Committee felt that it would be important to have the committee actually look at it and say yes, we agree that there is a test, and it's appropriate.

DR. DOUGHERTY: Well, could you explain what looking at something generically would mean, then?

DR. HOWELL: Where is Marie? Marie was there. Marie, would you like to comment? You were a part of this discussion about what you would think HRSA might do at this gatekeeping spot. You will need to come to the microphone so we can hear you.

DR. MANN: I think mainly it would be minimal what HRSA staff would be doing. It would be based on whether it meets the minimum filling out the questionnaire, the nomination form, the required submissions, all of the requirements, and then preparing that package.

Everything will go before the subcommittee, even if staff feels there was inadequate information. I think it is more administratively what HRSA would be doing, preparing the package, and then presenting it to the advisory committee.

Then the advisory committee will determine based on review if all the information is there, determine whether it agrees with whether it should proceed or not. So it will be minimal what HRSA does.

DR. DOUGHERTY: I guess the big question is will each of these in turn, and it sounds like HRSA will putting the package together, whether everything is checked off and so forth, but this sounds like a huge job for the Follow-Up and Treatment Subcommittee, unless there are criteria for both the Lab Subcommittee and the Follow-Up and Treatment Subcommittee for the kinds of things that they are supposed to look at. They're not looking at the evidence. I'm not sure what they're looking at.

PARTICIPANT: They're not looking at it.

DR. HOWELL: That was discussed. There is a plan to have specific criteria for each of these committees.

DR. BROWER: And just to follow up on that. On the Lab Subcommittee side, is there a test available. So any type of test that's reliable, whether it's off of a card, or a hearing test that is physiological on the follow up and treatment side, it's really not treatment. I misspoke of its benefit.

So we really define that as is there a benefit available. We would envision that both the Lab Subcommittee and the Follow-Up and Treatment Subcommittee would come up with their own standardized assessment for assessing the information to say yes or no, whether we would recommend to the full committee that these tests or benefits go onto the ad hoc working group.

DR. DOUGHERTY: Then I'm not sure what the ad hoc working group does. Is the Lab Subcommittee and the other subcommittee, that's one question, what the ad hoc working group is looking

for. The other question is what about all the other variables that were talked about yesterday and that were in the ACMG method, burden of disease, cost, public advocacy, all those kinds of things.

DR. HOWELL: You described the working group.

DR. DOUGHERTY: So they're not looking at the evidence for benefit. That would be the Follow-Up and Treatment Subcommittee. Or they look at it again to make sure that we got it right, because we are only doing a quick passthrough.

DR. LLOYD-PURYEAR: Yes.

DR. DOUGHERTY: Yes? Okay.

DR. HOWELL: But the working group would have a broad representation that would, I think, consider a whole variety of issues. The Benefit Committee, I think would look at concrete evidence for benefit. The lab would look at all the expertise that's required of the tests to be sure it's valid, and then the working group would have to expand that to cover the other important areas that have been discussed at this table.

DR. DOUGHERTY: I guess one more thing is if we could get some external help like we were talking about from David and others about putting criteria together and how to do that so that we don't have to reinvent the wheel for what the benefit group looks at and what the test group looks at, because in working with the ad hoc working group, which I'm assuming will have some core members, so that we make sure that all of these criteria kind of fit together in those three circles we saw yesterday where you've got evaluation and values, and maybe cost.

I don't see some role for what we asked David to do yesterday, to come up with an improved process in this.

DR. BROWER: I think what we asked David to do yesterday really is provide the structure and the criteria for what we're going to be doing. Some of it will be done in the Laboratory Subcommittee and the Benefit Subcommittee, and then the full majority of that will be done in the ad hoc working group. But the committee will have full visibility into how the Lab Subcommittee and the Treatment and Follow-Up Subcommittee make their decisions, as well as the ad hoc working group.

So if we decide as a full committee that this disease, this test or treatment goes down the chain, we already know ahead of time the data points they're looking at.

DR. DOUGHERTY: So I would add that as a sort of pre thing to this chart, saying that we will work to get sets of criteria for the different groups to work with. Would that be okay? That's the only thing that concerns me, besides the multiple —

DR. ALEXANDER: I think what we're doing here is a modified screening process in itself. HRSA's role is mainly to assemble the data and pass it on without even a whole lot of comment for the committee to see whether it meets the criteria for further consideration and pursuit.

The whole committee then decides if there is enough here to make it worth going further. They refer to the two subcommittees who do a further depth probe and decide whether there is sufficient evidence, benefit, and a quality test, and testing of the test to make it something that is ready for consideration for addition to the whole panel.

If in their judgment it meets that, then they come back to the full committee and say this is ready, it is worth the investment of time, dollars, and resource, for an ad hoc working group to be appointed to

consider this and bring forward a recommendation to the whole committee as to whether this is ready for addition to the panel or not.

So there are three levels of screening, if I may use that word, in itself, of depth of study and assaying of whether this is ready or not.

DR. DOUGHERTY: What I'm just trying to make sure is that there is an explicitness of the process and not just judgment of the group.

DR. HOWELL: I think that there was considerable discussion about the explicit plans for the laboratory, because that was the group that was looking at this. But the other groups would need to have the same thing.

In the laboratory area, these are a bit clearer to annunciate, because there are established criteria for laboratory tests that can be plugged in here. I think that the treatment group, I would like to emphasize the term "benefit," because I think that we all feel there is benefit to some of the screening tests that far exceed a specific drug, test, or medication.

DR. DOUGHERTY: I would add "harms" as well, given the presentations we had yesterday. The assessment of benefits and harms.

DR. HOWELL: I think that that will come out.

DR. DOUGHERTY: Well, actually it often doesn't. It most often doesn't. I guess I would put up there then in this chart the fact that these groups are using explicit predefined criteria.

DR. HOWELL: Well, this incredible background was generated after the meeting, I might point out.

DR. DOUGHERTY: Okay.

DR. HOWELL: Fortunately, there is an excellent diagramologist who is a member of the committee. Few of us know how to draw the circles and get the lines together in the right place.

Bill?

DR. BECKER: Thanks, Rod.

Amy, thanks very much, and your committee, for the thought and development of this model. I think it addresses the major concerns and comments brought out yesterday. I congratulate your subcommittee for putting it together so very quickly.

I agree with Denise's comments. It is probably something that we will need to learn from. Clearly we haven't even had the ACIP presentation, but I think it's a template where we can start, and it's a great place to start. I would favor it.

One request would be that on the ad hoc working group, that there not only be liaisons to the Lab and Follow-Up Subcommittees, but also Education and Training. I think it's critically important that even in the preconceptual phase when we are considering the composition of the panel, that education and training components be a considerable part of the ad hoc working group. So I would make that request.

Then the final is sort of a comment that I think is going to be vetted out. But so that I guess I get it out there, the entry point, the very entry point to the algorithm is sort of the submission of nominations, which I suspect is probably a process that needs to be worked out. I think that's something that can evolve and maybe we don't need to talk about right here. We don't even have a nomination forum, and I know that's something that Piero, Michele, and I are going to work on in the intervening time.

DR. HOWELL: I was going to say, before the next meeting we will expect a fabulous forum that you, Piero, and Michele will have developed. You always are volunteering.

DR. BECKER: As Michele and a couple of the breakfast folks heard this morning, we have a couple of ideas about that. Hopefully we'll develop those a little further.

DR. HOWELL: I think that entry point should be as broad as possible, but have obviously a format for doing it. We want to encourage people to come into the fold, but also be certain that there is some moderate level of information at the beginning so that they are not on the fly.

Are there any further comments about Dr. Brower and her committee? Or do other members of the committee have any comments who are here? Dr. Alexander has commented.

Piero, did you have any comments? Anybody? Peter?

DR. COGGINS: No, just to reiterate that we said that we would definitely have a set of criteria to judge everything against. I think another point you raised, in the ad hoc working group, some of the composition will be determined by the condition we're looking to approve or disapprove.

There has to be some standing membership there that's going to drive the process and make sure that it's an objective approach rather than just judgmental in terms of accepting new ideas to come through.

DR. DOUGHERTY: This looks great. I guess maybe we should discuss resources, though. The follow-up working group could each kind of run a Medline search or take turns on running Medline searches on conditions or talk to experts.

Is that how you want it done? Or is there going to be some resource to have a contractor or somebody who is knowledgeable about how to do some searches and interpret them to help guide us? And also the ad hoc working group. If we're going to have core members, that needs some resources, too.

DR. HOWELL: Comments?

DR. DOUGHERTY: That's my final question. But I think it's great.

DR. HOWELL: Comments from folks about how such might operate as far as the resources are concerned?

Peter, would you like to address that?

DR. van DYCK: I think we'll just have to start and see the volume. Certainly depending on what the nomination form looks like, part of that administrative work at the beginning could be to make sure that there are as many references as possible, and then print it up perhaps before it starts through the process.

There are certainly resources. An ad hoc committee may not cost anything, other than sending things back and forth. We may be able to get volunteers to do that, is what I would expect. So I'm not sure this is a terrible money resource. There are personnel resources that are necessary.

DR. HOWELL: One of the advantages of the conditions that we work on is that they tend to be rare, and so the number of references that you're going to have, it's not like we're working on prostate cancer or mammography as far as the volume is concerned. But they obviously will need to have analyses done.

DR. DOUGHERTY: Sometimes the fewer references you have, the more difficult the discussion is.

DR. HOWELL: But they're quicker to read. The discussions can go on forever. Speaking of discussions going on forever, the noon hour is upon us. Is there additional comments of Dr. Brower and her group? I think you all did a great job of I believe addressing the concerns of the committee and coming up with a system that hopefully will be workable.

DR. DOUGHERTY: Do we need to vote on this?

DR. LLOYD-PURYEAR: It's not a voting issue.

DR. HOWELL: No, it's not a voting issue. We are just going to do it.

DR. RINALDO: I would like to hear from the Follow-Up and Treatment Subcommittee that they are amenable to this process.

DR. BOYLE: Well, I don't want to speak for the whole committee myself, but I agree with almost everything everybody said around the table. This is something we have to test out and develop a procedure for. But I feel like this is a very appropriate way of dealing with it.

I agree with Denise in terms of it being transparent. I have thoughts about that last little yellow box and whether or not it is a duplication of the green boxes in terms of the activities and the work being done there, but that may evolve into something very different over time as we test out the procedures.

DR. RINALDO: Well, that little yellow box is very much the result of what was said yesterday about not having this done by the subcommittees. So we were really following the comments from yesterday.

DR. BOYLE: I'm not criticizing it at all. Actually, I think this is a fine way. You and I don't communicate really well. I just feel like I'm very encouraged by this. I think this is a nice way to proceed. I think it will evolve as we develop it.

DR. HOWELL: And I think that one of the reasons for being clear about the fact that there will be representation from the benefit treatment center and the lab committee is so that those two areas will have been pretty thoroughly discussed so that the broader committee can focus on many of the things that Denise was alluding to that were considerable.

Are there any other comments?

(No response.)

DR. HOWELL: Thank you very much.

DR. BROWER: And I think it's important, Bill, for that committee, that if they're going to address wider issues to have an Education Committee liaison. So I think that was an excellent suggestion. Thank you.

DR. HOWELL: Further comments?

(No response.)

DR. HOWELL: Let's go to lunch. We'll return, and right after lunch we'll have the advantage of public comment, and then some additional discussions and recommendations to go forth.

We are going to end quite promptly by 3:00 or before.

(Whereupon, at 12:10 p.m., the meeting was recessed for lunch, to reconvene at 1:00 p.m.)

AFTERNOON SESSION (1:08 p.m.)

DR. HOWELL: Ladies and gentlemen, we have a busy afternoon. As we have said repeatedly, we're going to be leaving by or before 3:00.

We now have the privilege of having a series of public comments. We'll start with the first person on the list, Jana Monaco, who is a parent and a board member of the Organic Acidemia Association.

MS. MONACO: Hi. Good afternoon. It is a privilege once again to represent the Organic Acidemia Association in support of universal newborn screening. The OAA's mission is to provide information and support to families of children with inborn errors of metabolism. It also provides information to health care professionals along with its families across the country and internationally.

Our organization also has many parents that are busy like me advocating for newborn screening in their own states, along with supporting various efforts to enhance the research and management of their specific disorders.

One of our recent developments is that of an isovaleric acidemia research fund so that we can start working on that process and help support Dr. Vockley.

As you know, universal newborn screening is near and dear to my heart because of my son, Steven, who was one of those misdiagnoses of isovaleric acidemia and suffered severe brain damage at age three and a half. My two and a half-year-old daughter, Caroline, is living a normal life with diet management and medication that he missed out on because she was diagnosed early.

They have inspired me to work with the State of Virginia to pass the recent legislation expanding the state's newborn screening program from nine disorders to match that of the ACMG report. That way, no one will have to show up with their little cards anymore at the hospital.

I have also accepted the invitation to serve as a regional collaborative on one of the workgroups, and also to serve as a parent educator for the LEND program here at Children's National Medical Center.

I see the opportunity to work with Amy Brower and her subcommittee as quite an honor, along with my other endeavors, as they are a validation that parents do play a vital role with these issues. I, like many other parents, do what I do because of the firsthand experience that comes to living with one of these disorders.

For us, it's a vested interest, and I hope this committee will fully incorporate parents into these subcommittees to move the process along.

In light of yesterday's discussions and presentations, I have to agree on behalf of our organization that education, follow-up, and laboratory infrastructure are the key areas to be addressed. As the subcommittees identify their goals, objectives, and work process, I'm confident that many of the issues identified in the public comments will be resolved.

I must stress that these are not new issues to our organizations. We parents address most of these issues on a routine basis because they do have a direct effect on our children's health. We even incorporate them into metabolic conferences, welcoming the experts to come and speak on the topics.

We also think OB/GYNs should initiate the discussion of newborn screening to help educate parents on these disorders during the prenatal period like they do with such things as AFP screening. Waiting until the baby is born to introduce this knowledge and the prospect of supplemental screening is far too late. OB/GYNs need to be a part of the process.

The education process is ongoing within our parent organizations as a direct result of raising children with a disorder. The evidence related presentations truly propose some critical concepts to think about. Evidence that newborn screening saves lives and prevents mental retardation and death truly exist. I have proof of that.

The fact that it might not be tremendously high numbers is irrelevant, and every child's life should count. Waiting for more and better evidence translates into more lost lives and brain damaged children because these disorders are very unforgiving when they are missed.

Scientific validity for screening does exist, and parents support it, regardless of uncertainty. One of our families has two children with ketone utilization disorder. Though the research shows that there are probably only 50 to 60 cases worldwide and would not be identified with newborn screening, the family fully supports universal newborn screening, and hopes for increased knowledge regarding KUD.

In light of all of this, we feel that Dr. Watson and his staff used their expertise to fulfill the duties commissioned to them, and produced a quality report of the universal newborn screening program. The methodology chosen was a very effective tool to reach people and obtain the data to complete the process.

Certainly as the process of universal newborn screening is implemented, the development of innovative means will continue to grow in regards to how, when, and who will include other disorders to the recommended panel. It is our hope as an organization, you will move forward with the process of recommending the report to the Secretary for his approval, with the understanding that the identified issues of the report will be ongoing tasks to address, and that as science and technology continue to change, so will the methodology of the process.

The focus should be on progress rather than perfection. They should not hinder the advancement of the report. Expanded newborn screening is taking off state by state, with or without this report.

It would be beneficial to have the support of the ACMG report in assisting the remaining states in developing their screening programs, and bring a sense of uniformity among the states.

You as a committee have devoted an incredible amount of time and commitment to the development of this report for recommendation, and have done a phenomenal job in addressing the various aspects of newborn screening, one for which we parents are truly grateful for.

I appreciate the fact that you have remained sensitive to those of us who have tragically been affected by these disorders amidst all of the technical data presented. The personal aspect of it all must never be forgotten. I thank you for your ongoing work and the opportunity to work with the Laboratory Standards and Procedures Subcommittee.

Thank you.

DR. HOWELL: Thank you very much, Ms. Monaco.

Are there questions?

(No response.)

DR. HOWELL: If there are questions, perhaps you can answer them. Apparently you have answered all the questions.

We'll move onto Jill Levy Fisch, who is a parent and National Director of Education and Awareness of Save Babies Through Screening Foundation. She represents herself, an SCADD family.

MS. FISCH: My name is Jill Fisch. I am the National Director of Education and Awareness for the Save Babies Through Screening Foundation. I want to thank all committee members for their continued hard work and dedication regarding newborn screening and the surrounding issues.

It is wonderful to see that certain states are expanding their newborn screening programs in anticipation of the acceptance of the ACMG report by the Health and Human Services Secretary. However, as we all know, there are still states severely lagging behind, and there appears to be no movement in these states to expand.

The death or impairment of a child should not be determined by the state in which they are born. For example, I have been in contact with the New Hampshire newborn screening program. Their hands have been tied by the legislators in that state. I was told that regardless of what happens regarding the standards set forth in the ACMG report, they may very well choose to ignore it and expand as they see fit.

We need to be able to exert more pressure on these states, as the lives of children are at stake. I would like to point out the benefits the children in Mississippi are receiving, as the newborn screening panel they use is the best in the nation.

In the past year, there were 22,618 births in Mississippi. Fifty children had a positive screen, which gave them immediate access to diagnosis and treatment. According to these numbers, 8,850 babies out of 4 million births in the United States would have a positive screen using the best panel currently available.

It is apparent that this committee is examining the decision-making process and how it will move forward in this regard. It is of vital importance for the decision-making process to be structured within this advisory committee. We do not want to have another committee set up, rather it would seem more practical for this committee under HRSA to devise its own structure.

This is a crucial time for newborn screening, and this committee has shown a vast knowledge of the issues at hand, as well as extreme fairness, integrity, and willingness to listen to the needs of families. Having attended all committee meetings thus far, I have seen firsthand the thought and time the committee has put forth by the vast array of experts consulted and expert presentations.

Parents are the experts in the patient/doctor relationship when children with rare diseases are involved. Parents bring the information to the physician to assist the physician in caring for the child. Because of the necessary height and level of advocacy, parents provide invaluable resources to health care issues such as newborn screening.

I would also like to stress the need for parent involvement in the decision-making process as things move forward, as well as aspects of the subcommittee work. Some of the subcommittees have moved in this direction, and I am grateful to have been asked to be a member of the Treatment and Follow-Up Subcommittee.

The knowledge and experiences that parents bring to these issues is invaluable. The Education Subcommittee currently does not have parental involvement. It is my great hope that this will be changing in the very near future. The parent can be one with a child with a condition currently screened for, as well as the parent of a child with a condition that may be screened for the in the future, such as Micki Gartzke.

Micki would be a wonderful asset to the Education Subcommittee, and so many children and families would benefit from her knowledge, caring, and commitment. Families in many states are still not being informed about supplemental screening. By the 35th week of pregnancy, ACOG must mandate that all pregnant women receive this lifesaving information. It must be a standard of care.

Unfortunately, I have heard yet another story of a hospital refusing to perform the supplemental screening. This family purchased the Pediatrix kit and brought it to the hospital at my suggestion. The parents were very anxious to have the supplemental testing. The hospital refused to perform the test, citing poor lab quality and inaccurate results. We all know this not to be the case.

My thought on this issue would be for the supplemental screening to be ordered prior to delivery and be the standard of care. This crucial testing cannot be left to the subjectivity of the nurse on duty. There was another family that was told by the nurse on duty that the hospital would not perform the supplemental screening even though the parents had brought the kit with them.

In this case, the family was able to get the testing done by the nurse who came on duty during the next shift change. Standards must be set. As a result of hearing these stories and many others, my question would be, should this order come from the pediatrician or the OB/GYN? If it is a physician-ordered test, the pressure would be taken off of the families, and it would become the standard of care, as it should be.

I would appreciate it if this issue could be addressed in an expeditious manner by the AAP and ACOG. I would also like to comment on the ACOG statement that the disorders screened for should have effective treatment. If the babies aren't identified, how can treatments be developed? Also, parents do have a right to know what is wrong with their child.

I continue to be grateful to have the opportunity to advocate for children born in this country, and once again thank the committee for all they have done to save the lives of children. I am also grateful of the committee's willingness to involve parents in the process as we provide insights in the lives of affected families like nobody else can.

Thank you.

DR. HOWELL: Thank you very much, Jill, for those thoughtful words.

Let me point out, as we continue this, that the committee has certainly sought family input, and I can assure you we are going to continue to do that. We will clearly have family input on all the committees, I can assure you.

I'm now pleased to welcome Micki Gartzke from the Hunter's Hope Foundation. Ms. Gartzke is a parent and also the Director of Education and Awareness for the Hunter's Hope Foundation.

MS. GARTZKE: Could I sit down when I talk?

DR. HOWELL: Welcome. Be sure to turn your microphone on.

MS. GARTZKE: Thank you, Dr. Howell, members of the committee, and HRSA for the opportunity to speak today.

Your outstanding dedication and your ongoing work to make recommendations to further assist states to expand their newborn screening programs is invaluable. Comprehensive universal newborn screening utilizing a tool like a uniform panel needs to be a regular practice in the United States.

The children not only need this benefit, they deserve it because they are our future. You're the ones that are going to get the job done.

My name is Micki Gartzke. I live in Shorewood, Wisconsin. I'm a Midwest girl. I'm the Director of Education and Awareness for the Hunter's Hope Foundation. Recently universal and comprehensive newborn screening for all children born in the United States has become our foundation's top initiative.

It started out because we knew that children born with Krabbe disease needed to be identified through newborn screening to receive access to the effective and lifesaving treatment of cord blood transplant for Krabbe disease, which I have copies of the New England Journal of Medicine recently published study if anybody would like a reprint copy.

We moved on to help all of the other diseases gain access to newborn screening for the benefits it provides those diseases, their families and children, because we just know it's the right thing to do.

This month being the month of July, the very month our country achieved independence in 1776, I recently attended a reading of the Declaration of Independence as part of our community's annual 4th of July celebration. I found it most insightful that the Declaration of Independence speaks directly to universal newborn screening with the well known line, we hold these truths to be self-evident that all men are created equal.

Well, we may be created equal, but that equality stops right now at birth with the state's newborn screening's inequality. I think our public health programs are one of our country's greatest gifts to all of our citizens. Our first public health program, the state-based newborn screening, is not living up to the long held acknowledgment that we are all born equal.

Historically, this lack of equality in newborn screening has had too much subjectivity involved. But this is now changing, and it is because of you guys that this is changing. Your commitment to excellence in making recommendations, using the best available evidence and the best available expert opinion. You're using high level of integrity and far reaching strategies. Much progress has been made toward the creation of a uniform nationwide panel.

In 2001, the year I became aware and consequently involved on a daily basis with newborn screening, there were only four states testing for 20 disorders or more. Today there are 25 states at that

level. So we went up 21 states in four years. There are 25 states that still need to step up. It highlight is there is much to be done, but it shows the great progress.

Along with all the parents I have ever spoken to, and it is in the many, many, many thousands now, I believe this committee is the committee to get the job done. They can do it efficiently and effectively. The structure of this committee with its subcommittees and its decision-making process I think is doing an excellent job.

Your continued openness to identify concerns, address criticisms, and work toward effective solutions continually spotlight that the benefit to the children remains the number one priority. We see no need for additional committees to be set up to repeat or possibly slow down the progress of expansion of newborn screening across the United States. HRSA has done an excellent and judicious job working with experts like you in all relevant fields before and since the establishment of this committee.

The infrastructure, implementation, and education continue to be the avenues driving progress. Education being of the utmost importance, from parents to physicians, the entire spectrum of medical care providers, including students training to be physicians. Parents will provide the demand for the education and the materials, but as I learned this morning, the physician buy in needs to be the number one objective accomplished through education. We need the physicians to buy in on newborn screening, or it's not going to happen in the manner that we're all working so hard to achieve.

There is so much that can be done so that all can be better informed about the vital lifesaving importance of newborn screening. I believe parent involvement in all levels of decision-making and advocacy are a major key to success. Like the others, I'll tell you a little story about parents of children born with rare diseases.

We have faced many challenges unlike any other challenge. We are the experts in our children's care. We bring the information and the ideas to our physicians. They're not providing them to us in most cases. They are learning from us, and they are usually open to learn that information from us. That is helpful, because they know that that is what provides their patient the best care.

The parents have access to the experiences of other parents, what they have done with their children in the past, and that is how the care is really getting taken care of at this point. So these physicians at this point do not know how to treat these rare diseases, and when this happens, it is very much an eye opener for parents.

This is how parents become advocates, because of situations like this. They get in the big system, and the system can't help them, and they can't help their child. Mothers and children, that's a very special relationship, and fathers and children is a very special relationship, too.

But when something happens to your child and the system established to help you can't help you, that changes everything. The playing field is different. That's how parents become their child's advocate.

Last week I spent seven days at our annual scientific and family symposium. We had parents there, 44 families, and they spanned the socioeconomic spectrum. Not only was our commonality our children's disease, but the other commonality was that we all had to get our children care. Nobody had access. Nobody's physician knew what to do. Everybody learned from each other and went back to their physicians and said, this is what this family did, this is what they tried, this is the drug they used, they are using a feeding tube now, they are doing this therapy, they are doing that therapy. That was the common thing we had. Young parents, old parents, some parents more educated than others.

We were there all together, and parent advocacy was our common thread. Our foundation pays to bring families to our symposium, families that would otherwise not be able to attend the event. We

want no disparity amongst our families, because we know that all parents are important, and there is value in everyone's perspective across the entire spectrum of parents.

We don't underestimate parent commitments and skills. Parents are willing to bring their skills and knowledge to newborn screening. Parents whose children were not identified, even though there is currently a newborn screening available for that disease, have specific valuable knowledge and experience that is of great importance.

Parents of children who have diseases for which a newborn screen may become available in the future also have invaluable knowledge and experience. As it is anticipated that in the future many more tests will be added to newborn screening panels, the assistance of these parents may prove to be even more vital moving forward from this point on.

Parents have played the key role in expansion. You've heard this before. Within the last year, we've had Virginia, New York, and Kentucky all moving forward, all with parent advocates playing key roles. Interestingly, I just heard that Mississippi, with it's top shelf screening program, had 22,618 births. Out of that number, they identified 50 children with positive screens. That's 1 out of 452 children. I'm not an epidemiologist, so I don't know how that translates across the country, but I just wonder with 4 million annual births, if you look at 1 out of 452 children, that means that maybe 8,850 children would screen positive using the most comprehensive panel available today. There are going to be more children that will be identified in the future as these panels grow larger.

The opportunity cost is too great not to find these children any longer. While it may be hard to quantify the benefits of newborn screening, children dying unnecessarily have too many far reaching impacts to American society at large and specifically for the families affected by the premature deaths. Time is of the essence. Children continue to be born, 11,000 of them a day. I can't help but wonder how many children each and every day are going unidentified only to endure an odyssey of disabilities and untimely deaths.

The resources for follow-up treatment studies, all aspects, there must be funding made available. There must be a standard of care. The stories continue to be told of the subjectivity of families being able to access the current supplemental newborn screening.

States that border defining access and subjectivity in hospitals from one shift to another are creating additional barriers. This is no way for medical care to be practiced in America.

My hope is that there is a mandate, policy, or something like that for OB/GYNs and/or pediatricians to provide information on newborn screening to expectant mothers before the 35th week of pregnancy.

The discussion yesterday regarding the consequences of no decision I found particularly interesting. But you all are going in the right way, you are all right on track. I want you to all please keep working together as well as you have because you are moving forward, you keep expanding your subcommittees, and you build this newborn screening program into the great asset it can become. I know you can do it.

Additional resources will follow this. I guarantee you that parents are a big resource, and we will help. I want to thank you. Your focus on the children and on the families, your commitment to excellence, and your dedication to creating universal access to comprehensive newborn screening is not only life saving, but it is also helping to create an even better America.

Thank you.

DR. HOWELL: Thank you very much, Micki. Again, we appreciate all the work you and your group continue to do.

MS. GARTZKE: Thank you.

DR. HOWELL: For the members of the committee, if you have not seen the article that she referred to, I would take her up on this. This is an article that recently appeared in the New England Journal. It is a major article that is from the University of North Carolina at Duke looking at stem cell transplants in infants with Krabbe disease.

It particularly addresses the issue of outcome versus the age at which the treatment is begun. It is a very important paper, obviously in the New England Journal, and is something I would recommend you read if you have not yet had an opportunity to see that paper.

We're delighted to have here with us, from Chicago today, Amy Brin, who is the manager of the screening program at the Division of Children with Special Health Needs at the American Academy of Pediatrics. Ms. Brin will be speaking today on behalf of Carol Berkowitz, who is President of the American Academy of Pediatrics.

Amy, we are glad to have you.

MS. BRIN: Thanks. Good to be here. Good afternoon. It is an honor to be here before you to submit the sentiments of the American Academy of Pediatrics board of directors.

"Dear Chairman Howell, the American Academy of Pediatrics board of directors greatly appreciates this opportunity to provide comment on the Health Resources and Services Administration's commissioned report of the American College of Medical Genetics, 'Newborn Screening: Towards a Uniform Panel and System,' to the U.S. Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children.

"As you know, our longstanding commitment to newborn screening has been manifested through our continued partnership with the Maternal and Child Health Bureau. Through the years, this partnership has helped improve the ability of pediatricians to care for newborns identified via the newborn screening process. We join HRSA/MCHB in acknowledging the many benefits that newborn screening provides to the health of newborns and their families. Moreover, we support HRSA/MCHB in their endeavors to unify state newborn screening programs in order to address the wide disparity that currently exists.

"In accordance with the Federal Register's call for public review of the ACMG report, the AAP's board of directors submitted the following comments from our expert committees at the beginning of May, 2005.

"While we endorse the concept of expanded newborn screening, we strongly maintain that a clearly defined follow-up system must be established to support its effects on pediatric practice. Through our endorsement of the ACMG report, we join fellow national partners such as the March of Dimes in the understanding that this advisory committee is charged to make such implementation recommendations.

"We acknowledge that such a process must be a dynamic one, incorporating pragmatic structural changes in the operation of the state program, as well as evolving tests and treatments. We salute this advisory committees's construction of subcommittees to address the issues of follow-up, laboratory standards, and education, as well as the crosscutting issues of finance and technology, as it illustrates a deep commitment to attain a quality, comprehensive newborn screening system.

"We further offer the following points of emphasis. One, the follow-up system. The role of the medical home is essential to ensuring the quality newborn screening process. The 2000 AAP Newborn Screening Task Force report established the medical home necessity in successful short term and long-term follow up for identified newborns.

"As the expansion of newborn screening seems inevitable, we look forward to our continued partnership with other national leaders about how to support the medical home in this role. As mentioned previously, it is necessary for a defined, appropriate, and comprehensive follow-up system to be implemented. While we acknowledge that such a charge was not part of the ACMG's expert panel's work scope, we do note that the report's implications require that such a model be identified.

"The integration of expanded newborn screening on our state's public health systems, laboratories, medical homes, specialists, and families demands that such a system, as well as the resources to support it, be in place.

"Two, physician liability. Malpractice suits against pediatricians related to newborn screening have increased. The proposed system must ensure that results are reliably sent to the medical home, and that information about the suspected disorder is included. An expert contact number should also be given.

"Liability for informing the medical home and family about the need for additional testing should reside with the state.

"Three, education of pediatric professionals. The fully operational newborn screening program is complex and naturally encompasses a vast number of health care professionals. As the ACMG reports, recommendations are germane to all pediatric professionals. We strongly suggest development of a communication plan to inform and educate these audiences on the ACMG report recommendations.

"In turn, we pledge to utilize our resources to distill and disseminate such information to our 60,000 members. It is only through such coordinated efforts that we can engage the pediatric health care community to meet the needs of these newborns, their families, and their communities.

"Please note that in our May submission of comments to HRSA/MCHB, we also included some editorial considerations.

"At this time, we'd also like to inform you of our immediate plans to engage in these areas of further definition as described above. Beginning in 2005 and through the support of our partners, HRSA/MCHB and ACMG, we will be developing our first clinical report to outline the medical homes role in the newborn screening follow-up process. The publication of this report will solidify our commitment to expand newborn screening, and our acknowledgment that our members, as well as all pediatric child health professionals, need unambiguous clinical guidance to know their role in this expanded system.

"Earlier this month we established an expert multidisciplinary body from the pediatric domains of primary care, genetics, neonatology, neurodevelopment, neurology, quality improvement, and informatics to draft this operationalized clinical report targeted at the point of care.

"The report's scope will explicitly delineate the primary care child health professional's role in quality care to identify newborns and children, specifically defining their role and co-managing the condition with a subspecialist and the family.

"Moreover, the backbone of this clinical report will be an algorithm which will provide explicit marching orders for electronic health records developers to note the specific pediatric functionalities their health information technology must have in place in order to support the medical homes provision of care.

"Whereas defining the content of this document to such a granular level, its outcomes can naturally be incorporated into EHR standards, developing organizations and pediatric initiatives such as HL7 or the Public Health Informatics Institute in which you were all briefed at during your January meeting by Dr. David Ross.

"As this advisory committee has, we recognize the role of information technology and the provision of quality care, and in doing so, consider its implications in drafting our intellectual property for providers and for the public.

"It is our hope that this clinical report will assist in identifying clinical standards of care for these newborns and children. We look forward to the opportunity to further partner with ACMG's national coordination center for regional genetics and newborn screening collaborative groups to evaluate the implementation of this clinical report. We believe that through ongoing evaluation of such standards, the pediatric community can then ascertain best practice models.

"Once again, we applaud HRSA/MCHB's leadership and commissioning of the ACMG report, and it's continued forethought regarding expanded newborn screening as we both share in the mission of improving the quality of lives for all children, youth, and their families. We look forward to continued dialogue about how we can assist and enhance this domain of care.

"Respectfully submitted, Carol D. Berkowitz, President."

DR. HOWELL: Thank you very much, Amy.

That's obviously invaluable to have the input of the American Academy of Pediatrics and its 60,000 members. Obviously that group has been involved in newborn screening, and working with this committee and so forth will be very helpful as we go forth.

Are there questions of Ms. Brin about the Academy's recommendations, comments, and so forth?

Coleen?

DR. BOYLE: Just a thought, and we can table it for next time, but in terms of a liaison capacity for the American Academy of Pediatrics, I don't know if that's something we've talked about and discussed.

DR. HOWELL: I don't think that was on our list today. I think that might be the elephant in the room, because obviously we will need to be certain that the academy has defined the liaisons to the appropriate areas and so forth.

I think that perhaps Steve as an ex-President of this organization may not have specifically mentioned that, but I'm sure that was much in your mind.

DR. EDWARDS: I was listening to what Education and Training was looking at. I would suggest that the Follow-Up Committee, because that was one of my choices as far as an individual about where I would like to be. I would hope that maybe you could consider an AAP representative for the Follow-Up Committee.

DR. HOWELL: But obviously that's something that we will need to discuss, the appropriate organization of formal input from the academy because of their critical role. Thank you very much.

DR. LLOYD-PURYEAR: Coleen, you mean to the committee.

DR. HOWELL: Yes. I interpreted that.

We'll continue with our public comment at this point. We'll come back to the liaison, that's well put. Again, we welcome Ms. Fisch.

MS. FISCH: I'm back.

DR. HOWELL: Jill says she's back. She's here now presenting for Theresa Murry. This time she is going to take a new persona, and she's going to sit. I introduced Jill earlier.

MS. FISCH: I'm reading on behalf of an FOD family.

"My name is Theresa Murry, and I am a Save Babies Through Screening Foundation volunteer. My story is a bit different than those of newborns who are either diagnosed too late or misdiagnosed. My story is that of a young girl that lived to be 20 years old, and who died mysteriously and suddenly after a camping trip with friends.

"My daughter Michelle had only been sick really only once in her life. That was when she was two years old. The doctors at Texas Children's Hospital tested her for over 70 different diseases and possible illnesses, all tests which came back negative. After a week in intensive care in a comatose state, she suddenly improved. The doctors stated that 'whatever she may have had' must have been 'cured' and there wasn't enough of whatever virus 'it could have been' left to detect in the tests they were running. Her illness at that time was deemed a 'fluke.' For the next 18 years, she lived a very normal and very uneventful medical life.

"At 20 years old, she went camping with friends. She climbed a mountain and came back to the campsite tired and not really willing to eat much, so she slept instead. A few hours later, she became very ill, and by morning, she still hadn't eaten. Her friends thought she had contracted the flu. Her condition worsened to the point to where they took her to the emergency room, and she was then transported to Herman Hospital in Houston.

"After many tests and several hours of waiting, they determined that she 'needed to sleep it off,' convinced that it was some type of drug use or alcohol, though neither had been detected in her system. She was moved from the emergency room to 'observation,' where she died within a few hours.

"After 4 months, the Harris County medical examiner ruled her death as though she 'died of natural causes, cause unknown.' As her parent, I was told, 'these things happen' and 'sometimes people just die and we don't know why.' I cannot express the anger and hostility that took over my life and the frustration our family felt as we were treated as if we were 'parents in denial' or that somehow Michelle had contributed to her own death.

"Our answers came 14 months after she died from the doctor who treated her in the emergency room. He also didn't understand how a perfectly healthy girl could die so quickly at 20. With our permission, he continued to have tests run from 'samples' that had been kept at the medical examiner's office.

"Michelle had died of MCADD, a rare hereditary disease that is caused by the lack of an enzyme required to convert fat into energy. People with MCADD cannot fast for very long. Remember, she hadn't eaten after climbing the mountain with her friends.

"My point in telling this is that even though I strongly support the screening of newborn children, I feel it is only the first step.

"Recently I read that a geneticist at a Louisiana Children's Hospital told one mother who wanted these tests run on her children that she needn't worry about it. She was told by the geneticist that there

was no way her sons, the youngest of whom is two and a half, could have MCADD, because that disorder only affects babies.

"As the mother of a dead 20-year-old, I can confirm that this is ridiculous. How many other parents have lost a child to a disorder that our professionals have not been able to diagnose simply because they didn't know where to look or didn't even look in the right place? I sometimes hear of young people who died after a sporting event, or sudden but brief illness, and wonder. I can confirm it doesn't get much worse for it to be undetected by a coroner as well. Our society teaches us that they are our last hope for answers.

"I feel that every death, especially that of a young person or individual under 50 that is ruled 'died of natural causes, cause unknown' should be tested for metabolic disorders as a possible cause of death. Though I realize that in no way will it bring back a lost loved one, it will help to put the death in perspective. Without answers, there is a gaping wound that will not heal that includes anger, dismay, guilt, and confusion.

"Thank you for the time. Theresa Murry."

DR. HOWELL: Thank you very much, Jill, for that very moving note about the mother of a young woman with MCADD deficiency.

Our final person speaking this afternoon in the public comment area is Dr. Alan Hinman. Again, Dr. Hinman, as you've heard from earlier, is a very experienced member of the CDC team. He is here to speak to us this afternoon.

DR. HINMAN: Thank you very much, Dr. Howell. I'm a former member of the CDC team. I retired nine years ago from CDC. I'm Alan Hinman with the Public Health Informatics Institute, which is a not-for-profit organization that has been working with the Maternal and Child Health Bureau for the last five years on trying to integrate child health information systems. Our basic premise is that health and health services can be improved by the timely provision of accurate and comprehensive information.

As an example, looking at the CORN report for 1999, of the 4 million and some PKU tests that were done, 3,494 were reported as not normal, as a result of which, 302 cases of PKU or clinically significant variants were detected, a rate of about 11 follow-ups per case diagnosed. However, there were 154 persons with non-normal tests who were apparently lost to follow up. If you divide 154 by 11, that suggests there may have been 14 cases of PKU missed in 1999.

We don't know that that is the case, but that is what was known to the program people who reported the data. If you look similarly at tests for congenital hypothyroidism, there were 52,217 not normal tests, resulting in a diagnosis of congenital hypothyroidism in 1,550, a rate of about 32 follow-ups per case diagnosed.

There were 1,371 non normals who were lost to follow up. Applying the same ratio of 32 follow-ups per case, that suggests there might have been as many as 42 cases of congenital hypothyroidism missed in 1999. Again, we don't know that that's the case.

We also know from similar data which are reported on the number of days between birth and initiation of therapy for primary hypothyroidism for the cases for which there are reports, only 44 percent were known to have treatment initiated within 15 days, which is the recommended cutoff. You should be under therapy by 15 days.

Twenty-four percent were known to have had therapy initiated after 15 days, and for 32 percent it wasn't known to the people who were reporting to the CORN system. Again, we don't know when these children were put on therapy. What we know is that we don't know.

We also know that currently according to folks in the National Center for Birth Defects and Developmental Disabilities, the loss to follow-up rate for newborns with abnormal hearing screening is on the order of 40 to 50 percent nationwide. So I suggest that there is an information problem, and it has at least some potential for having serious clinical repercussions at the present time.

A study that the Genetics Services Bureau funded found that 4.5 percent of primary care pediatricians were not notified of screen positive results. The results were reported to tertiary care centers, to the hospitals, to somewhere, but not to the primary care pediatrician, and that 26 percent of the time, screen negative results were not reported to the primary care pediatrician. In this case, no news is not necessarily good news, it's just no news.

Again, I suggest this is an information problem. I am pleased that the Follow-Up Committee is going to be addressing issues of information systems and bringing information to those who need to have it, and urge that this be given priority.

I would say a couple of things about this. We talk about integrated health information systems. What we mean by that is that the information is presented to the user in an integrated fashion. It doesn't really address what the hardware and software is, but whoever is an authorized user has access to all the information available about the child. That may be a pediatrician, it may be a public health program, it may be a family member or parent if they are authorized to have access to this information.

Parents have talked about the fact that they are the purveyors of information about their children. That's because physicians don't have it. We put the information in a way that it can be given to the providers so that one can see at one's screen what is happening with a child.

If you think particularly in the hearing arena with a 50 percent loss to follow up, these are children who are being seen at 2 months, 4 months, and 6 months for immunizations. Wouldn't it be nice if the pediatrician who was giving the two-month DPT had available on the screen in the computer the fact that this child had a failed hearing screen and not been followed up, or that an abnormal dried blood spot screen had not been followed up, or that it had been followed up and had been found that there was no problem.

So I just encourage continuing priority to be placed on developing information systems. Thank you.

DR. HOWELL: Thank you very much.

Are there questions of Dr. Hinman?

(No response.)

DR. HOWELL: It's my impression that there is a federal initiative going on in electronic medical records, is that correct? Can you bring me up to date on that?

DR. HINMAN: There is a lot of work going on in developing health information systems and health information networks nationwide. A lot of it is on developing electronic medical records.

I will say, however, that the primary emphasis on this is electronic medical records for adults. One of the things that the Academy of Pediatrics is concerned about, and that I think we all are concerned

about, is the special information needs of children, which are different from those of adults in terms of medical records.

Adults, you don't have to worry about growth and development charts, you don't have to worry about dosing by weight. There are things that are different. One of the issues I think is to be sure that the needs of the child are addressed as this health information initiative goes forward. I also have to say that the public health issues are addressed.

If you look at most of the diagrams that describe these systems, they show public health, often the coroner, receiving information. That's really unfortunate, because the public health system can provide information as well, which can be very useful. For example, in Michigan, the physician logs onto the immunization registry, and the first screen is a screen of information that's helpful.

You can now administer the forced dose of Prevnar, because our supplies are good, or here is where the influenza vaccine is. This is not just a one way sucking up of information, which many people think of for public health.

So I'd say that there is a pediatric steering group with representation from NACHRI and the other children's hospital organization, the Board of Pediatrics and the Academy that is meeting regularly and holding conversations with Dr. Brailer and with Dale Nordenberg from CDC who is on part-time detail to deal with child health issues in this arena.

DR. HOWELL: Thank you very much.

In a very timely fashion here, I think that completes the folks who have signed up for public comment. That takes us back to winding up our business here in the next hour for committee business and discussion.

Let me ask, before we get to one of the principal things that I would like to spend a good bit of time, the letter, the document that we're going to send to the Secretary, I would like to discuss that with you a little bit more, a good bit more, but before we get to that, are there other issues other than the letter that we're going to compose to the Secretary? Within that letter will be recommendations from this committee about the ACMG report, and also recommendations and comments about the public comments on that report that we will send to the Secretary. That will be in the letter.

So other than that, are there other issues that you want to discuss for the meeting? Michele reminds me to look at the calendar, which is in the very back of your book. Next year we're having three meetings.

DR. LLOYD-PURYEAR: And to give me any changes, and we'll finalize it in October.

DR. HOWELL: Fundamentally, the thing that's in the back is a blank calendar with the dates that have been tentatively suggested. If you'll notice, they're in October, the dates that are already set are the 20th and 21st. Then some other meeting dates in January, the 19th and 20th. May the 18th and 19th, and then the third and final meeting of 2006 at the 28th and 29th of September.

DR. EDWARDS: I have a conflict in May.

DR. LLOYD-PURYEAR: Okay.

DR. EDWARDS: It's the third weekend. The third Friday in May always.

DR. LLOYD-PURYEAR: Okay.

DR. HOWELL: Now, what is the discussion that we just had? What did you say? You just changed the dates?

DR. LLOYD-PURYEAR: Yes. If everyone could look at the dates of May 25th and 26th instead.

DR. EDWARDS: She's asking if we could do it Wednesday and Thursday.

DR. HOWELL: So the suggestion is the 24th and 25th, which is a Wednesday and Thursday, in view of the fact that that is Memorial Day weekend.

I think Michele has vetted these dates with the rest of the committee, is that correct?

So anyway, those are the meetings for next year. Anymore comments about the meetings for next year? Any other business, other than the letter that we want to put together for the Secretary?

Steve?

DR. EDWARDS: The question that I guess Coleen raised about the American Academy of Pediatrics, I was thinking that she was referring to the subcommittees. But then somebody clarified I think that she was talking about liaison committees. It's my understanding that we cannot have anymore members in this committee, but I'd like to understand what the distinction is there, and what the opportunity is as far as liaison members are concerned.

DR. HOWELL: We'll ask the experts. Peter, could you define again for the group, or Michele, what are the exact rules?

DR. LLOYD-PURYEAR: It's in the charter. The charter provides for liaison representatives from organizations. These are non-voting individuals, representatives from organizations that are nominated by organizations and represent their organizations.

So they participate in the deliberations, but they do not vote. What else? We don't pay for them. They don't get paid. Their travel is supported by their organizations. They are not subject to the approval by the Secretary of HHS. Again, their organizations approve whoever is representing the organization.

DR. HOWELL: So the mechanics of that is that this committee could recommend that a given organization identify a representative to this committee, and that person would serve as a liaison member, be non-voting, but would be participatory in the activities and would not be funded in travel in support for the meeting.

Duane, is that your understanding? Duane is an expert on committees also, needless to say.

DR. DOUGHERTY: It was my impression that Dr. Edwards was the AAP representative.

DR. HOWELL: Dr. Edwards is not an AAP representative, although he has strong credentials in that area. But Denise, he is not.

DR. LLOYD-PURYEAR: He was not the liaison for the American Academy of Pediatrics. He was a member at large representing all health care professionals.

DR. HOWELL: But again, appointed through that mechanism, but not officially as the liaison from any specific organization but health care in general.

DR. EDWARDS: Having heard the discussion then, I would at least like to open discussion of the possibility of having liaisons from — well, we heard from OB/GYN today certainly as far as our Education Subcommittee is concerned. I think it's pertinent. But I think it probably has a wider degree of pertinence just from education, looking at the American Academy of Pediatrics, as well as the American Academy of Family Practice.

So I'm not formally proposing those, but I would like the committee to at least evaluate those as possibilities for liaison members.

DR. HOWELL: Can we have comments about that? Actually Steve has recommended obviously the three major physician groups that deal with newborn screening at the clinical level, family practice, pediatrics, and obstetrics and gynecology as a discussion, as potential liaison members to the committee at large. Can we have comments from the group around the table?

DR. ALEXANDER: We heard today the presenter from ACOG almost request liaison membership. Three of the people who testified for the public this afternoon recommended them participating with us as well. So I would certainly participate in that.

Therein, it would certainly make sense to have Academy of Pediatrics and the Academy of Family Practice liaison members as well. So I would support Steve's suggestion.

DR. HOWELL: Further comments from anybody at the table?

(No response.)

DR. HOWELL: No one has an opinion at all over there? Any opinion?

DR. BECKER: Rod, I would support that suggestion as well.

DR. HOWELL: Okay. I see nodding of the heads and so forth.

Piero?

DR. RINALDO: Just to say the silence means yes.

DR. HOWELL: Well, one might infer that, particularly from this group.

(Laughter.)

DR. HOWELL: But certainly it makes imminent sense for these three groups to have an active involvement with the committee overall, because I think that there is a lot of involvement that will be at the clinical arena.

Denise?

DR. DOUGHERTY: I have to have a comment. I'm just wondering what the role of say pediatric nurse practitioners is in caring for children identified by newborn screening, and whether that group, NAPNAP, should be part of this, or another nurse group. I'm not sure.

DR. HOWELL: Bill?

DR. BECKER: Well, obviously they have a role, as implied by the raising of the topic. I can tell you that that particular group is being considered for inclusion on the Education and Training Subcommittee. At least we would feel that that would be an appropriate place for their input to be a part of this process.

DR. HOWELL: Piero?

DR. RINALDO: Well, if we go down that path and we recognize professionals who clearly have a defined role in newborn screening, then I think it is hard enough to mention genetic counselors, especially for metabolic patients. They have a vital role in the follow up.

DR. BECKER: And Piero, another group that we discussed today is a potential subcommittee liaison member as well.

DR. HOWELL: Well, if we go down the particular road we're talking about, we quickly are on 495, I can tell you. It would be very difficult not to have the American College of Medical Genetics at the table. It seems to me, and I'm sympathetic, Denise, with your comment, but it seems to me that certainly at the outset we should consider for membership as liaison members the three very large independent groups that have a heavy involvement.

I would suggest that we try to focus there. Again, nurse practitioners, genetic counselors, and the other genetic professionals, pathology, for heaven sake and so forth, all have major roles. But I would suggest we try to remain a little focused at the outset with the three big groups and so forth.

DR. EDWARDS: Well, I did not make it as a recommendation, but with everybody seeming so conciliatory, I would like to make that as a recommendation then that we invite as liaison members representatives from the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, and the American Academy of Family Practice.

DR. HOWELL: Is there a second for that? That a motion that you made. Is there a second to that?

DR. BECKER: I'll second it.

DR. HOWELL: Then we can have a discussion.

DR. LLOYD-PURYEAR: I need to clarify language, for the record. They are not liaison members, they are representatives of organizations. They are not liaison members.

DR. HOWELL: What will be their official title?

DR. LLOYD-PURYEAR: We have liaison members that are representing the Secretary's Advisory Committee on Genetics, Health, and Society who are also non-voting, and the Secretary's Advisory Committee on Infant Mortality.

DR. HOWELL: Yes.

DR. LLOYD-PURYEAR: These are representatives. They are not members, they don't vote.

DR. HOWELL: All right.

DR. LLOYD-PURYEAR: That's important.

DR. HOWELL: But I think that aside from the technical commentary about their definition, I think we would agree that what we'll ask these folks to do will remain the same.

So we've had a motion and a second. Michele has clarified the definition of what they will be called. Does everybody favor that? I see nodding of the heads unanimously in the bright sunlight over there. Great.

Is there any other discussion? Joe?

DR. TELFAIR: Yes, I think that while I would agree that the recommendation for representation of the organizations for the larger group, the physicians, be recognized, I think the point was made earlier, and also I would like to make the point because I've heard the discussion, that there are multidisciplinary providers that exist who have a significant role in newborn screening and they exist at all levels.

I think that if this committee is considering that level of input, as it was demonstrated, even in the review of the report, that there be some discussion among maybe having those as representatives like the Follow-Up and Treatment Committee has had as advisors or consultants to the subcommittees, that we consider that also and make sure that we bring that up as a point to be made.

I recognize that they cannot necessarily, because this would make this a bit unwieldy, but I would just for the record like to say that they be recognized at some point of having input into the deliberations at the subcommittee level.

DR. HOWELL: I think that's a good point. And again, the subcommittee makes recommendations of additions to their committees. But, for example, some of the groups, for instance, the pediatric nurse practitioners, would strike me as being extremely relevant to some of the follow-up programs and so forth, and some of the other groups might be more relevant to the Laboratory Committee or something. But I would encourage everybody to think of people and add people to their committee.

DR. LLOYD-PURYEAR: There are some financial implications to this. Representatives get paid by their organizations, but consultants and members, we pay for. If representation is what you want, and the input from that organization, you could do it as a representative sometimes, and not always as a consultant.

DR. TELFAIR: Well, I guess I would agree. There are sort of low cost, no-cost ways of using people and getting their input. That's a HRSA quote, low cost, no-cost.

(Laughter.)

DR. TELFAIR: That's a use of people, but using their expertise or taking advantage of their expertise. I don't mean using in that sense.

(Laughter.)

DR. TELFAIR: Never mind, never mind.

DR. HOWELL: Denise is an expert on how to get things out of people free, I'm sure.

DR. EDWARDS: Let me ask a follow-up question there that then comes up. These groups are three of the representatives that we had considered for having at the Education and Training Subcommittee. But then if they were to come to this meeting as representatives, then we could adopt them, and then still have our five or six other positions for committee members, is that correct?

DR. HOWELL: Oh, yes.

DR. EDWARDS: Thank you.

DR. HOWELL: Oh, yes, without question. The final order of business that we want to complete today is we tried to capture some of the discussion from yesterday about really two areas. One is, and please, I'm going to pass around, I'll ask Michele to pass around in just a minute, a document that we worked on which I would dramatically encourage you not to wordsmith, but to look at content.

We tried to capture the major elements that came out of the discussion of the report yesterday that you want to convey to the Secretary. We would like to tell the Secretary that we're sending this forth. We have read the report, and we make the following series of recommendations as we move forward. Finally, after doing that, we would pick up on Steve's comment yesterday of recommending that the Secretary accept this report and take action to see that the states would move forward on screening.

So Michele will pass these around, and I will be right back. Some people I see are still reading. This is not anticipated to be a final letter, but basically some of the points that would be covered in a document that would go forth.

As we look at the thing, obviously the first sentence is just repeating that as you know, we sent a letter to the Secretary last September, that's in the first bullet. It points out that we discussed the report additionally this past January. Thirdly, that the committee has reviewed the public comments that came in that we discussed yesterday.

The next thing is the fact that the committee endorses the report and general recommendations, and concern about methodology that was expressed by some of the commentators fairly stringently. Although this was, again, reviewed, and the committee felt that all of those issues were there, that the basic report and its final decisions were appropriate, and that the process is felt to be a dynamic process that we look upon as being variable.

Then there is a list of things that are here that we need to do going forth to make this whole thing work. These are some of the points that this group will be looking at that needs to be done. The committee is starting on those deliberations.

A final recommendation, Steve had made a strong recommendation yesterday about recommending to the Secretary that the Secretary accept this and really move ahead to make this happen.

Now, the one thing that as I look at this, and the discussions that we've had since lunch that is not here that we ought to talk about, is some of the things that we really have got cranking up in the process that we've got that are going to require some resources. I wonder if this committee shouldn't at least insert, I don't know how or what, but to say that as we move forward to solve these problems and to get consultants to do things and to help get the methods straight, that we make a brief comment about the fact that it would be extremely important and helpful for additional resources to be available and so forth.

Again, I think that that would be something that would need to come from this committee, because Dr. van Dyck and company can't appropriately, I think, request that. I guess you could, but it seems appropriate that the committee could say that we need adequate resources to do this and so forth. I'm aware of the fact that resources are scarce as they can be, but at least we should recognize that some of the things we want to do are going to require some funding. It would be nice if we at least made a mention about that.

Can we have some comments about these points that are listed on the paper and so forth?

DR. EDWARDS: Well, I would just like to put it on the table by recommending the adoption of this statement. I won't try to wordsmith, but I would like to say something like instead of the last sentence, I'd like it to be a stand-alone type statement so that it could say after reviewing the recommendations of the American College of Medical Genetics, and after having reviewed the public commentary on those recommendations, that then we recommend that the Secretary take appropriate action to facilitate the adoption of the ACMG recommended screening panel by every state newborn screening program, and appropriate adequate financial resources for that implementation.

I would make that in the form of a motion.

DR. HOWELL: Dr. Edwards has made a motion. Is there a second to that motion?

DR. RINALDO: Second it.

DR. HOWELL: Dr. Rinaldo seconded that motion. We now can have some discussion on the document that has been recommended and seconded.

Amy?

DR. BROWER: And not to wordsmith either, but I wonder if we can add the word "strongly" recommend, if that makes a difference from just recommend. I would support saying strongly recommend.

DR. EDWARDS: I think it makes a difference. I consider that as a very friendly amendment.

DR. HOWELL: And you agree with that? Both the persons that made the recommendation and the second consider that and so forth.

Other comments about the document? And again, this will have to be formatted carefully and appropriately worded and so forth. These are the points that would go in such a document from this committee to the Secretary.

Denise?

DR. DOUGHERTY: One thing about inserting the need for resources, I think that is really something that needs to happen. However, this is one of those rare committees where some federal people are voting members.

I'm wondering if we should not vote because of that reason. I'm not sure how this would play out, because I'm not familiar with all the variations of committees. But for our names to be on a letter saying there should be more resources, I'm not sure that that's —

DR. HOWELL: Well, I think that's very easy, then. The Secretary could just take it out of your respective budgets.

DR. DOUGHERTY: Exactly.

DR. HOWELL: And that would not be a problem.

DR. DOUGHERTY: He'll do that anyway.

DR. HOWELL: We need several hundred thousands of dollars. Just divide it among the feds and so forth.

DR. EDWARDS: Couldn't he just call it a conflict of interest and abstain from voting?

DR. DOUGHERTY: Well, I would like to know what the guidance is, though, and what the feds are supposed to do in this kind of situation.

DR. HOWELL: What would be the guidance, Peter, from the federal side of this committee?

DR. van DYCK: I'm not aware that it's a particular problem, but I think it is probably an appropriate role to abstain from the vote for the federal employees.

DR. HOWELL: They can't hear you, apparently.

DR. van DYCK: Oh. I'm saying it's probably appropriate for the four federal employees to abstain from a vote that would suggest additional money.

DR. HOWELL: Is there a way that we could get the additional money thing? The document is a very important document, I think, from the committee. I must confess I hesitate to have it go forth with abstention of our distinguished colleagues here. On the other hand, I appreciate the sensitivity about the money issue and so forth.

DR. DOUGHERTY: But the other thing is that, as Peter described, the agencies are going to have to either help develop a document that goes through clearance and approve it so that we will have our own opportunity to comment to endorse whatever we do. So I'm not sure that it's that big of a deal for us not to be voting as part of the committee.

DR. HOWELL: I think some of the committee may not be completely aware of this, but it is policy when a recommendation comes forth from an advisory committee that the federal agencies that have involvement in that area — NIH, HRSA, CDC, AHRQ — have a document that goes forward from that group concerning the ACMG report, for example.

It is my impression that that will be a detailed document, particularly with some of the criticisms. Is that correct, Peter? Is that appropriate to discuss here? So that's what Denise is alluding to.

DR. RINALDO: Well, I think we need to ponder a little bit of what is more important, to add a generic statement at this time about the resources. I don't know if it's a reality of the consensus, because I think that adds significant value, at least in my mind.

So I don't know. It would imply that there is a need for resources to allow this to be a document that is really supported by the whole committee, rather than eliminate half of it. I'm concerned of somewhat the perception similar to the deliberation I believe we had in September last year. That, in my opinion, I think would be a disservice at this point.

DR. HOWELL: Bill?

DR. BECKER: I don't have any comment on the issue about the resources statement. Mine is a different one, so if you want to finish that and come back to me.

DR. EDWARDS: I certainly respect Piero's point, and would be happy to do it either way. I think it really sounds nice if you say the committee unanimously endorses. It obviously would be stronger.

As Piero said, if they adopt, then there is an implied necessity for providing funding if you adopt the report. It is only implied, though. So I think he has made a good point, and I would be happy to change it, to drop the financing portion if that's going to be the stumbling block.

DR. HOWELL: Dr. Alexander?

DR. ALEXANDER: When you have language that says take appropriate action to facilitate adoption, the first appropriate action is to provide some funds to help make it happen. It's implied here whether you specifically say it or not.

I'm not sure you had that much by pointing out the funding aspect of it. Leaving the language general like this would enable us to vote for it.

DR. HOWELL: So you would suggest just as it is stated, facilitate appropriate action, and that would imply that? If we took out the other, that would make it perfectly adequate then for the federal representatives who vote on this committee to consider the document.

DR. DOUGHERTY: In that case, if you want our vote, I have a few suggestions for some wording changes that would make it reflect the entire committee's views.

There is sort of a downplaying of very few commentators having said something about the methodology, when in fact it was some committee members.

DR. van DYCK: Can you speak up a little bit, Denise?

DR. DOUGHERTY: Okay.

DR. van DYCK: We're really having trouble hearing.

DR. DOUGHERTY: Okay. There are just some wording changes, very minor, I think, that I would like to suggest so that this does reflect the view of the entire committee.

DR. HOWELL: Speak out.

DR. DOUGHERTY: Okay. Well, one, I would say that yes, the committee, and I don't know if you want to finesse this or not. It's fine to say in September the committee voted to endorse and recommend the report and its findings to recommendations to the Secretary. That's not exactly what happened.

What happened in fact is you sent the report but did not recommend it. At least that's the language I read here. In this letter that's in Tab 6 —

DR. LLOYD-PURYEAR: This is 2004.

DR. DOUGHERTY: Oh, okay.

DR. HOWELL: Yes.

DR. DOUGHERTY: But did that letter ever go forward?

DR. HOWELL: Yes.

DR. DOUGHERTY: That's fine, then.

DR. HOWELL: It did recommend.

DR. DOUGHERTY: In the third bullet, which says the majority of comments were favorable to the report and it's findings, I don't know that we did a real count. Because one of the things that really struck me when I was going through this was that the real plurality of comments were postcards from people wanting SCID to be included in this. Then there were another set about Krabbe disease. So those were not endorsements of the report.

DR. LLOYD-PURYEAR: Actually, the Krabbe disease ones all endorse the report. You are right about the SCIDs, and they're not included in this count.

DR. DOUGHERTY: Okay.

DR. LLOYD-PURYEAR: We did do an analysis of each and every comment.

DR. DOUGHERTY: Okay.

DR. HOWELL: We do have those numbers, but that is accurate.

DR. DOUGHERTY: Okay. I wasn't aware of that, because we just discussed this in general terms yesterday.

DR. LLOYD-PURYEAR: You had the comments, though.

DR. DOUGHERTY: Yes, but I didn't know that some people were taking out some of the comments, and then calculating the majority. Do you know what I mean?

On the fifth bullet, I think if we substituted "some" for "a very few," of the commentators, I would be happy. That's the only instance in which we kind of diminish what a particular public comment was.

Even though they were few, they were strong. And then I guess in the last sentence, I'd be happy with taking out "science" and putting in "methods."

DR. LLOYD-PURYEAR: On the last sentence of which?

DR. DOUGHERTY: Of that bullet five.

DR. LLOYD-PURYEAR: Method?

DR. DOUGHERTY: That's methods available.

DR. HOWELL: Okay.

DR. RINALDO: So you want methods?

DR. DOUGHERTY: "Methods" instead of "science."

DR. RINALDO: Is there any other word instead of "some?" It is already in the same sentence.

DR. DOUGHERTY: The first one?

DR. RINALDO: Yes. There were some concerns from some commentators.

DR. DOUGHERTY: Several?

DR. RINALDO: No.

DR. DOUGHERTY: Oh, okay. Take out the first some and put in another one.

DR. RINALDO: Nice try.

DR. DOUGHERTY: Okay. Take out "some," but also take out "a very few."

DR. HOWELL: Add "some." Take out the first "some."

DR. RINALDO: I think it really becomes fairly trivial. I think that the numbers that Michele is pointing the finger to on one and there were five —

DR. DOUGHERTY: Well, there were more.

DR. RINALDO: I don't have the number.

DR. BOYLE: I feel like we're being very reasonable here in terms of a few changes that would make us be able to vote unanimously here.

DR. HOWELL: I would agree with Coleen. I think that we should, you know, the thing is there were very few. But I think that if others would feel it would be more satisfactory to say "some," I think that that will apply.

I think it's important that we all be comfortable with this document. It's a compromised document, but we want to send the Secretary a clear message. I think Denise has made some very thoughtful suggestions here.

DR. DOUGHERTY: I guess the other thing that's missing is just to say what I said yesterday about how some people pointed out some minor errors in the report, and they will be corrected.

DR. HOWELL: Right. Maybe we can just add a brief thing saying that some —

DR. DOUGHERTY: They won't be corrected?

DR. HOWELL: We can't correct the report.

DR. DOUGHERTY: We can't.

DR. HOWELL: We cannot. We can only comment on the report. It's not our report. Although we take great possession of it at times, it's not our report.

DR. BECKER: You can note them, but even if you want to say anything about them, you can note them, but I'm not sure that —

DR. HOWELL: Were there other comments? The person who made the motion, Dr. Edwards, and the seconder, would you accept these modest changes as friendly?

DR. EDWARDS: Yes.

DR. HOWELL: Further comments about this document?

DR. BECKER: Okay, Rod, no wordsmithing, but it is a style sort of approach. At the bottom of the first page, the listing of the particular items.

DR. HOWELL: Yes.

DR. BECKER: I don't know if Secretary Leavitt is a techie or not, but maybe listing the lab stuff first might not catch his attention. Although he did come from EPA, so he might be a techie.

What I would suggest, though, and it might be a grabber, particularly for an agency of health and human services, to list the medical home bulleted items, just pull it up towards the top. The second item, you could make it education, but if you wanted to leave that where that was, I wouldn't have a problem with that.

I think the medical home is hugely important for an agency like health and human services, maybe to get to that one first.

DR. HOWELL: Is there any concern about the order of these?

DR. LLOYD-PURYEAR: There was no prioritization.

DR. HOWELL: Yes.

DR. BECKER: Well, then maybe just take a look at it and give it some thought. I mean, it is just an appearance thing.

DR. HOWELL: But I think it's important to think about what might be the first thing that hits your eye, and that's very helpful.

DR. BECKER: And then philosophically, there is one item not in the list that was discussed yesterday. It is kind of implied in our summary statement at the end, but it is the policy-setting process that was one of the items that we identified as an element of some of the comments that we received.

Now, again, our request is sort of like back with the resources thing, Steve, and I think this is to Duane's point. We are recommending that the Secretary take appropriate action to facilitate adoption of the ACMG recommended screening panel. That implies a policy-setting process.

I don't know if that's good enough, but I want to put it out on the table for us to consider, because it was something we discussed yesterday.

DR. LLOYD-PURYEAR: I'm not sure if you're talking about a policy-setting process for the committee, because we're proposing a policy-setting process to the Secretary, the committee is. Or do you mean a policy-setting process for the state newborn screening programs?

DR. BECKER: That actually was the specific type of comment that we received.

DR. LLOYD-PURYEAR: So a policy-setting process for state newborn screening programs?

DR. BECKER: That's correct. Because see, we're listing in this letter, proposed letter, that there were some concerns about issues of the ACMG report. The policy-setting process was one of those things that was brought up. That's fair, decision-making process, yes.

DR. HOWELL: Any comments? Good. Greg has been waiting.

DR. HAWKINS: Yes, just one comment on the next to last, where we said the committee has begun to examine these issues. I wonder if when we say we have begun to examine these issues, if we could just kind of spell it out, that we have formed subcommittees to address that.

I think we should go into detail and show them the actual action items that we've done rather than just say we've begun. So if we say we've formed three subcommittees and we've —

DR. HOWELL: So we'll add then a little thing about what has begun without being lengthy. My thought is as we were trying to put things on paper, I think the absolute maximum of this letter must be two pages. So it has to have headings, it has to have an HHS heading on the thing, it can't go beyond two pages, and it has got to be 12 point type.

DR. HAWKINS: You can't slip in 11.

DR. HOWELL: It has to have room for a big flourish of signatures. Anyway, what else would you like to see on this?

Denise, we're not going to hear much more from you here.

DR. DOUGHERTY: No, no. I have one more. Under this last bullet on the first page where there are several bullets under that where it says, "committee process and infrastructure for future evaluation of new technologies."

I think we are really evaluating new conditions for inclusion and new technologies, right? Because we may be considering conditions that should be tested by existing technologies rather than just refer to new technologies. That's all.

DR. HOWELL: I think that improves the wording there a little bit.

Amy?

DR. BROWER: I would just like to see if we can make sure that "strongly" is inserted, and "unanimous."

DR. HOWELL: Strongly, and with all the smiling and nodding, it had better be unanimous, or there are going to be a few people off the 8th floor on Pennsylvania Avenue.

(Laughter.)

DR. HOWELL: Without parachutes. Leave it to Denise. She is an expert. She's checked, and the doors are all locked. She was worried about that.

Joe?

DR. TELFAIR: Yes, just to add on the second page at the top, the second bullet. Because of the issue related to access, I just wanted a point of clarification. If we talk about health systems, we're also talking about health services research as well.

DR. HOWELL: And how would you think that would better be worded?

DR. TELFAIR: Well, because of the issues related that we talked about the other day, you have health systems and outcomes research. I was wondering, were we speaking of services as well? I know sometimes there is an interchange, and Denise knows what I'm talking about. Is that adequate? I guess I would have to ask Denise, because this is your neck of the woods.

DR. DOUGHERTY: Yes. That's adequate.

DR. TELFAIR: Okay, fine. Then the other part of it is —

DR. HOWELL: Health systems.

DR. TELFAIR: Because there is a discussion that goes on, I just wanted a clarification.

The other point I'd make is that in the third bullet on that page, there are literacy issues. There are linguistic issues, but there is also literacy issues as well that need to be indicated here.

DR. HOWELL: You're talking about the attention to cultural literacy?

DR. TELFAIR: Literacy.

DR. HOWELL: And so add "literacy" in there.

DR. TELFAIR: Right.

DR. HOWELL: We certainly heard a lot about that at one of the earlier meetings.

DR. TELFAIR: That was it.

DR. HOWELL: Does anybody else have anything to add or comment on? I gather that the changes that you put in here make you comfortable with the document? We will work then on a letter and try to get that put together as soon as possible.

This will be the content of the letter. We may change a little wording or order, but everything will be here as you see it, and so forth. If everyone now has said his or her peace, can we have a motion and a second, and those persons have accepted the modifications that have been made, the wording that has been made.

So I have a motion and second to changes in the wording. Can all those favoring this document please raise his or her hand?

(Show of hands.)

DR. HOWELL: And it is unanimous. Thank you very much. We'll get that cooking.

You have been very efficient today. I said we'd finish at 3:00 or before, and it's before.

Dr. Rinaldo has words.

DR. RINALDO: Can I make a comment?

DR. HOWELL: Yes.

DR. RINALDO: It might be a bit surprising coming from me, but I actually want to express my appreciation to Coleen and Denise for the efforts they have made to find a common ground with some of us. I actually think this is an example of a truly working committee. So thank you.

DR. HOWELL: Having heard that comment, I expect the Pope to come through the roof.

(Laughter.)

DR. HOWELL: Thank you very much. We'll see you later.

(Whereupon, at 2:50 p.m., the meeting was adjourned.)