SECRETARY'S ADVISORY COMMITTEE ON GENETIC TESTING

Eleventh Meeting

Thursday,
November 15, 2001

Congressional Ballroom Salons II and III
Bethesda Marriott Hotel
5151 Pooks Hill Road
Bethesda, Maryland

IN ATTENDANCE:

Chair

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C O N T E N T S

C O N T E N T S

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

DR. McCABE: Well, good morning, everyone. I want to welcome everyone to the 11th annual meeting of the Secretary's Advisory Committee on Genetic Testing. The public was notified about this meeting through an announcement in the Federal Register on October 19th, and a posting on SACGT's website. We appreciate the public's interest in our work and, as is our custom, we have provided an opportunity to hear from members of the public during this meeting.

Our meeting will focus on a number of important issues in education, informed consent, rare disease testing, genetic discrimination, and FDA's progress in the development of a framework for the regulation of genetic tests.

This morning Dr. Boughman will lead off with a report on the outcomes of the November 14th roundtable meeting that explored some of the major questions the work group has been tackling, including how genetics fits into current or future health practice, the major genetics educational needs of various disciplines or professions, and obstacles and gaps in the integration of genetics into health professional education and practice. I want to thank everyone who attended the Education Roundtable yesterday and welcome those from the Roundtable who are attending the SACGT meeting this morning. The work group's plans for an Education Summit in February will also be discussed. Then Dr. Joseph Henderson from Dartmouth University will present a novel educational tool developed through support from CDC. Later today, Dr. Koenig will present the Informed Consent Work Group's draft information brochure on genetic testing for the Committee's consideration, and she will walk us through the work group's progress in the

development of recommendations for informed consent for tests in clinical and public health use. She will also be seeking the committee's input on the direction being taken with that project. We will then be briefed by key Congressional staff on the status of efforts to pass genetic anti-genetic discrimination legislation. We will end the day with an update from the FDA on the agency's progress and further development of the new paradigm for the regulation of genetic tests.

Tomorrow morning Dr. Lewis will briefly update the Committee on the Access Work Group's progress. We will then spend the morning discussing issues on rare disease testing. Ms. Davidson and Dr. Michael Watson, co-chairs of the Rare Disease Work Group, will lead the session and we will hear a number of important presentations on the development, oversight, availability, and accessibility of genetic tests for rare diseases. Tomorrow afternoon Dr. Hans Andersson and Marie Krousel-Wood from Tulane University will present data from a CDC-funded study of laboratory reporting of genetic test results. We will close with a brief discussion of the request SACGT has made of the HHS agencies for information on efforts to enhance knowledge of the validity and utility of genetic tests.

We have scheduled public comment sessions for both days. I want to encourage members of the public here today who are interested in making comments on issues relevant to genetic testing to please sign up at the registration table outside of the meeting room.

Finally, I want to conclude by noting that our report on the development of a classification methodology was submitted to the Secretary, and copies are available to the public. The report will also be posted on the SACGT's website next week.

Let's now hear from Sarah for her important reminder about the ethics rules.

MS. CARR: Thank you. Being a member of this Committee makes you a special government employee and thereby subject to rules of conduct that apply to government employees. The rules and regulations are explained in a report titled "Standards of Ethical Conduct for Employees of the Executive Branch," which you received at the beginning of your appointment. At every meeting, in addition to reminding you about the importance of following all the ethics rules, we always like to review the steps we take and ask you to take to ensure that any conflicts of interest are addressed. As you know, before every meeting, you provide us with information about your personal, professional, and financial interests. We use this information as the basis for assessing whether you have any real, potential, or apparent conflicts of interest that could compromise your ability to be objective in giving advice during committee meetings. While we waive conflicts of interest for general matters because we believe your ability to be objective will not be affected by your interests in such matters, we also rely to a great degree on you to be attentive during our meetings to the possibility that an issue will arise that could affect or appear to affect your interests in a specific way. If this happens, we ask you to recuse yourself from the discussion and leave the room. As always, if you have any questions about the rules of conduct or conflict of interest, our committee management officers will be happy to address them. One of them, Mary Nuss, is here with us today.

Before I end, Mr. Chairman, I would like also to take a moment on behalf of the entire Committee and SACGT staff to congratulate you on your recent election to the IOM. We know what a great honor it is, and much deserved. Congratulations.

DR. McCABE: Thank you very much. Also, I'll just mention that we hope to have Pat Barr and possibly Reed Tuckson connect by phone with us during the meeting.

SACGT views a well-trained health care workforce as a critical element of enhanced oversight and a fundamental way of assuring appropriate test use and interpretation. The priority we place on this issue is reflected in the intensive efforts of the Education Work Group. At our last meeting in August, the work group presented a great deal of information about the state of genetics education in the health professions and led the Committee in a discussion of a proposed summit to bring together leaders in the field and the community to explore critical issues in genetic education. Yesterday afternoon the Education Work Group convened a roundtable meeting on genetics education. The participants who represented a wide range of health professional disciplines and organizations were all extremely knowledgeable and insightful about the issues in genetics education of health professionals. The roundtable participants provided the work group with a deeper understanding of the issues and offered a great deal of helpful guidance in the planning of a much larger public education summit to be held next year. Dr. Boughman will report on the outcomes of the meeting and lead the Committee's discussions of where we go from here on this important issue. Joann, thank you very much for the meeting yesterday. The group was really very engaged, and I think it was a very profitable meeting.

DR. BOUGHMAN: Thank you, Ed. Thank you very much. I was pleased to have Ed say that the roundtable and the work group have explored the questions around genetic education, not that we have answered them, because we in fact do not yet have all the answers. I also thought it was appropriate that you all are in the light and I'm over here still in the dark. That's how it feels sometimes.

The Education Work Group has been working for quite a while now, and back in August of 2000, if you remember, all of the work groups were established, with the charge to the education group to gather information, to conduct literature reviews, identify gaps and needs, and to make some recommendations either individually or in the form of a white paper. We have maintained, as SACGT in general has, to consult with stakeholders and assess both public opinion, public input, and in our case the public education efforts as well.

In February of 2001, we had a meeting and discussed the literature review draft and the white paper. The situation at that time was that many groups had recognized the needs out there. Some groups -- and by that I might mean discipline-specific groups, institution-specific groups, a variety of folks -- were creating certain kinds of plans. There were curricular content pieces being developed, such as the core competencies that have been worked on by NCHPEG. There were some model programs out there that were moving. We still had issues that the Education Work Group has been grappling with, and I put these into phrases.

We found genetics migrating into other health care disciplines but not meshing into the basic material of those disciplines. We found ourselves infiltrating but not integrating into the basic materials. A constant issue has been the role of geneticists in providing these services versus how all other practitioners were going to be providing these services.

So we acted a little bit like scientists at that point and said let's step back and gather more information rather than charging ahead. In the spring and summer of 2001, we continued to gather information and, for the Committee members, you know that in the literature review and

so on -- and at this point I'd like to thank Susanne Haga as the chief staff to this committee. She's done a marvelous job of pulling volumes of information together, and here are some of the topics in the material that we had put together.

Then in May we proposed to the Committee to host a summit. If you remember, then, in August the Data Work Group kind of superseded us, if you will, but first things first, and the Committee decided that the Education Work Group could step back a little bit, and during the August 2001 timeframe we came up with the idea of rather than proposing a summit for November, because we were still having trouble getting our hands around things, that we would go with a smaller roundtable kind of representation and, in fact, have a candid discussion.

We are now halfway through the Day 1/Day 2, and yesterday we did have a very lively and candid discussion. The table was, I guess, the same size as this one, and it was pretty much non-stop, lots of great ideas that we'll review in just a minute.

Our hopes were to clarify some of the barriers, identify some of the successes, focus our discussion points, and recognize some potential for steps, bring those ideas to you, see if we could crystallize any recommendations for the Committee to take forward, and design a more efficient and effective summit for the February timeframe.

The list of participants, the members of the Committee in your book have the list of participants from the roundtable yesterday. The way we approached this was that we had a kind of roughed-in table where we wanted people who represented the formal curricular phases of training. We wanted individuals who could better represent the context or the position of

practicing professionals from the ongoing activities out there. We then thought about the various kinds of professional groups that we might want or need to have here, so we had allied health, we had nursing, we had medicine, we had primary care, we had specialists, we had a wide variety of individuals and made it clear to them that when they came in, while they were representing the perspective of that discipline or their own background, it was not expected that they were representing the viewpoint or the opinion of any one group. Ergo, our conversation was much more open and wide-ranging.

We gave these three goals at the beginning of the afternoon: to explore the integration of genetics into current and future practice; to discuss major curricular needs of these disciplines from the viewpoint of core competencies, training programs, faculty training and development; and then to identify some of these obstacles or gaps.

We also gave them the tasks of being actively participatory -- they took that very seriously, thank heavens -- to identify focal areas and help guide the whole committee's discussion, and then to talk about areas in the summit. Here are the discussion questions, and the exact content of these are not so important. We tried to give a framework to a discussion that was, in fact, free ranging. But we basically broke it down into three major bullets. The first was the integration of genetics into clinical and public health practice and the educational needs of current providers. We wrote down some questions that might help guide the discussion. We then moved into content and curricula of genetics education, and some of these are pretty specific, some of them are fairly general. Not only did we find ourselves moving from question to question within some of these categories, we moved back and forth between the categories. But I think it was useful to start out with a framework because people recognized that they were

moving from one category to another, and one of the things we found out was that labelling, categorizing, trying to see where things fit is a part of this complex issue. In fact, we're putting together the puzzle in finding out which blue pieces are sky and which ones are water. Then we moved on to gaps and needs in genetic education.

The other thing that we did was that in the work group we mixed people up around the table. So some of us from the work group who had been involved in many other conversations were interspersed among individuals who had been invited to the workshop. We tried the approach of assigning work group members to pay special attention to one or the other of the areas to help us bring out themes to reiterate some of the points that they heard that were made that were either unique, an underlying theme, or something that the Committee and the work group might get their hands around more specifically.

So what I'm going to do in the next few minutes is go through these three areas, and what I would like to do is have, at the end of each one of these three, if work group members or participants in the roundtable have things that they would like to add, that's when we can jump in and then pull it together in a few minutes.

If we go back to number 1, the integration into professional practice, one of the early and very specific comments that was made was that, yes, there are a lot of groups that are recognizing the needs, but there are still some groups that need to get past the denial stage. They're still saying, "That doesn't affect me," and we've got to, in fact, clarify, very specifically demonstrate to groups that in fact genetics is important to them and their practice in one way or another. We get then into the phase of increasing the awareness, and several people made the point that

you've got to get the message clear. This came in the manner of having geneticists, having those of us who talk and think about these genetic services, define very clearly what the behavior is that we are expecting of these practitioners. Don't say, "Think genetic." Don't say "Approach your patients differently." What's the behavior? There were several points that, in fact, pharmaceutical firms, other organizations have done very good jobs in marketing and being very specific about here's the behavior we want you to change and here's how we're going to facilitate that change. In fact, people from a variety of disciplines were actually really very good about helping us figure out what some of those changes should be, and I'll get back to one of the very interesting themes I thought yesterday.

Several groups made it very clear that medicine of the 21st century is going to be evidence-based medical practice, that the folks out there in the real world want to know when these services, when the tests, when the actions are acceptable medical practice. They want the evidence. That told us in a couple of ways that translational research, getting that evidence, doing the outcomes research, demonstrating how changed behaviors result in better outcomes, is absolutely critical. We had some discussion about some of the model programs out there that were quite interesting. One of the other ideas in the development of evidence-based practice was that there was a general affirmation, I would say, of the NCHPEG core competencies, with the interesting caveat, at least interesting to me. I heard messages loud and clear from a variety of disciplines that they knew about these core competencies, they saw them, they read them, they concurred with them, but they understood that they needed to take them away from the table, massage them, and put them into action items for their own discipline. That, to me, was a very important comment made, and one of the parts that had been frustrating to work with, what do we do next to work with these things, I think we heard yesterday that they're ready to have

us pass them the ball. That may mean how are we going to support and strategize with them to get those massaged and put into their own disciplines.

Another idea of the professional practice aspect was the team approach, and lots of people talked about this both in model programs and from a variety of viewpoints. One of them had to do with one of the things we've been struggling with, and that's the genetic workforce issues. The point there, and I'll just make one point, is if in fact we expect and believe that genetics should be infused in the day-to-day practice of other health care professionals, what then is the role of geneticists and how do we mesh that and make the referral systems appropriate? And even if we are moving genetics into all these other practices, there still remains the need for the genetic specialist, and there was concern voiced yesterday repeatedly that the pipeline for that group of genetic specialists is not as large as it should be, so there was a focus on that.

The other aspect of team approach, if we are going to be coordinating these teams, putting everybody together, we still need leaders for those teams arising out of all of the disciplines across these areas, and so we do need to focus on faculty development as well.

The final points that I'd like to make here. We heard clinical tools mentioned many, many times yesterday. We need tools. We need examples. Give us things that work that we can take into our practice immediately.

One of the things that's exciting about working with groups of bright people who are really engaged and active listeners is that you see "ah-ha's" around the table. They're very obvious on people's faces. We had a discussion about the family history, and there were two or three

comments that were made that were very insightful and I think very important, and certainly there were ah-ha's from me. The family history was defined first and foremost as the most important of the genetic tests. It was defined as a predictive test. And it was also defined as a common denominator that should be implemented in all of the health care specialties in some way or another. The family history as a tool is extremely important. Then we got into some really interesting ideas about ways that that could happen and a couple of examples in computer-based programs, and so on. To me, that was very interesting, and I would like for anybody else who was there to comment on that in a minute.

One of the other things in the tool set that people talked about very often was computerized point-of-care technology. Several people pulled out their pocket computers and said, "If I just had the genetic tools here, it's not quite the same as just in time. That somehow connotes people not having the readiness. But point of care is very different. It just connotes convenience of the material that they already have but don't need to have all in their own computer.

The other clinical tool that several people commented on was give us lists or resources or ideas of what the truly credible sources of information on genetics really are. There is so much out there. How do I, a non-geneticist, sort it out?

So I'm going to stop there for a few minutes and I would like for folks to chime in.

MR. HILLBACK: I very much agree with the way you've summarized this. I thought it was an excellent day and a lot of really interesting folks came and thought about it. I tried to organize it in just a little different way to try to take it back to some of the fundamental issues

that I've always seen, so let me just lay it out for you.

I thought that one of the most crucial things that you mentioned was this dividing the roles clearly. We heard that over and over in lots of different ways yesterday, that each group needs to understand the other person's role. Someone said the geneticists need to think in the other guy's shoes, what role are they in. I almost get back to the point that when you start to think about that and when you go through the stuff that NCHPEG has done that Joe McInerney has presented, you realize that the objective there isn't to make geneticists out of everybody else. It's to allow them to work with geneticists and with the genetic information in a safe, relaxing to them, easy way. That's really what we have to do, because genetics for the average practitioner, whether it's an M.D. or a nurse or any other specialty, this is just one more set of tools in a big toolbox, and I think we may even have over-sold the idea that genetics is not going to be just a tool but it's going to be the tool that does everything. It's got a screwdriver and a hammer and pliers, and magic besides.

So I think when we get down to some practical things, I just listed four points under the practitioner side. After we assume that we're not going to over-sell this and we're going to be realistic and say we understand this is one more set of tools, that you need to know how to hold a hammer at least, and then we'll show you where to hit it and we'll show you how to use it. So one thing was to go back to what NCHPEG is saying, which is the primary education function -- and I started off yesterday thinking the issue was different for existing practitioners and people in school, and the more I listened, the more I came to the conclusion that the fundamental issue is the same. How we get it to those people is probably different, to the two groups is probably different.

So the four points on the practitioners: Teach them a fundamental framework, don't try to teach them to be geneticists; teach them how to do the fundamental analysis, how to synthesize it. Someone said just get people to think genetics a bit each day with each patient. Maybe it's only for 10 seconds as they look at the patient and think about the patient. But if they just have that one thought, they'll at least look that way. Then, as Joann said, start with real, useable examples that people can do today. If you keep talking about the future and what you need to know in 10 years, then the doctors will say, fine, then we'll learn it in 10 years, we won't learn it today, we won't bother to get into this. So in every area, we need to have some real examples. The next was where to go for facts, where are the credible sources, and that gets to the electronic databases, the PDAs, the Palm Pilots, whatever else might be there. Finally, how to use the genetics professionals, not to assume that they're there to try to take over your practice or take a patient away. How do we make that work?

Then on the other side, from the geneticists, again they need to understand what their role needs to be going forward, and as I said, think in the other person's shoes, the other professional's shoes, and then figure out how we increase both the numbers and the availability. How do geneticists work with all these other practitioners? If they are a crucial tool, how does that fit?

Then there was an interesting thought. My last comment is there were a lot of interesting thoughts about more joint programs. Those were joint rounds, they were at point-of-care kinds of things. But someone else, and I can't attribute this to the person who said it, said we ought to have more cardiogeneticists or neurogeneticists, and we ought to find programs that will increase the numbers of those people who can be the translational leaders. We have geneticists on one

side and neurologists on the other. Where are the neurogeneticists? There are some, but are there enough? Maybe programs focusing on increasing people who can walk both sides of the street and think about both sides will help with this transition.

So those are some of my take-aways and my way of organizing what we heard yesterday, but I think it's very consistent with the way Joann summarized it as well.

DR. BOUGHMAN: Elliott kind of slid into 2 and 3 as well, as we did yesterday. Ann, did you want to comment on this section?

MS. BOLDT: Yes.

DR. BOUGHMAN: I don't know, you all give me some guidance. Should I run through 2 and 3 and then have a more general discussion? Go ahead and comment, Ann.

MS. BOLDT: Okay. I was just going to comment to underscore the importance of the family history as a genetic counselor, of course, who recognizes how important it is to see that, and the patterns that we see, not only the medical history but also the social histories. But it was brought up by I think Skip Elsas that there's a disconnect between the medical school students in terms of what they're being taught and how to draw a pedigree, and then also the practicing physicians telling them that they shouldn't draw a pedigree. So as they're talking and doing their clinical rotations, they're drawing a pedigree, and then "Oh, no, no, no, you shouldn't do that." So I guess we need to emphasize that this does need to be a multi-tiered approach in terms of the education, and we need to underscore that as well. So we need to attack this in all different

directions.

DR. BOUGHMAN: Ed, did you have something?

DR. McCABE: Just that I think it would be good to go over 2 and 3, because I think it was obvious yesterday that it was very difficult to keep all these topics separated, and the discussion sort of flowed freely. So it's probably good to run through them and then not be constrained by any one of those.

DR. BOUGHMAN: Okay. In Area 2 there was more focus on formalized curriculum, if you will, although CME, depending on how you look at it, falls into both. But in the content and curricular area, one of the basic comments that was made was that it's not just knowledge and skills. It's knowledge, skills and attitudes, and that in fact we might use genetics for getting into curricular areas in discussion of doctor-patient relationships, that that may be a basis from which we could work.

There was no debate at all about whether genetics ought to be taught in formal courses or in an integrated kind of way. Everybody rejected either/or. Everybody wanted both/and. We talked a little bit about some of the curricular areas where it's taught as a basic science, and this primarily was focused on medical schools, but it is now translating into many other areas.

With problem-based learning going back to Elliott's comment about case history-based issues that we have some opportunities there, but there still are major disconnects that during clerkships, certainly in the third and fourth years of medicine, during the rotations for other

professionals on the wards, they are not seeing and hearing genetics as they should.

Another point here with the affirmation of the NCHPEG core competencies, with the caveat that the disciplines need to kind of hone the definitions and bring the areas within those competencies that are the essential elements and the most relevant to them.

There was more talk about the appropriate review and revision process for curricula, that genetics is changing rapidly and that there needs to be an ownership of the genetics portions of the curriculum in the variety of schools, and that this should not just be ownership by a geneticist or a few geneticists, that these individuals across disciplines are representing a variety of viewpoints really need to get together and take ownership; and that the disciplines themselves, whether these are the boards or the professional organizations, also need to take some responsibility about getting things into their curricula and training programs.

Throughout the afternoon, some of the model programs that are out there were presented and referred to, including the Genetics and Primary Care, some new degree programs or specializations in public health and genetics, some combined specialty residencies, one of the ideas that Elliott just referred to, and some special fellowships. There was a mention of a mini-fellowship, even for currently practicing individuals that might come back and be re-trained or trained more specifically in genetics to go back to their own specialty. Once again, for content and curriculum, there were pleas for resource materials, including specialized case studies and additional web-based resources.

That led us to a clearer definition of where gaps and needs are, and this represented in some respects some summaries and pulling out of some important bullets, I think. We need to define

better the desired behavior change. We need to, in fact, now move on to step 2. We've got some generic guidelines and competencies developed. We now need to get those into the disciplines and get the disciplines to take ownership of them. We need to continue to enhance faculty development, train the trainers, get the leadership out there. There needs to be continued or at least adequate expansion of the genetics work force to meet the increasing need. There was a clear call for support of translational research. There was a clear call for continued support of these model programs and/or possibly new and innovative kinds of programs. These last two bullets, I think in a lot of different ways it came out that there are some good models out there, there are some good programs, but there is real concern about the ability to continue those programs with the budgetary situation as it is coming down here at the federal level. Support for special fellowship programs, the mini-fellowships, the variety of different kinds of training programs. These could be small, they could be large, they could be federal, they could be state, they could be institution-based, but there needs to be a focus here. And, once again, the credible resource list.

A couple of the other points that I just pulled out were the common denominator that was brought up many, many times and somehow we need to get our hands around this was around this idea of family history, and there were several conversations about the electronic medical record. The Education Work Group still has a pretty big agenda. I'm not sure we're quite ready to take on electronic medical records in the United States, but I think that there may be a smaller piece of that that we somehow want to utilize as a starting point.

I would say, and I'm very pleased to be able to say, that while we have decided that we weren't ready for a summit, while we decided on having a relatively informal roundtable, this was not

meant to be a consensus conference. We thought we were bringing people together who together with us would have quizzical looks on their faces. During this discussion, I heard two or three very specific recommendations that I think the afternoon roundtable would like to bring to SACGT for consideration of fleshing out and making very specific, and one of those had to do with continued support for the Title VII programs that a variety of groups have felt were very successful, and that this clarion call for more translational research because of the medicine of the 21st century and health care of the 21st century being evidence-based, and we've got to get our act together with regard to genetics. I think those two themes, at least, were very specific and should be considered by the full Committee and on behalf of the work group. For starters I would, in fact, put those out on the table for discussion points, recognizing that there are other challenges to put together the agenda for the summit, which we'll do in a few minutes. But I was very pleased that a roundtable that was -- I don't know, how many hours were we here for? Four hours? Four hours. It was a very full and rich afternoon, yet I was quite pleased that we got as focused as we did as quickly as we did. Once again, I'd like to thank all the members who were there.

Let me now turn it to the group. We have several of the invited participants from the workshop here and our work group members. David, good. David Gale.

DR. GALE: I didn't mean to get front and center that quickly. I think there's one other issue you slipped over rather quickly. The genetic community needs to work with the accreditation bodies of this country in the disciplines, and with the credentialing bodies, and I'd like to see that broken out as an issue, because I think if we're to move genetics education into the disciplines, we're going to have to work between and among those groups.

DR. McCABE: Someone made a comment about boards driving content, and you affirmed that very strongly, as I recall.

DR. GALE: Yes. There are about 50 different accrediting bodies nationally that look at the various disciplines, and in order to get it into the accrediting issues, it also has to be in the scope of practice of many of these disciplines, and it is not now there. I think there needs to be at the summit discussion between and among those various accrediting bodies and the credentialing bodies.

DR. McCABE: Thank you.

DR. BOUGHMAN: David was shy to introduce himself. Dr. David Gale from allied health sciences. He's in Kentucky but wears a variety of national hats and has been involved in one of the genetics and allied health programs that has been supported in genetics education.

DR. LEWIS: One of the things I heard over and over yesterday was people's need to have credible resources, and somebody suggested that we have an SACGT approved list of websites. I just wanted to comment on that area because I'm not sure we can be in the business of saying what's credible and not credible. But I think what we can do is help people get a list of tools that helps an individual evaluate websites to see if they're credible, and there's lots of resources out there that I use in my teaching. I think that there are ways to help people figure out how to look at a website and determine for themselves its credibility, because I think that is a big issue, that people who don't know how to do this and who are only used to looking at peer-reviewed

journals where everything already has credibility because of the peer review process don't necessarily have the skills to learn how to go out and critique materials that haven't gone through that kind of peer review process.

DR. KAHN: My name is Ruth Kahn. I'm from the Division of Medicine and Dentistry, HRSA, and I was a member of the Education Work Group. I wanted to pass around a colored picture, and I don't know if there's enough for the audience outside, but at least it will give you a view of how the Bureau of Health Professions and Maternal and Child Health, who are collaborating on a number of projects, view their work with other agencies. I would just suggest that, as time goes along, we will be able to advise the general public on some curricula materials that will be made available. Marie, do you want to just speak to that a moment, on the GeneTests and GeneClinics material?

DR. MANN: Well, just specifically, we have funded a contract to develop a curricula that is going to be made available probably within the year that's going to incorporate a lot of the issues that were raised. They will be case-based approaches that can be used by the general practitioners to enhance their understanding of genetics. This will be done in collaboration with what's existing at the University of Washington with their GeneClinics.

DR. KAHN: Thank you. We did address yesterday the Genetics in Primary Care Project that is an effort to educate faculty in the primary care disciplines on how to get through case-based learning the issues of genetics into the learning for their students. We are enlarging that effort by working with the physician assistant community this year by another demonstration project that's being carried out by Duke University. But I would encourage the Committee to look at

whether or not two efforts are really going to make an enormous dent in the enormous numbers. I don't have any suggestion for what you might say, but I think that while these can be models and begin to address it, they can't nearly reach the multitudes of people out there.

The other point I wanted to make is that the slide that I passed around is the Bureau of Health Professions and Maternal and Child Health effort to help us visually examine the gap and identify those agencies that we are engaged in with partnerships, with NIH, AHRQ, CDC, states' organizations and universities. Although we have not yet received clearance for it, we are just in the very initial stages of developing this, we are anticipating that we will begin some satellite broadcasts to bring to the university, to the practicing community, some information about genetics, and that's about all I can say on it because it's really in its infantile stages. So I just encourage you to think about that.

The other point I wanted to make is that we've been very, very careful in the programs we've been designing to ensure that geneticists and educators are working together. We've been struck by the fact that people in large academic centers say to us afterwards, "This is the first time I've ever met a geneticist," or "This is my first opportunity to work with them." We're going to build a bond now that's going to allow us to do this more easily. So if we've served as a catalyst in that area, probably that's the most important work we've done.

MR. McINERNEY: I'd like to come back to this notion of credible resources on the web and simply remind you that there is an organization -- I think many of you have already heard of it -- called GROW, Genetics Resources on the Web, which is headed by Alan Guttmacher at the Genome Institute, and NCHPEG is working closely with GROW to see if we can collaborate a

little more effectively. But early on in the discussions in the GROW meetings -- and GROW comprises about 50 separate organizations that have a presence on the web in genetics -- we took on very early this notion of approved sites or sanctioned sites. Those individuals in the group who have some background in the law very quickly called us off on that because of the liability implications. Now, that doesn't say there aren't ways to try to demonstrate to the broader community that the sites that you are affiliated with are, in fact, effective and credible, and we are working and do have a set of internal guidelines that we ask GROW members to adhere to, to demonstrate that their information is in fact credible and reliable and ethically based. So there is a resource out there for us at this point.

MR. BAKER: Joann, I want to come back to a point you made in the integration comments about the emphasis on ensuring that the different disciplines or the audience owns the competencies. An important lesson learned was when we started looking at the public health community at how and where they felt genetics fit into what their roles and their functions and their competencies were. So in order to create an urgency and a demand for that training, one of the things they did was take the NCHPEG competencies and digested them and pulled out the pieces that were relevant and put it in language that made sense to them, and therefore challenged the educational institutions to provide that training, because they then owned those competencies and said I want to be trained in this, so then the training demand is created. Finally, when it's done by the community and for the community, they end up really creating some support for this.

DR. LEWIS: I think one of the themes that I heard loud and strong yesterday was the workforce theme, and as a non-geneticist generalist, one of the things that I'd like to talk about is

the appropriate role for a variety of health care professionals at various levels and that everybody doesn't have to be a tertiary level 3 geneticist, but that what we really need to do is that we need to work to develop an appropriately differentiated workforce because lots of problems can be handled at the level of primary care and don't necessarily need the referral. What we want to make sure of is that we have enough referral level 3 type people available for folks who need that kind of assistance, and we need to make sure that we've got a lot of people in the workforce who can do -- that 90 percent of the work can be done by 90 percent of the people, and then that small number of people are appropriately positioned and appropriately trained to educate the generalists for what we all need to know to be effective providers, and then save the skills of the most highly educated, most highly skilled individuals for the incredibly complex cases. So I think it's not necessarily a numbers issue but it's a looking at what are the levels of competencies we expect at various levels of providers. There are lots of areas, for example, in my own discipline there are 2.6 million nurses who are pretty strategically placed throughout the country who can do a fair amount of very comprehensive history-taking if they're properly educated and then can identify patterns that need to be referred. So I think that it's a workforce issue. It's not just necessarily numbers, but it's looking at appropriate differentiation of competencies at the various levels.

DR. LANIER: I'm David Lanier from the Agency for Healthcare Research and Quality, AHRQ. I'm sorry I wasn't able to attend the roundtable yesterday afternoon. I had a last minute conflict. But listening to the information that's been provided here, I guess I'm feeling a little bit conflicted. On the one hand, some of the conclusions that were made by the group are definitely not only down our alley, but you've been singing the same song that we've been trying to sing for 10 years in terms of support for evidence-based practice, for team work,

interdisciplinary teams, for clinical tools, point-of-care technology, all those things that we've supported greatly. But what I'm struggling with is the extent to which genetics itself is specifically unique in this. What is there about genetics that's different from the broader area, from other issues seen in practice, in primary care, whether we're talking about prevention or we're talking about detection of depression or some other clinical conditions? That's what I'd really like some help with. We've made some attempts to support, in a small way, some genetics efforts, but what is there specifically about genetics that is so different?

DR. BOUGHMAN: I might try to respond to that, but first I would say that I was sorry you weren't there yesterday either. There was a specific comment and recommendation to billionize AHRQ.

I'm not sure that this really is different for genetics than the other kinds of approaches that you took. I think it was if not new information, it was a clarified picture for those of us who have been focused on genetics education, that there may be modes that are already being used by disciplines out there that we, in fact, could take advantage of; or, in fact, if we are a little bit ahead of the curve, let us utilize the technologies, the methods that will be a part of the mainstream practice. If we are thinking about some of these tools -- and let me just use this as an example, the structured family history -- then let us think about it and talk about it with the right people so that we don't create an odd man out there that does not integrate, does not flow well with the general practitioner's daily activities.

The thing that I heard more strongly than I had heard before, and maybe it's just because I haven't been in the right rooms with the right people, but the disciplines and the practitioners, the

curriculum people really are ready, willing, and I think if not now, very soon will be able to take the materials and so on that the genetics community might be providing, that they are more ready than I had anticipated the general world out there to be, and that helped clarify roles from my perspective and said that SACGT needs to be creative in its facilitative role to get materials from one to the other.

MS. BOLDT: Well, this is a different subject, but there was also another theme that emerged, that of reimbursement, and there's definitely overlap between the Access Working Group that we've talked about. We know that reimbursement is an issue for genetics professionals, but the neurogeneticists actually mentioned too that it's not as enticing for some neurologists who want to go into neurogenetics because of the time-intensive, comprehensive nature of that work-up, and that they're not getting reimbursed. So it's not only an issue in just the genetics professional arena. Reimbursement is also another issue that we need to be considering and looking at.

MR. HILLBACK: David, I wasn't trying to answer or respond to your point, but I wonder if part of the difference in genetics is that I do believe in some cases we've sort of over-sold it to the general practitioner and they see this tidal wave, or what feels like a tidal wave, coming at them, and maybe they're just trying to run rather than figure out how to cope.

I guess I'd go back to comments from both Dr. Gale and from Tim. When I think about the summit that we're going to have, it would seem to me that a very profitable part of that, a very useful part of that could be to focus on how do we help, we the genetics community, the broad genetics community that we represent here, how do we help the other parts of medicine figure out their role here in the sense of looking at what NCHPEG has done, adopting it, modifying it,

bringing it into their own house, and then connecting further with those groups into the groups that manage the education and the accreditation, et cetera. It seems to me that's a continuum, and that that by itself could be one of the major topics, one of the major areas of focus of this summit, because that to me is very practical. Once it's somehow even part of standard of care, it gets adopted, it gets used. If we could get that started, even in a small way, then those groups are taking the lead and we don't have to push. Then it starts to be a pull situation. Once it's a pull situation, then I think it's inevitable.

DR. KHOURY: Joann, this is wonderful. I was furiously taking notes here, and a few months ago I had my own ah-ha moment in genetics in public health. After five years of trying to sell genetics to public health programs like cancer and heart disease and asthma and kept getting politely rebuffed, saying "When you have a genetic test, come talk to us." There are no genetic tests for asthma today. There are no genetic tests for most complex, chronic disease, et cetera. I came to the realization a few months ago that family history as a tool is ready for everybody's consumption, including public health professionals. I want to elaborate on this and pick up on the theme of evidence-based practice, family history being a tool. I asked my internist -- I was in for an annual check-up last year, and I asked him, "Do you ever use family history for anything?" He knew that I was a geneticist and worked for the CDC, so he said, "Of course, it's the most important area." I asked him, "Well, what do you mean by that? Give me some examples." And he started reciting all sorts of diagnoses that he has made because of family history, from hemochromatosis to multiple sclerosis, all kinds of things. I was pleasantly surprised, because my idea up to that time was fairly abysmal of what internists and primary care people do. I don't know how much of this came up yesterday, but there is family history, and there is family history. There is all kinds of family history. If you do a survey -- actually,

we are collaborating with the American Cancer Society to look at the prevalence of family history for a wide variety of cancers. These are cross-sections of normal people who have no cancer.

Let me give you an example. About 10 percent of people in that ACS survey have a positive family history for first-degree relatives, one or more with colon cancer, about 10 percent. When you think about that, that's a substantial fraction of the population. However, only 1 out of these 10 are early onset colon cancer, under the age of 50, or two or more first-degree relatives affected. This is the 1 percent of the population that you want to identify and refer for a more in-depth genetic assessment, counseling, perhaps FAP testing and HPNCC, et cetera. But what do you do with the majority, which is all of us, because we all have family histories of one thing or another? It seems to me when you apply the evidence-based practice guidelines, we are making public health recommendations that all people over age 50 should have recurring rectal exams, sigmoidoscopies, et cetera, for early detection of colon cancer, and we know from the literature that people with undifferentiated first-degree relatives with colon cancer have twice the risk of colon cancer. That could be on the basis of multiple gene variance, multiple environmental factors, a combination of behavior and genes, and very few of those are the high-risk single-gene disorders. We know that at the age of 40, someone who has a first-degree relative with colon cancer, their own risk is the same as a person at age 50 without a family history. So it would make sense even without any genetic testing or assessment for people who have a first-degree relative with colon cancer to perhaps begin their check-ups earlier than the general population, perhaps at age 40.

So that that example and move it across all diseases, which means all of us in this room, because

we all have our family history baggage, be it cancer or heart disease or any other thing. It seems to me a very small fraction of that baggage merits a genetic assessment because of the high-risk single-gene disorder situation. The vast majority of that baggage is for the primary care and the specialties to deal with, which is to use our accepted guidelines for preventive strategies, smoking cessation programs, exercise regimens, five a day, colonoscopies, breast exam, et cetera, to see whether or not family history could be used as an additional tool to get people to move, get people to reduce their risk behaviors.

Which brings me to the topic you have mentioned here, because family history is a predictive tool, and in order to use it as such, we have to approach it with the same scientific rigor that we've been discussing in the evaluation of genetic tests, meaning analytic validity, clinical validity, clinical utility, and ELSI issues, because we know, let's say, for analytical validity, what that means for family history, we know family history is a risk factor for most diseases, but we don't know how to collect it, we don't know how reliable that is. Think of it in the same vein as you think of a lab test, because you have analytes and metabolites, and here we have people telling you that his brother has prostate cancer, or forgetting that his brother has prostate cancer. So we don't know what that is. So you go through that same spectrum of analytic scientific evaluation, leading up to clinical utility, because clinical utility is really where the rubber meets the road. It is not enough to tell a person that they are at a higher risk of lung cancer because their mother died of smoking-induced lung cancer. We want to change their behavior by either getting them to stop smoking or not to start.

Which leads me to the evidence-based practice. We have a series of evidence-based practice guidelines for chronic diseases that we've been desperately attempting to move into public health and mainstream preventive medicine, and one example was a recent analysis of how good those

practices are in the real world. The equivalent of evidence-based practice guidelines from AHRQ are the Community Preventive Services Task Force, which CDC has, and in a recent analysis they looked at efforts to get people to increase their physical activity. We know that physical activity is good for us, but we don't know what is the evidence for or against using different ways, like school-based education programs, mass t.v. campaigns, et cetera, to get people to move.

I think an important public health agenda would be the ability or using scientific tools to evaluate whether or not family history can be used to change people's behavior. I think this is a long, tortuous argument, but this is basically where public health, preventive medicine and genetics can come together, because only a small fraction of that merits that in-depth genetic analysis, the single-gene disorder. The rest of it is undifferentiated family history that 10 years from now maybe we'll have the tools with the Human Genome Project to measure the many, many genes or gene arrays that make us, let's say, at three-fold increased risk for a disease given family history. But we're not there yet.

So my answer now to most public health people who ask me what's the relevance of genetics to us today in the absence of rare single-gene disorders that we want to refer to the clinical community, I'd say, “What's your family history?” Everyone has a family history of some sort which, for at least a third of the population, should lead them to take active non-genetic steps -- i.e., not genetic testing or anything -- but either behavioral modification or diet or sometimes pharmacology or treatment to reduce their burden of disease. So this is really a great bridge.

The last point I was going to make is that we in public health are going to take this very seriously

and we're going to adopt a public health scientific methodology for the issue of exploration of family history, including expert workshops, and we'd like to collaborate with SACGT all the way.

DR. BOUGHMAN: I would just say that that concurs. The Preventive Medicine Task Force was mentioned twice yesterday by participants as a good model for some of the kinds of things that we're talking about.

DR. McCABE: I just have one comment that I didn't hear in the summary, but before I mention this I need to disclose a potential conflict of interest, and that is that I'm the father of a journalist. But I heard yesterday some discussion about the need -- that's perhaps why I heard this -- the need to educate journalists about genetics also, because, in fact, an awful lot of the education of both the public and health professionals occurs through journalists. We really need to engage the journalist community in terms of understanding the importance of genetics, the importance of the family history in medical care, all of these issues, and I think that's a very effective way of getting our message out beyond the confines of the academic health center.

MR. HILLBACK: I think there were two alternatives for what we should do with journalists. The other one had something to do with guns and bullets. You picked the alternative that I think was good for the family situation.

DR. MANN: I'm Marie Mann from HRSA. I just wanted to affirm a couple of the comments that have been made, specifically what David was saying, how do we convey the message what's unique about genetics, and what Elliott said, that we don't need to overwhelm the primary care providers and make this so difficult that they would run away from it. As we're developing

the summit, I think it's important to have sessions that deal with what is unique, how can we use this information, whether it's the family history or any of the specific genetic information and testing. How can we use it to improve the care of our patients? If we can get that message across, then people will want to get to know that information, will want to be educated.

MR. HILLBACK: We talked a lot yesterday about leading a horse to water, and Priscilla talked about a conference that was in '98 in New Orleans that a lot of us were asked to be faculty of, and the faculty outnumbered the attendees, even though a lot of people were offered free airline tickets to fly to New Orleans for a weekend to go to the session. I think the issue is to make this accessible, mentally accessible, not just physically accessible. I like Muin's idea, which I think a lot of people said in different ways yesterday, and Muin wasn't there. I think a lot of people said that the family history maybe is a very good bridge. They didn't say it in those words, so those are his words, but when he said it the light went on with me that, gee, I think a lot of people said that yesterday in different ways. Maybe this is a way to get people comfortable that, yes, I do a family history in my practice, I just don't quite think of it in the way I could, and maybe that's a transition that they could be comfortable with.

DR. BOUGHMAN: Okay, before I go even to Pat, and before we break also, I would like to make sure that any of the participants who were there yesterday at the roundtable who are sitting in the audience, if they have anything that we have missed that you'd like to underline, put in bold, or whatever, I want to make sure that we give those folks a chance we invited and who shared their experience and expertise with us.

DR. BOUGHMAN: I'm taking silence as assent. Should we go ahead with a couple more

comments before we break? Okay.

DR. CHARACHE: Well, first I'd like to thank the group for this elegant summary of the issues that we've been hearing about. To me, in thinking about it, two things strike me. One is the absolute need to integrate the genetics into the professional practice, your number 1 point, because otherwise it's not going to be effective. In doing that, it seems to me that the number 1 challenge under your "gaps and needs" is to define the desired behavioral change.
I see this as a very major problem. We have a new chair of the Department of Medicine who made it clear in his first lecture on grand rounds to the department that he considers genetics as the future of internal medicine. So the strength of that discipline in internal medicine is recognized. I'm quite sure that if we pointed out to him that we'd like to see him request that any medical presentation at grand rounds consider genetics and how it might interdigitate with what they were presenting, that this could very well happen. Certainly, it would be extremely interesting in my field of infectious diseases as an example. But I think what we have to do before we even make such a suggestion is define what we want the outcome to be, the behavioral change. So I see this as a high-priority first order of business that you called to our attention.

DR. LEWIS: I've been thinking about the other themes I heard yesterday that maybe we want to put on the table, and one of the themes that I heard yesterday was in terms of some of the access issues that I'm working on with the Access Working Group. One of them was the genetic test, the family history as being a genetic test, and as such, working on reimbursement mechanisms for it. But the second theme I heard in terms of reaching out to diverse and under-served and at-risk populations was making sure that we involved the AHECs, and I want to

make sure we capture that.

DR. BOUGHMAN: Thank you.

PARTICIPANT: I think we should say what they are.

DR. BOUGHMAN: Area Health Education Centers that are distributed around the country. Each functions a little bit differently, but they infuse in rural areas to a great degree and utilize expertise from regional tertiary centers.

DR. LEWIS: And they're involved in education of health professionals, and also there is a certain amount of consumer involvement. So it would be a great opportunity to partner with the patients we serve as well.

DR. BOUGHMAN: Right.

DR. SHORT: Two points. One is so you know, I'm sure the AMA is not the only group, but the AMA has an annual science reporters meeting, and they have actually done and are doing again this year genetics. The point is whether or not some of the messages that are being articulated here, perhaps taking those to the organizers of such a reporters meeting would be helpful. I would be glad to do that.

The other point is that I really wanted to affirm Tim's description of looking at the competencies of particular different disciplines, and then how does genetics relate to them. Actually, the

Family History Working Group of NCHPEG attempted to survey the various groups in terms of what was the typical opportunity for them to actually bring up the family history in a typical clinical encounter, and how that would have any relationship to what their general clinical services they were providing; i.e., if you were a physical therapist, how often did the family history come up in the course of the top five clinical issues that you had to deal with? I think that allowing people not only to identify their competencies but also that process of self-discovery of how genetics is relevant to what they do I think should be a point perhaps of the summit. I think in our earlier discussions about the summit, the idea of having the various team players take on a genetic problem, or a problem that may have some genetics, but to really illustrate how genetics is relevant to each discipline as they would be encountering that particular case.

DR. PENCHASZADEH: I just wanted to reflect a little bit on the concerns about the uniqueness of genetics in all of this. I wanted to support this notion of the importance of family history because of the practicing geneticist and involved in teaching for many years, it's been the motor that has made genetics really get its place, at least in the minds of many general physicians and specialists of a different nature. I do think that genetics is distinct in the sense that it has developed primarily outside of most of the clinical disciplines, on the one hand, over the past 20 or 30 years, and secondly because the distinctness is not so much in what it is but in what it is perceived to be by the general medical profession. I see that very commonly in everyday practice. Whenever physicians encounter a genetic problem, they run out of the problem and they immediately come to the geneticist to advise them on what this means, what it is. So I think for that reason and because genetics crosses every medical discipline as no other specialty does, and it's in dire need of knowledge on the part of the general professional, I think

that makes it very distinct.

DR. McCABE: Another comment that I heard yesterday was that drug companies, pharmaceutical manufacturers, have been very effective at changing physician behavior, perhaps the most effective at changing physician behavior because it's key to their bottom line, and we need to learn. Perhaps we can't get an army of detail persons out there visiting every physician, but at least we need to know if this has worked in one sector. We need to try to learn from the behavior of those individuals so that we can, in fact, influence physician health professional behavior.

DR. KAUWELL: First of all, I did want to congratulate Joann on doing such an excellent job in summarizing the material from our conference yesterday, our roundtable discussion.

DR. BOUGHMAN: Gail, could you tell us who you are and what you do?

DR. KAUWELL: Gail Kauwell from the University of Florida. I am by training a registered dietician. I want to make a comment I guess to get it on the record, because the people in this room may come and go, but the document will be there. I think it's really important -- people have mentioned physical therapy and disciplines and have used those types of words today, but I want to make sure that we have for the record, at least what I think this group intends when they say disciplines is that they don't mean just medicine, nursing, physicians assistants, but they also mean allied health. Dr. Short mentioned, for example, physical therapists. I just want to make sure we get it in the record, because I think sometimes the memory will be short and when it comes time for programs and funding and things like that, they'll go to a concentrated area and

miss some of the other important disciplines, allied health included in that word. So if I could just offer that up, I'd appreciate it.

Excellent job in terms of the summary, I think, and I appreciated being a part of it.

DR. BOUGHMAN: Thank you very much for reminding us of that. I would like to think that the cross-section of people represented on the Secretary's Advisory Committee is so well aware of that and that it's so obvious to us that we don't say it out loud frequently enough.

The other aspect that I would just reiterate is that one of the themes that did emerge yesterday in a variety of ways was the doctor-patient relationship. Excuse me, the provider-patient relationship. Thank you very much, Judy. The first comments actually came from the physician community, which I thought was terrific. The consumer as partner was mentioned in a couple of ways. We did steer away, not purposely and not as a sign of neglect, but we did not include the broad-based consumer educational issues yesterday because we thought we had plenty to handle in the four hours as it was. But that, too, was not ignored. It was mentioned and I think is very much on the minds of folks.

MR. BAKER: To reiterate a real quick point from yesterday's discussion, in the end we're talking about relevant dose of genetic information that fits into broader training efforts. So it's not drawing attention to that because it's not only the free-standing new training programs like GPC or a Center for Genomics course, but it's also those existing ongoing educational efforts and the challenge of how do you create a plug-in module that fits nicely and neatly into the way people are already learning. We need to keep our focus on that so it's not needing to build a

whole new machine, a whole new methodology, a whole new educational curriculum. There's a lot of training going on in health, a lot of training going on in medicine in various diseases, and the plug-in concept is very important to keep in mind.

MS. BOLDT: Another thing I think we also are always aware of but don't always say as frequently as we need to but we recognized yesterday is the need to educate diverse and multicultural populations as well. So just to put that out on the table for the document.

MS. DAVIDSON: First of all, I want to apologize that I was unable to attend yesterday's session. It sounds like it was something really not to be missed. But I did have the benefit of a short summary from Joann last night, and she was, of course, speaking to me as the consumer representative, and I just wanted to bring to this discussion also the importance of consumer panels in the process of health professional education. Picking up on Elliott and Muin, it's one of the way that we at the Alliance and other consumer groups have seen consumer panels in action, in medical schools, in grand rounds, and they're a very effective way -- certainly different, but a very effective way to demonstrate case-based practice and to just give people a beginning window into the importance of genetics or family history, a different way of looking at medicine. They are a very powerful educational tool in themselves.

DR. BOUGHMAN: Thank you, Mary. It's about time for a break. I couldn't let you go without making a picture. I'm known now for drawing diagrams, and I can't yet diagram out our summit. We're going to do that in the 30 minutes when we come back from the break. But the pieces that I think we have, the what for the summit includes these essential elements of the concept of definition of the roles of the various disciplines, genetics in the disciplines or the

disciplines vis-a-vis genetics. This concept that people out there want to know what tools are available and the people that have the tools and are developing the tools somehow need to have that forum, that the process of that integration. One of the groups we didn't have around the table was accrediting bodies, per se, although we had a couple of organizations that are involved in one way or another, at least accrediting the schools but possibly not the continuing education or the examination process, per se. It's all built on this idea of elevating the awareness. I'm not sure whether the journalist/consumer piece fits in here or not. Of course, the summit would be open to the public, but we can't in probably one day address all of the issues.

We were reminded yesterday of some of the basics. I think I have some of the what down there, but who do we want to give the platform to? Who would be in the audience? We were charged yesterday to clarify our message. This is an opportunity to have specific messages translated. Is it examples of successes that we want out there? Is it provocative challenges to the variety of disciplines? Is it presentations of a discipline that has, in fact, gone through the process of integration, an institution-based example? The when would be the timeline of the day, and the how is do we have a message that is so basic that we would like to have a plenary session, and who would we want to provide that? Do we want to include panels, and would they be factual, here's how we did it from three different disciplines, from a different perspective? Would we want to, for example, have a genetic case or have a case presented and have members from three or four different disciplines on a panel say if this were my case, here's how I would deal with it, here's how I see that family history as a general practitioner, here's how I see that family history as a nurse in an AHEC and what I would ask for next, here's how I as a geneticist see that, so that conversation could then be how do these different disciplines work together to provide the complete health care picture for that individual.

Those are some of the kinds of ideas that have floated up. One of the others was, in the facilitative role, should the summit include the opportunity for several different kinds of tools to be presented, almost in exhibit kind of format, so that individuals could go and interact with selected people that they had the most interest in pursuing rather than everybody sitting in small rooms and being captive audiences?

So when we come back from our break, and I hope that there's some conversation about this and great ideas become crystallized, I guess I would summarize the morning as well. I think, if not ah-ha's, I've heard some reaffirmation from folks that the messages that we heard from the various disciplines and the participants yesterday were very welcome messages because it did exactly what I think SACGT and certainly the Education Work Group was looking for, and that was helping us bring into focus. We knew there were gaps, we knew there were needs, but we got some very specific challenges yesterday. So, Ed, do you want to give us our guidance, then?

DR. McCABE: Yes. Thank you, Joann. When we return from our break at 10:45, we will then begin planning for that February summit. We will resume shortly at 10:45. Thank you.
(Recess.)

DR. McCABE: Let's get started again. Joann will be leading the discussion, and we will need to wrap this up at 11:15, Joann. So if we could continue now and focus not on yesterday but more on the summit and the plans for the education summit.

DR. BOUGHMAN: We have two or three things that we have to do, and we are going to defy

all usual expectations. This group, which is even larger than a committee, is not going to build a camel. We're going to build a horse. I don't know whether all of you have heard that a camel was really supposed to be a horse but it was put together by a committee.

We need to define the parameters, at least the skeleton or concepts, of how we want an educational summit to go, so we need to address the when, where, who, what, how kinds of things, and I'll start it off by saying that the Education Work Group had spoken about a model not unlike the day that we spent in Baltimore before, where there would be some plenary session at the beginning that included top-notch kinds of folks that shared key information and also were somewhat provocative. We then had a session that was more interactive with some panelists and some multiple perspectives that were presented and gave people some context. Then after lunch we actually had more active discussion groups and interactions that were facilitated. We had thought that we might approach the day something like that, but then we came back and had a lot of trouble with topics and styles and so on. But in the next 20 minutes or so, I would like to get hopefully some opinions or some ideas that would emerge somewhat clarified, and Elliott is just chomping at the bit over there.

MR. HILLBACK: What's new? What's old? What I listened to both yesterday and then the comments today, I tried to write down what I thought were four areas, at least three of them I'm very confident I would like to try to take on. One is the fundamental issue that Tim and others talked about, which is how to incorporate genetics into their world. We certainly won't get all groups present, but to try to get enough other groups, and that means both some of the various organizations that represent M.D.s, nurses, dieticians, and other important groups, and some of the groups that evaluate the performance of those groups and try to set standards, and try to

figure out how we carefully take what NCHPEG has done and customize it and get it accepted, et cetera. So that's one for me.

The other one that I think is sort of an interesting corollary to that is one that a lot of people raised but which Muin crystallized, which is that the family history is the bridge. If the comment we're getting from various practitioners is put up or shut up, show us something that's real, that is genetic. We've always said that's the best genetic test we have today, and it probably still is, and it's very practical. It could be a very interesting set of workshops.

Then the third area for me is sort of on the other side of the coin, okay, if that's the way this is going, let's go back to the genetics community re-defining its role and thinking about the workforce issues that have been talked about a lot yesterday and a lot more this morning, and maybe the fourth one is advanced tools. I don't know whether that's over-reaching and overkill and maybe ought to be saved for another day, because the first three, to me, if you can't fill a huge set of rooms on those three topics, but also I think get something done on each one of them and move the ball forward, I think that makes an interesting day for me.

DR. LEWIS: A couple of the principles that I think are important for the day. One is that we need to make sure that the speakers represent a variety of disciplines and that it not be a particular discipline talking about how things translate into health education for a variety of disciplines, but that the presenters need to come from a wide variety of disciplines, and that includes not just the panelists but also includes the plenary session speakers.

The other thing that I think is really important is that it not be just geneticists doing the talking but

that it be people who have already been converted and have figured out that this is the way to go. Is this going to have an awful lot more credibility if you have non-geneticists as some of the speakers as well? Because I think part of what that will do is it will say that this isn't a mystique but it's something that many of us have been able to translate into practice.

DR. BOUGHMAN: Okay. The questions that I have -- and I'm going to put Joe McInerney and Priscilla Short on the hot seat for a moment. One of the questions that I have is why should SACGT have this party, and who would come? Is this the best way for us to facilitate and get the message to groups that we want to see get the message? Is it a corollary or an addition to other mechanisms by which we might be working to get the message out there? The specific question -- Priscilla mentioned that the AMA meeting is going to have something about genetics. Was that for the science writers that you said? Okay, so that's more specific. But should we be going to the audiences, or who would we expect to come to us?

And then, Joe, I'm going to ask you about the NCHPEG meeting.

DR. McCABE: I just would argue that there is value in the Secretary's Advisory Committee on Genetic Testing holding this. We are advisory to the Secretary. One of our roles is to recommend resource allocation to the Secretary. I think where we've got to be cautious is that we don't have a meeting where we say we're in need of education, education is good, but we need to focus very specifically with some action items that can be made as recommendations to the Secretary.

DR. BOUGHMAN: Okay. So, in fact, for those around the table and in the audience who did not have the pleasure of seeing in action that kind of philosophy at the last Baltimore meeting,

what really started out as a pretty diffuse meeting -- at least for me it wasn't the typical kind of one-day meeting. But at the end of that day, I think a lot of people had learned a lot of things and we had some messages that we could actually take back to the Secretary which supports the idea of moving into some actual discussion groups and getting information out of the participants at the summit.

DR. McCABE: And I would remind everyone that at a time when the literature in genetics was saying there is no genetic discrimination in insurance and, by implication, employment, that was not in the literature. We heard anecdotes. Certainly they were anecdotes. We weren't hearing the evidence, but we heard information that I think crystallized the Committee's letter to the Secretary regarding genetic discrimination, that this was, in fact, a major concern of the public, and that came very specifically out of the stories that we heard at that meeting.

DR. BOUGHMAN: At the break, Joe McInerney pointed out that NCHPEG is having its meeting on January 31st and February 1st, and we had been talking about target or potential dates for the SACGT summit in the middle of February. Joe, maybe you could talk a little bit about what the NCHPEG meeting would be about and how these two things might conflict, complement, whatever.

MR. McINERNEY: I think Dr. McCabe's point is well taken. Certainly, NCHPEG is not an organization that exists to recommend policy. It is an organization that intends to improve genetics education for health professionals, and our annual meeting does attract a broad cross-section of health professionals, most of whom are not specialists in genetics. They come particularly to learn more about genetics and how they can educate their constituents. Our

meeting will be here in Bethesda.

I'll just run through the agenda very quickly for you to let you know where there is overlap. Wayne Grody from UCLA will discuss the science and technology of genetic testing, again at a level appropriate for non-geneticists. Ellen Clayton from Vanderbilt will discuss ethical, legal and social issues in genetic testing. Then Dr. Collins will chair a panel on what health care professionals need to know about genetic testing, and why. We then will have the first of two poster sessions where we will invite not just NCHPEG members but any other health professionals who have been working on the integration of genetics into their own disciplines, people such as Gail Kauwell, for example, and others who have used the NCHPEG core competencies or other mechanisms to increase the presence of genetics in education and in scope of practice. They will be able to display those. We'll also have a plenary session where we will pick three very good model programs from across a range of disciplines for plenary presentation to the group. The second day, Dr. Short will present the reports of the NCHPEG survey that some of you heard back a couple of months ago, with a little more data added. We will have a second poster session as well, and then Dr. Collins will finish with a discussion of some of the things we were talking about at the session yesterday: what does genetics do for me now, not just the future, but what does genetics do for us now and why we should be paying attention.

So there is some overlap with the concerns of this group. But again, Dr. McCabe's point is important, that our meeting is not to recommend policy. On the other hand, I am concerned about the close proximity of the two meetings.

MR. HILLBACK: It's interesting that all the speakers you've named are geneticists or related to genetics.

MR. McINERNEY: No, that's not true. The individuals who will be presenting the posters, and also at the plenary session, will not be geneticists.

DR. SHORT: I think in the survey work that we've done with NCHPEG and one of the logistics that we continue to grapple with, which I think other people have as well, if you put together a meeting to discuss the issue of genetics and you ask cross-disciplines, you get the genetics-friendly person sent by that organization. That does not translate into investment by that organization in the importance of the topic. You hope that the messenger that they send has credibility back with the organization, but that's always a question. I think to learn from the HuGEN experience, I think that could help determine who we think should be in the audience. I think that, as you said at the bottom of your other drawing, awareness, I think there are the disbelievers who are probably in positions of perhaps greater power than their representatives that they send to various advisory committees. So I think taking a page from the HuGEN experience in terms of perhaps turning those people that are in positions of power to increase their awareness would be something to consider.

DR. KHOURY: I'd like to second both Ed and Elliott's remarks and expand on them. If we keep in mind what SACGT's mission is, which is to provide advice to the Secretary, and therefore to all the agencies that are represented at the table, and then influence directions, resources, filling in the gaps, et cetera. I see that mission as complementary to but not necessarily overlapping. There could be some overlap with organizations like NCHPEG, et

cetera, but we need to keep our eyes on the ball. I think what you heard yesterday and the discussion this morning was very important, not only what I said in one agency in HHS, but I think across the landscape, because you're beginning to identify some of these gaps that groups can take on in the future, like NCHPEG or some of the other organizations. So I like your action-oriented agenda, what are the gaps, what should be the priorities, what can SACGT recommend, be it Elliott's three-point list or four-point list or some other list of some sort, rather than getting too much into the nitty-gritty. You need to get not only the friendly people but you need to get the critics to talk and get those people who are saying genetics can't do anything for me today to speak as much as the genetics-friendly faces that Priscilla mentioned.

DR. BOUGHMAN: Before I call on a couple more people at the table, I want to put a challenge to the other participants at the roundtable and other folks who have come to the audience today recognizing that there is some degree of genetic friendliness or you wouldn't have chosen to be here in this room today. I don't want to spend my time, and I certainly don't want to spend the time of a lot of other people, duplicating or conflicting with other people's work. I'm going to throw out the idea that to have the summit 10 or 12 days after this NCHPEG meeting, in fact, raises some questions, and that two kinds of alternatives might be to either piggy-back immediately onto NCHPEG in some way to keep a few people here that might be interested and attract more, or separate it enough in time, say to late spring, that we might utilize any information that came from NCHPEG but to clarify and differentiate the goals of these two organizations and to have a different outcome-based process from SACGT meeting.

DR. LEWIS: Looking at how Ed defined the goals of SACGT and how Joe defined the goals of NCHPEG, I am wondering if, in fact, these two meetings will attract exactly the same people or

whether they won't. I believe that some of the people that we want to come and help us make policy are the accreditors, the certifiers, people like leadership in professional organizations at a policy level who aren't necessarily people who are the genetics-friendly people of the world, but the CEOs or the chief operating officers or the presidents of some of these associations who maybe aren't sending their genetics-friendly people. So if the level of people we invite to our summit may be different than the level of people who are going to the NCHPEG meeting, I don't know if there's a conflict, but I do see what you're saying about the value of maybe including this rather than with our February meeting, with our May meeting or our June meeting, whenever that is. I just worry that now we'll put it off for a year, because we had originally started talking about doing this in August. So that was one piece. But I'm wondering if, in fact, it may well be similar organizations but different principals within the organization if we want to focus on not necessarily getting all the genetics-friendly people, and I think that's a key point Priscilla had.

DR. CHARACHE: Briefly, it sounds as though the beginning parts of the NCHPEG meeting, the material has already been covered by this group over time, Wayne Grody's talk and the talk on ethics and so on, that the discussion by Dr. Collins on what we need to know and why is really more targeted towards how we're going to get there. So there is not a complete overlap, as well as the difference in the goal, which is to come out with specific recommendations. So it seems to me that there's really not a conflict, and if there is a delay in the meeting, I should think it would only be by a month or so, rather than getting into unacceptable delay.

DR. COLLINS: Two quick comments. I do think, even though there is a somewhat different cast of characters that you might want for these two discussions, that there probably is a fair amount of overlap. If you try to organize two meetings within two weeks of each other, people

will assume that something is really wrong here, and perhaps it will actually damage the attendance at both meetings because people will assume that neither one is relevant. So I would consider it a bit risky to go down that path.

I liked Ed's formulation of the way in which this fits into SACGT's particular mandate, but I think probably we need to think carefully about what that means, because if this is being formulated as an opportunity to make recommendations to the Secretary about education in genetics, then they need to fall into the areas where the Secretary has authority. There are certainly aspects of what one might hope for that the Secretary really doesn't have the ability to step in and fix. You'd want to try to think carefully through what that means in terms of the areas to emphasize in such a policy-oriented discussion.

DR. BOUGHMAN: Well, just as a comment there, and also to address Judy's concern about delay, I didn't actually expect us to have the agenda done by the end of our 30 minutes here. I think our charge as a Committee is to, in fact, advise the Secretary on actions that might be taken. I think implicit in that charge is to inform the Secretary of the status of the environment out there, to present the context as a basis for the specific recommendations. One of the things that was, I think, quite revealing yesterday was not just what the geneticists are doing but, in fact, there are many of these organizations that have begun to take actions and make progress, and I think that was certainly very gratifying to me, and it seems as if a delay of several weeks or whatever is certainly not going to slow down that progress. More progress might have been made, some of the successes would be more solidified and presented and shared in a more clarifying way so that we could not only crystallize a few of the recommendations but base those recommendations on actions that are taking place out there in the real world. That's just one of

the senses that I've gotten.

MR. HILLBACK: Yes, I'd like to sort of second that. I think Francis made a really good suggestion. We do need to remember areas that we ought to focus on, and I guess what I would propose is that the education committee set up our own conference call soon to sit back and say within our charter and within everything we heard yesterday and today, where are the areas that we ought to do more research over the next X months, including some of us or all of us going to the NCHPEG meeting where the rubber is going to meet the road? But in the meantime, maybe we should be talking to the accreditation organizations more. We should be doing some other homework on some of these issues where we may be able to make real recommendations to the Secretary or real recommendations that work, and I think also where we can play sort of the intermediary to maybe bring some groups together, and then from that decide what our meeting ought to look like.

You know, I had my list, but the more I think about it, that's where my list was as of today. If we take Francis' suggestion and say, hey, what can we really tell the Secretary about, compare that to all our notes, compare that to what happens in the next few months, then we can put together a meeting. I have no problem if the meeting doesn't happen until the end of April if it's the right meeting, skipping it a few more weeks to hear what happens in NCHPEG and then re-format our meeting based on what we've learned there, what we've learned on some of these other pieces of research. I think that will make it a better meeting. So that would be my recommendation, that we not just sort of pause, hit the pause button, but that we go into more action in the sense of the committee meeting and thinking through the three or four topics that we really want to take on, and narrowing our scope.

DR. McCABE: Let me make a suggestion. Dr. Koenig has agreed to abbreviate her discussion this afternoon. I think that will give us another 45 minutes, maybe even an hour, to pursue this discussion, so that we can -- it will give us 15 minutes? Oh, sorry. I thought she was abbreviating it to 15 minutes, not 50 minutes. But we can have at least 15 minutes this afternoon to pursue the discussion. People can think about this between now and then.

DR. BOUGHMAN: And chat over lunch. Even for those who won't be there this afternoon, I would just like to say that I don't want anybody to leave feeling unsatisfied just because we don't have the formalized agenda. The work group is a working group. The advice and input and participation that we got yesterday I think has informed our process tremendously. You can bet that the participants are going to get some phone calls soon, and I think Elliott is right, if we don't get all the conference calls and one-on-ones done this afternoon, we'll have a conference call soon. But, in fact, even this last 20 minutes or so have further clarified the challenge that we've got, and I certainly hope that those of you who participated in yesterday's roundtable, our messengers of high credibility and assertiveness, will go back and share the insights and enthusiasm and focus that there is nationally now on some of these issues, and give us feedback. You're part of the process now. We've got your name and number. If you don't call us, we're going to call you, and keep contributing to the process. Now that you've seen the way we work, know that this is a venue for you to get information from your disciplines, both the challenges and needs as well as advice, into this broad-based group here and the Secretary's Committee. With that, I'd just like to thank everybody again for all of their input and energy on this.

DR. McCABE: Thank you, Joann. We will continue this discussion later in the day.

At our meeting in August, Dr. Charache mentioned that she had seen a demonstration of a novel educational tool at the last CLIAC meeting which she thought would be of interest to SACGT given our intensive focus on education. The program was created by the Interactive Media Laboratory at Dartmouth Medical School through a cooperative agreement with CDC's Office of Genetic Testing, which is part of the agency's Public Health Program Practice Office. We're very pleased that the program designer, Dr. Joseph Henderson, could be with us today to demonstrate the concept to us. Dr. Henderson is the director of the Interactive Media Laboratory and professor of community and family medicine at Dartmouth Medical School. Dr. Henderson has a broad background in research, medicine, and communication technologies. After early work in neurophysiology research, he developed a computer-aided diagnostic method for the U.S. Navy and did graduate work in epidemiology that led to the design of a novel interface and a multimedia data set dealing with Vietnam War trauma. His work culminated in development and application of a model for technology-based learning called the Virtual Practicum. The program we will see today is based on this model of learning. Dr. Henderson earned his medical degree from SUNY Buffalo.

Dr. Henderson is joined by Mr. Andrew Faucett -- maybe both of you could come to the table, please -- a genetic counselor in the CDC's Office of Genetic Testing. Mr. Faucett is part of a collaborative program between CDC and the Association of Teachers of Preventive Medicine that focuses on the integration of genetics in public health. Mr. Faucett was trained at Sarah Lawrence College and has been active in the leadership of the National Society of Genetic Counselors, is currently a member of the board of directors of the American Board of Genetic Counseling.

Mr. Faucett will begin with a brief introduction and then turn to Dr. Henderson for the demonstration and discussion of the genetic testing in clinical practice, a team approach. Before he begins, however, I should warn all of you that I play a bit part in this, and though I'm not giving up my day job, when I introduce myself to people I meet in Los Angeles, I'll say I'm a physician, and they'll say, well, I'm not a physician but I play one on TV. Thank goodness I am a physician and I don't have to worry about ever having to play one on TV, as you'll soon see. But thank you very much for both of you being here.

MR. FAUCETT: I'd like to thank the Committee for inviting Dr. Henderson and myself to present two projects from CDC that were designed to help with the integration of genetics and genetic testing into the health care system. I have to say that the discussion this morning was quite a set up for what we're going to talk about.

The first thing I want to talk about is the project Genomic Competencies for the Public Health Workforce. This is a joint project of the Office of Genetic Testing at the Public Health Practice Program Office and the Office of Genetics and Disease Prevention. This project provides an example of that massaging that we talked about earlier. We started with the NCHPEG competencies and then worked with a group that was considering the integration of genetics. The key to the success of this project was the involvement of many individuals currently working in public health who were interested in genetics but not geneticists and not the leaders in genetics. This outcome was their product which they support and are currently promoting in their respective areas of public health, and this slide just indicates a number of people involved. There were also over 60 different individuals who looked at the project as we went along.

This process was a combination of expert opinion and consultation which involved over 100 individuals working in public health. The project began with a meeting of team leaders in March, followed by development of lists for each of the six areas of practice, revisions by email and conference call, an in-person team leader meeting to edit and decide on a final format, review by multiple public health professionals, and then release on the Internet in June of this year.

To kind of summarize the outcome a little bit, the result was a list of three competencies that we felt really applied to everybody in public health, and then targeted lists, one for professionals, and then one for each of the discipline-specific professional groups that we worked with, leaders and administrators, clinicians, epidemiologists, data managers, health educators, laboratory professionals, and environmental professionals. These lists are designed to be used as a starting point for discussion. I think one of the things that's important as you look at this practice is to realize that you're not going to get all of the competencies that you want integrated, but you've got to start somewhere. Hopefully, as groups in public health reevaluate their competencies, they will incorporate some of the genomic competencies. If you have any questions about the project or for more detailed information, there's a lot of information on our website, and there's a lot about the process that we went through in developing these competencies. So I would encourage you to visit the website.

Now I'd like to introduce a joint project of Dartmouth Medical School and the Office of Genetic Testing, Genetic Testing and Clinical Practice, A Team Approach. This project is a cooperative agreement to create an interactive multimedia educational program using the virtual clinic that Dr. McCabe described. It's an educational format designed to re-create the learning

environment found in most medical schools, that of a mentor in case discussion. It simulates interaction between health care professionals and patients facing genetic issues. One of the major goals of the program is to highlight the issues that make genetic testing different and to offer a team approach as the best way to provide patient-focused quality care. This team includes clinical professionals, geneticists and genetic counselors, and the laboratory as active participants in the team. This program includes face-to-face patient visits, demonstrations of genetic counseling, lectures from leading experts, patient interviews, an introduction to genetic laboratories, tours of the cytogenetics, molecular and biochemical lab, activities, and a guide to resources on the web.

Now I'd like to turn the program over to Dr. Henderson, who will actually demonstrate it.

DR. HENDERSON: Thank you, Andy. It's a great pleasure to be here. Thank you for inviting me to participate. I'd like to echo Andy's comment that you've provided a wonderful tea up for this program. Also, hearing the discussion, which I enjoyed very much and took a lot of value from, it tells me to think about how I want to present this program to you.

I think what I'd like to do is touch lightly on highlights but make the point that we are aware that we need to emphasize the value of the family history, so I want to pick one of the cases that gets into that. I also want to say that the program is not quite finished. We're still polishing it and we have not yet put the activities for the program in. There is an error in your handouts describing the program. There are not three cases but four, and there is not going to be a beta version available in 2002. It will be a final version ready for deployment early in 2002. So we hope the review process will be relatively quick and the number of revisions will be relatively

few. If all goes according to plan, the program should be available sometime in March of 2002 for use in ways to be discussed, I hope.

We have a mini-fellowship, but it's a mini-fellowship that can be accessed from any location at any time, as long as one has one of two things, either a broadband connection to the Internet, and that can be done via land line or satellite -- we've demonstrated both -- or via CD-ROM plus dial-up connection if you want full functionality, or CD-ROM with no Internet connection if you don't desire or can't get web access.

So let me log in and let the program and its mentors speak to the program's design. The program is intended for the generalist. We have this particular list of generalists. The projector can't do justice to the quality of the images and the text, of course, but please believe me that this is all legible by someone sitting in front of the screen.

This is approved already for up to 10 hours of CME credits granted by Dartmouth Hitchcock Medical Center. It satisfies the necessary requirements.

(Virtual mini-fellowship follows.)

VIRTUAL DR. McCABE: Sounds good, Michelle. Glad you've made it. There's a lot of ground that we can cover, so let's get started. First, some introductions. I'm Ed McCabe. This is Wayne Grody and Michelle Fox. Wayne is a clinical geneticist who is in charge of our molecular genetics lab at UCLA Medical Center. Michelle is a certified genetic counselor also at UCLA. I'm a clinical geneticist and chief of pediatrics in the Mattel Children's Hospital at

UCLA.

If this is your first time here, I strongly recommend that we start with a short orientation to the program. I'll tell you about the scope of the program and how this mini-fellowship is structured. Would you like to do that?

To begin with, this program is about the use of genetic testing in clinical practice. Our emphasis is on the increased use of genetic testing by practitioners like you who aren't specialists in clinical genetics. This reflects a growing trend resulting from technological and scientific breakthroughs on many fronts and the increased use of genetic screening for a broad range of conditions. This virtual mini-fellowship anticipates a time in the relatively near future when genetic testing will be a routine part of general clinical practice.

That said, this program is firmly grounded in the present. It deals with problems and situations that can be seen today by practitioners like you. The technologies and practices of clinical genetics are complex, and they are unfamiliar to many of today's practitioners. Our main goal is to help non-geneticists use genetic testing and services appropriately. This involves developing a better understanding of genetic testing and the testing process. Perhaps more important is understanding how the generalist provider, specialists, and laboratory professionals can form an integrated team to provide better patient care.

Here are the central topics and issues covered in our program. This program also emphasizes your role as a coordinator of care. Care providers like you will be playing an increasingly important central role in the application of clinical genetics. You will be responsible for assuring

appropriate levels of specialty care while providing excellent levels of comprehensive ongoing care. You'll be able to explore any or all of these issues using a variety of learning methods.

Now, let's talk about how this virtual mini-fellowship is set up. We'll be working in -- what else? -- a virtual clinic. The clinic's layout reflects the kinds of learning you can do and gives you a way of choosing among them. We believe strongly in the value of learning through experience. That occurs mainly in this examining room where you'll have the chance to interact with simulated cases. There are a total of four different conditions involving seven separate patient visits. You can do as many of the cases as you like in any order. You can select them using the patient roster located in the main hallway. I'll tell you more about this when we get to it.

In the room marked "B" you'll be able to see counseling sessions conducted by experts in various fields of clinical genetics. Our goal is to show you how they might manage the situations you encounter in the situations. The conference room is where you can hear discussions of the cases you see. We've brought leading experts together for these discussions. The resource room has several areas, each offering different ways of learning about clinical genetics. One of the most valuable is the interviews area where you'll find remarkable documentary-style interviews with some real people whose lives have been affected by genetic conditions either as patients or as family members. I strongly recommend going there. The web or Internet area lets you access a site on the World Wide Web for this program. The site maintains a set of pointers to other websites relevant to clinical genetics. Last but not least, the lectures areas. Here you can attend mini-lectures given by leading experts in various aspects of clinical genetics.

The last major area for the mini-fellowship is the laboratory area. This area provides an orientation to the laboratory and how genetic testing is done. It also provides the perspective of the laboratory professionals on the genetics team.

Finally, I just wanted to list the colleagues who will be assisting with this mini-fellowship. I think you'll agree that they're extremely well qualified.

DR. HENDERSON: Now, this is an example of something that's not yet polished. We'll be adding pictures of the faculty members and obviously getting this information just the way the various participants want it. We haven't gone through that step yet.

We have Mark Green from NCI discussing colon cancer and cancer in general; Randi Hageman discussing Fragile X; Sharon McDonald discussing hemochromatosis; and Brenda Finucane demonstrating a counseling session with a real family with Fragile X; Andy Faucett, whom you know; Betsy Gettig, another genetic counselor; two lecturers, Francis Collins, whom you know, and Alan Guttmacher also give lectures in the program.

VIRTUAL DR. McCABE: I recommend you let the patient simulations form the backbone of your mini-fellowship, with visits to the resource room and the laboratory interspersed. If you do all of the simulations and everything in the resource room, you could spend from 5 to 10 hours in your mini-fellowship. If you only do the simulations of most professional interest to you, and a couple of the resources, you could spend as little as 2 hours. You can visit the clinic as much as you like, so you needn't do everything in one sitting. For continuing education, you'll be credited for the number of hours you spend using the program.

The best way to start is by seeing one of your patients. To do that, select your case from the roster by clicking on it. You can also visit the learning resources room or the laboratory. Just click outside the roster. The fire evacuation map leads to an overview of the virtual clinic. It's your choice.

DR. HENDERSON: Now, we selected cases that at least one would appeal to the various generalist specialties. We have something for the obstetrics community, something for the medicine, and obviously everything is for the family practitioner. There's something for the medicine community. This ends up being a family with strong indications for HNPCC, and this is a family with hemochromatosis. This is the Fragile X family. Everything is played by actors except for this case where we actually had a Fragile X family who agreed to act. So you see how it works. Let me just show you the beginning of each of these so you can get a sense of what they look like.

VIRTUAL DR. McCABE: Since this is your first simulated case, I'll warn you that using the computer can be a little awkward, and there are limits on what you can do that aren't there in real life. For example, in actual practice, the family history would be much more interactive. On the other hand, these cases feel fairly real and raise several important issues about genetic testing and clinical practice. This encounter should make a good warm-up.

Your patient is Joan Singer, a woman in her late 20s. Ms. Singer is two months into her first pregnancy. She was offered a test for cystic fibrosis as part of routine prenatal care. The test shows that she carries the DeltaF508 mutation for CF. She was given the results of the test by

phone, a practice that is far from ideal, and she's been scheduled to see a genetic counselor. However, she has some immediate questions that she'd like to go over with you. You can look at her chart if you'd like. Turn the doorknob when you're ready to go in. I'll see you when you're done.

DR. HENDERSON: Ms. Singer has had one prenatal visit and tests. I'm just going to go through this rather rapidly, but you can see we're doing our best to kind of reproduce the clinical experience as one might experience it. This is obviously a typical kind of test report. So let's go ahead and go in.

VIRTUAL PATIENT MS. SINGER: Thanks for seeing me on such short notice. I'm a little bit concerned about this test result, and since I heard it I can't really get much work done. I don't even know if it's something that I should be concerned about, you know? When they explained the test to me I said, "Sure, why not?" I guess I really should have paid more attention. But then the person on the phone said that a positive test result really isn't that unusual and that I'm okay and everything. But still, I really didn't want to wait to see the specialist, so thank you. What can you tell me about my CF test?

DR. HENDERSON: Now, this program isn't about CF, so we just basically go straight into -- we're obviously educating physicians or residents or medical students who aren't real familiar with CF as we present this message. Again, forgive me for not giving you enough time really to look at the program closely.

Now, all of the cases follow the same format. We meet the patient, there's some kind of text

screen, and then we go immediately into family history. I don't know if you saw the ending of that previous text screen was that we told our patient that we would like to get some information before doing any more.

Let me ask you all, what would you like to ask about first?

PARTICIPANT: Pedigree.

VIRTUAL PATIENT MS. SINGER: Well, this could take a while. We have a really big family. I've got four brothers and two sisters. They're all younger than me. I'm 28. Christa is the youngest, and she's 12. Meg's 15, and then the four boys came like clockwork every two years, boom boom boom, when I was 4. So they would be 24, 22, 20 and 18, and they're all healthy.

DR. HENDERSON: Now I'm going to jump through this. That's the complete family history. Let's do a little more. You get one more choice. Obviously, we want to ask all the questions. What else would you like to ask about?

PARTICIPANT: The partner.

DR. HENDERSON: Partner. Actually, that comes up in her questions. This is a case, by the way, where one of the dilemmas is dealing with parents who have very different values with regard to continuing a pregnancy or not. In the second encounter, the husband does come to the session and we get a family history from him as well. Of this list, what would you like to ask?

PARTICIPANT: Ethnic background.

VIRTUAL PATIENT MS. SINGER: My dad's parents came from Scotland years ago. My mom's side of the family is pretty much standard Midwestern. My great-grandparents came from Norway.

DR. HENDERSON: Now, we give her a little more information. Please understand, this format simply doesn't support true patient interaction, obviously. I mean, there's no way to anticipate all the things one might do, so we're trying to focus on key issues. That's particularly brought out in this aspect of it. I can't do this, I don't know how to do this. I can't provide all the variability that the free exchange in a typical counseling session or patient education session would occur. So my goal here is not to duplicate a session but have people reflect on key issues that might arise in a session, and that's what this particular format is about. So we conclude the giving of information with asking if she has any questions, and she does. The way it works is she asks a question and we select from among three choices, and the choices kind of delineate the issues that we think that question brings out. This is an example of polishing. We just kind of messed up right there. Or we can ask about issues.

VIRTUAL PATIENT MS. SINGER: Are you sure about these results? I mean, could the lab have made a mistake?

DR. HENDERSON: So this first one is maybe a little technical. We talk about positive predictive value, negative predictive value, and we encourage learners to explore the answers.

These are pretty close. Well, actually, they're not pretty close. I'm sorry. I'm not reading this. This one is simply wrong.

VIRTUAL PATIENT MS. SINGER: No one in my family has CF. How could I be a carrier? I mean, who would I have gotten it from?

DR. HENDERSON: And so forth. I'm going to break into this case. I'll show you a couple of other cases. This is Mr. Martin.

VIRTUAL DR. McCABE: Your patient is John Martin. Mr. Martin is 46. He recently retired from the Navy and he's getting ready to start a second career as a high school teacher. His younger brother was recently diagnosed with advanced-stage colon cancer. Mr. Martin is here because he's concerned about familial cancer. We've requested John Martin's medical records, but they're not available yet. You'll find some useful information in his chart, however. I'd recommend that you take a look.

DR. HENDERSON: Now, Mr. Martin actually has done some research and he's actually giving us a pedigree. So here is our proband. Here's a brother with colon cancer. He has an aunt who had some kind of female cancer, and he had a dad with some kind of stomach cancer.

VIRTUAL PATIENT MR. MARTIN: Doc, I've got a few concerns. You see, they found out that my brother Frank has cancer of the bowels. They operated on him and just closed him up without doing much and said it was too advanced and had spread to other places. Now they're giving him chemo and all. Plus he's not the first one in our family to get cancer. So I went on

the Internet. There it was, FAP. Sounded just like what he had. Then there's this non-FAP kind of cancer, and they talked about genetic tests we could do to check things out. So my question is, do I need to be worried? Does my family need to worry? And plus, I'd like to see about those genetic tests just to be sure.

DR. HENDERSON: Now, in this particular case, we just solidify the diagnosis. But the point here is that there are two encounters with Mr. Martin. His family history is very suggestive, but it would be great if we could pin down the diagnoses for the father and for the aunt, and that's basically what leads to the second encounter. One of the things we can ask him is if he could get some more information. Obviously, we'd like to know what his brother has. That's obviously an important thing as well. In fact, we get his brother's operative report, we get his pathology report, and we can see that in the chart when we start the second visit. Then he's also able to get death certificates on his aunt. Amazingly, the physician had completed secondary diagnoses on those death certificates. So we did confirm that the aunt had endometrial as well as colon cancer, that the father had colon cancer, and Mr. Martin does meet the Amsterdam criteria. Then the issue is do we do genetic testing or not, and it's left unresolved.

I'm just going to take you down the hall and show you some of the other resources in the program. This is where we can do lectures. Ultimately, we'll be able to do activities as well. We can view the entire lecturers' subtopics. Dr. Collins was kind enough to let us record a lecture he was already scheduled to do.

VIRTUAL DR. COLLINS: Well, let me go through what we've learned about the genome in the course of the last few years. Again, in particular, I'm going to talk about where this is all

going to take us next. The reason we're doing the Genome Project, just to be very clear about it, is a medical one.

DR. HENDERSON: A lot of control there, right? Alan Guttmacher does this one, Francis does these, and then Betsy Gettig and Andy Faucett give these lectures. These are not actors. These are real people who present the patient/client/consumer point of view.

VIRTUAL PATIENT: I saw him just about a week before my mastectomy, and I looked him straight in the eyes and I said, "Philip, I will get breast cancer someday. I will have to have a mastectomy someday. So I'm going to do it now, and that way I don't have to do radiation, I don't have to do chemotherapy, and I get to keep my lymph nodes."

VIRTUAL PATIENT: I remember getting on my own bike but I don’t remember being able to ride around the park. My mom brought me a tricycle when I was young. The only place that tricycle got a ride was on the back porch.

VIRTUAL PATIENT: My sister got pregnant and actually gave birth this past December 31st, and the baby had several problems and was on a respirator and some of these other things. After doing some testing, they found out that the baby actually had myotonic dystrophy. The number of repeats on the baby's chromosome was 1,500, which is basically a death sentence.

VIRTUAL PATIENT: To me, genetics is really a unifying thing, and I think a lot of people right now are sort of scared of it and afraid and feel like it's going to fragment people. Genetics is really one of those things that says, yeah, that's true, everybody has these little things that are

different about them, and it's really differences, it's not disabilities. It's really genetic differences. Everybody has them, and if you want to make disability a little minority group, it's the only minority group that you can join at any time in your life, and you will join it if you live long enough. So, welcome aboard.

DR. HENDERSON: Let's just do a couple of these. Is there any particular segment that anybody would like to see? Which of the three segments would you like to look at? The first one?

VIRTUAL PATIENT SUZIE: I should have taken theater when I was really little, just as classes that you take, but I kept getting more and more involved in doing shows and that sort of thing, and I've always had fairly good reviews and fairly good responses from -- not always. I had a lot of long learning period time. But in the last few years, and people come up to me and say, oh, your league audition was the best league audition I'd seen, and it would seem like 800 people over the course of five days -- oh, it was the best -- and these are major theater directors. And I'm looking at them knowing that they've never called me into that theater. And I'm looking at them and I'm looking at them, and I finally go, well, why don't you cast me? And it's just like it had never occurred to them. It's this thing, it's this barrier. There's still that social taboo about disability that people just won't be able to accept it. If you want to make disability a little minority group, it's the only minority group you can join at any time in your life. You will join it if you live long enough. So, welcome aboard.

DR. HENDERSON: One more.

VIRTUAL PATIENT: Actually, my mother was very upset when she learned that we all had this disease. She was saying how she thought she had four very healthy children and there was no problems and so forth, and all of a sudden 30 years down the line she discovers, oh wow, there's something wrong with each of them. They each have some problem. It's scary. You read some of the things in there that wouldn't cross your mind once or twice. Anesthesia. My father's had several heart operations and so forth, and that might be something in my future. Now, all of a sudden, it's scary enough to go under the knife, but now you have to worry about the amount of anesthesia you get. It's just other things you have to concern yourself with that you didn't have to before. It's just something that sort of hit us out of the blue sort of thing. No one was expecting it and no one really realized they had it up until six months ago. So it's been a bit of an impact on the family, and I'm sure it will be even more in the future.

DR. McCABE: We should probably wrap up now.

DR. HENDERSON: Yes. Let me just show you one more thing, and that's the laboratory.

VIRTUAL DR. GRODY: Welcome to the genetics laboratory area. We can give you an overview of how genetic testing is done. Mainly, we'd like to help you understand how the clinical and laboratory teams can work together to improve patient care. Behind me is the molecular genetics laboratory. To your left is the biochemical genetics lab, and to your right is the cytogenetics laboratory. Or you can head back to the clinic area. Before you begin the tour, I can give you a quick overview. Would you like to do that?

DR. HENDERSON: I'll just do basically half a minute of this and then we'll stop.

VIRTUAL DR. GRODY: The most important point I'd like to make is the following. More than any other clinical laboratory area, genetic testing requires very open lines of communication between the clinic and the laboratory, and in this case the genetic counselor as well. It's important that the laboratory knows why you are ordering that test, the family history of the patient, the ethnic group --

DR. HENDERSON: Okay, we'll stop there. Lights up, please. And the microphones.

DR. McCABE: We can have about five minutes of discussion before we break for lunch. One of the questions that came up somebody asked me, Joe, or Andy, how much does this kind of thing cost to put it together? Because I know the amount of time that it took in a production facility and the amount of work that's gone into writing all of these cases and everything. So just not exactly but a ball park figure. Is this the kind of thing that a group other than a federally sponsored project would be able to take on?

DR. HENDERSON: Well, let me answer the second question first. Yes. There are a couple of answers to that. We have had funding from non-federal sources; for example, the Robert Wood Johnson Foundation. So it's possible to get funding from foundations. I've actually had a project funded by Merck. I'd say this program probably about $600,000 of direct costs.

DR. McCABE: Do you want to comment on what it was modeled on, because you talked to me about it.

DR. HENDERSON: Yes. This was modeled on -- for those of you who may be educators, you may be familiar with Donald Chung, who was on the faculty of MIT. In his book "Educating the Reflective Practitioner" and other writing, he laments the tension in academic educational settings between rigor and relevance, and that this is a reciprocal relationship. He says, "In academia we tend to take the high ground, where we have theory-based, fact-based, rule-based learning, and we don't do a very good job of preparing people to work in the swamp," which may not act according to facts and roles. He advocated the use in academic settings of what he called reflective practicums. So I outlined those two paragraphs in his book and I said what if we could take all those elements and make them technology based? And all of the elements of that reflective practicum are in the virtual practicum. The rest of our research at Dartmouth has to do with the underlying technology. My guess is you've never seen an interactive multimedia program of that quality in terms of the use of media, in terms of the quality of the image. It works exactly as well as that over the Internet if you have a broadband connection. In fact, it works a little bit better because it's faster than the CD-ROM on the local computer. So in addition to developing the program, we're looking ahead generally to how we can use the evolving Internet for health professional education.

DR. COLLINS: It's very impressive. I am curious as to how you're evaluating it by field testing it with practitioners and how you incorporate that feedback into altering the plan.

DR. HENDERSON: There are two different kinds of evaluations. One is what we call beta testing, usability testing, where we have actual practitioners sit down and I watch them personally using the program. We've already made changes to the design as a result of those observations. And also, bug testing. We have an army of Dartmouth students pounding on this

program, finding bugs. Unfortunately, every time we update it, we have to do the same thing all over again.

The other thing is that just yesterday we started testing the program in terms of does it have an impact on clinical practice. There's a separate group funded under the same initiative that is looking at a group of 30 primary care providers in northern New England. Half of the group is using the program for five hours, the other half is not. This is a pilot project, and we're using tests of knowledge change, but also we're using simulated standardized patients who actually go to the office and present with a problem that may have a genetic basis. I'm not terribly familiar with the design of that study. I believe strongly that the developer should not be involved in the evaluation, so I take a very hands-off approach.

DR. LEWIS: So after this is developed, is it going to be something that's going to be available on the Internet free of charge? Is it going to be a tuition-based program? Is there going to be a cost for the CME? How is it going to work?

DR. HENDERSON: My goal, and I know CDC's goal, is to have the program as widely used as possible. That said, there are a couple of other issues. One is perceived value. In our society, if you give something away, it's suspect in some way. So I could see accessing it over the Internet because that's the norm, it's free on the Internet, but if you get a CD-ROM for free, are you likely to use it? I don't know the answer, but I'm perfectly prepared from Dartmouth's viewpoint, I've already gotten clearance from my institution to just get the program out there. We're not concerned about revenues. That said, we know the field evolves rapidly. Who is going to pay for updates to the program to maintain its usefulness? There isn't a good granting

process to allow for that, so that's one argument for having some way of generating income. I'm taking a very short-sighted view, though, to just get the program out there.

DR. McCABE: The example is a case on hemochromatosis which deals with the controversies as they exist today, but they will be very different a month from now. So one does need ways to update this. One of the ways you can do that is through the text so that you don't have actors presenting all of this but can deal with the text, and that text can change much more easily than getting people back in to re-say their lines.

I think we're going to take a break. There will be a casting call over lunch. Joe will be seeing you in another room for that.

DR. McCABE: Thank you very much, Andy and Joe, for bringing that.

DR. McCABE: We will resume shortly, at 1:00.

(Whereupon, at 12:06 p.m., the meeting was recessed for lunch, to reconvene at 1:00 p.m.)

AFTERNOON SESSION (1:05 p.m.)

DR. McCABE: Let's go ahead and get started, because we have a lot to do this afternoon. Before we get started, I think I heard -- Pat, are you on the phone? Pat Barr?

MS. BARR: Yes, I am.

DR. McCABE: Hi, Pat. How are you?

MS. BARR: I'm okay, and hello to everybody.

DR. McCABE: And Wendy Uhlmann. Are you on the phone, Wendy?

MS. UHLMANN: I'm on the phone.

DR. McCABE: Okay, great. Good to have you. We're going to turn now to Dr. Koenig for her presentation of two products of the Informed Consent and IRB Work Group. The first is a proposed information brochure for the general public entitled "Genetic Testing: Some Basic Questions and Answers." The brochure is at Tab 6 of your briefing book. Following presentation and discussion of the brochure, Dr. Koenig will provide us with a progress report on the work group's effort to develop recommendations for informed consent for genetic testing clinical and public use. A report on that effort is also at Tab 6.

Before Dr. Koenig begins, I want to welcome Ms. Wendy Uhlmann, who is joining us by phone today. Wendy is a member of the Informed Consent Work Group and has played an especially key role in the development of the brochure, and as I mentioned before, also welcome Pat Barr on the phone. So, Barbara, if you would then proceed. And remember, we will take as much discussion as we need, but we are going to try to save 15 minutes at the end of this before the public comments. So from 2:15 to 2:30, if at all possible --

DR. KOENIG: We're going to switch to the other topic at 2:15, if possible?

DR. McCABE: Yes.

DR. KOENIG: Great. Good afternoon, and thank you very much. I'm anticipating that we're going to get some help, the Informed Consent and IRB Work Group will get some help with our activities so far. Let me begin by just putting up this slide. You have a copy of this slide in your packet. This committee is co-chaired by Ben Wilfond, who has taken an incredibly active role in the products that we've developed so far, and then we have a very active committee, including a number of consultants who have worked on informed consent issues in their own research, as well as a very active group of individuals from agencies.

I'm going to do two things. I'm going to divide this presentation in half. In the first half we're going to discuss the work group's draft information brochure, which is called "Genetic Testing: Some Basic Questions and Answers." This is a final draft. It's gone through a number of iterations, and we're now at the point that we need to ask for your approval, for the approval of the full SACGT, and possibly to then talk through the issues of how we're going to get this out to the public. The second part of the talk today will be to go through our harder task, in some ways, which is what we're calling our “points to Consider for Informed Consent for Clinical and Public Health Genetic Tests”. We've worked on that quite a bit in terms of trying to think through some kind of a set of procedures for assigning levels of informed consent to certain tests. So we're going to try to ask you if you think we're on the right track in terms of where we are with those activities. So these are the things I'll talk about first.

In terms of the information brochure, we'll explain how we drafted it, the purpose, the target

audience, the goals, the content, the reading level, and then move to what our questions are for SACGT. This was meant originally to complement activities that other groups were doing, to complement, for example, a document that might be for providers. So we wanted something that could be a draft brochure about genetic testing oriented toward potential patients. So staff drafted originally a document, and it was meant, as I said, to parallel the Data Group's provider template. We then have spent a great deal of time revising it. Wendy Uhlmann has revised it two or three times very successfully, and we've had a number of meetings where we've discussed it. One of the things that has happened in the context of those discussions is that the brochure has moved a little bit in terms of its focus from being something that might be useful in a particular clinical setting to an idea that what we've really created is going to be a much more general kind of brochure for the public at large. So the purpose of the brochure is to provide basic information about genetic tests to the general public and to serve as a model for communicating information about genetic tests. Just to make it clear, this is not meant to be any sort of an informed consent document in and of itself.

The other key element to keep in mind is that this is meant to be a generic document. It's not supposed to be focused on any particular genetic test, because I think those of you who read it on the way will recognize that it probably wouldn't be adequate for most specific testing contexts. So it really is not going to be something that you would hand to someone considering a genetic test at that particular point in time. You wouldn't give it to someone who was considering at that point in time CF testing, for example. So the goal is to broaden and enhance awareness of genetic testing and provide basic information about tests and issues. Though not an informed consent tool, by increasing general understanding, we hope that it might facilitate subsequent informed consent discussions.

So what is the content? We specifically went to a question and answer format which we thought would be most useful. So it's very basic. What are genetic tests? What are their purposes? How are they similar and different? What are their limitations and possible outcomes? To continue with the content, it covers questions on health insurance policy and employment and privacy discrimination, provides information and services resources, and then lists questions to ask yourself as well as your health care provider if you're considering genetic testing at any point.

We have some concerns about the reading level. I think it's at the 10th grade level at the moment, according to the computer formulas, but it still seems a little difficult. So one of the options that we have at this point is to consider hiring a professional writer who could review, revise and design the final document.

We also have felt that it might be important to actually get public comment on the document itself in terms of things like readability, tone, utility, and then how to disseminate it. Priscilla just told me actually that she has been in touch with some professional associations such as the ACP, the American College of Physicians, and the National Medical Association, who are interested in providing comments on such a document. So that's good. So what we would like to propose to the full SACGT is that we, as a next step, post the brochure in the Federal Register, on our Website, and then do a targeted mailing to public advocacy groups, genetic counselors and genetic specialists, and primary care providers, and possibly other professional associations, to get a sense about whether they think this would be useful for them.

The specific questions that we would ask in that sort of small public consultation are is the document useful as a source of general information for the public, and how would you use it? Is the content appropriate? Is it understandable? Is it complete? Is it tone appropriate? We had a lot of discussion about not to make this sound frightening, yet not to make it sound like a sales document as well. Is it culturally appropriate? What modifications would we need to make it more culturally appropriate? Should it be produced in other languages? If so, how should we decide which ones to use?

The specific questions we'll need to ask right now is to whom and how should the brochure be disseminated? For example, when we were first developing it, a lot of the clinicians on our group felt that it would be a very useful brochure to just have in their office, in their waiting room. But should or could the brochure serve as a model for more specific test brochures? So, for example, one way of thinking about this is that it might be a template that specific organizations could perhaps use as a base to then add more specific information about a certain genetic test, like sickle cell or whatever, although that's probably not a good model since there are a lot of educational materials.

We then also asked some questions. One of the things that came up especially from the consumer advocates on our committee was the issue of who really should develop these brochures and how should they be developed in the future, so that's a question. Should this really be an SACGT role? Is it something that we want to keep under our control, or is it something that we just want to make a recommendation that HHS in general should create some similar documents?

I'm going to go back up to that. Now I'd like to stop the presentation and ask for comments on the brochure itself and what directions. I'll leave up the questions or we can go back to any particular questions. Any comments on the brochure?

DR. LEWIS: This is a process suggestion. I'd suggest that before we put the brochure out for public comment, we take care of the readability issue, because most of the literature says that patient education materials should be at around the 6th grade reading level. I think if we want to get comments from the public in terms of its usability, if we're going to a diverse public that's broadly representative, I'd like to see us take care of the reading level issue before we send it out, because otherwise I think we would then need to send it out again. So it seems to me that that is a key piece. I was really pleased with the level and the tone of the content, but I do think that the readability is at least at 10th grade.

DR. KOENIG: Other comments? Does anyone like the final result, particularly those who were interested in our doing this?

PARTICIPANT: Yes.

DR. KOENIG: What about the issues in terms of are the questions that we plan to ask in terms of the public consultation appropriate? Are there any additional questions?

MS. CARR: May I say, they're all the questions, the two slides together.

DR. KOENIG: The two slides, right.

MS. CARR: This is one set of questions we'd be asking the public, and the previous slide?

DR. KOENIG: And the previous slide. You can look at all the questions in your packet.

DR. ZULLO: Will there be anything in it specifically directed at pediatric testing?

DR. KOENIG: No, because the point was to make it generic. It does mention, of course, the broad categories of testing, like prenatal testing, which I guess is some form of pediatric testing, but it doesn't focus on issues of testing children. It, of course, has no information at all about the research, or little about research. Do you think that that's an issue or a problem?

DR. ZULLO: Well, I know that the article in Pediatrics that AAP just put out talked a lot about it, should we be doing it, and I just thought it might be another resource to give people if you could link them to somewhere else. I don't know what the rest of the Committee thinks.

DR. KOENIG: Does anyone want to address the pediatric issue? Ed, what do you think?

DR. McCABE: Well, I think there are a number of issues that relate to pediatrics and the testing of children and the appropriateness, when it's appropriate to test children. Taking a lot of those issues that came out of the committee that were in the recent Pediatrics, I think it would be a challenge to get those down to a 6th grade level. But certainly some of the issues about the basic things about not testing for diseases in which there's no intervention that's useful in childhood, that would be the kind of thing that one might include.

DR. PENCHASZADEH: For all the importance that the issue of testing children has, I think that for this level of goal, I think if you start to add -- of course, there are many things that one may want to add. I think I would personally end it there, because we would not do a good service to the issue of pediatric testing just by adding a single sentence, or even a paragraph.

DR. McCABE: Perhaps if this is to be a model, that would be a next generation that could be considered.

MS. BOLDT: I was just wondering in terms of your targeted mailing, is that a complete list or could we add? I would want to add the state genetic coordinators, state legislators. I mean, I think they should have a chance to review these documents specifically too, because that will be a great way to disseminate that information to their individual states.

DR. KOENIG: Okay, that's the point. This is the point, and I think Sarah is getting all these ideas down, and we'll add to our list. People can certainly make suggestions later.

DR. SHORT: I had to give a talk on the issue of were genetic test results different to an Illinois group of the ACP and ASIM, and I was using the example of the difficulties of informed consent in genetic testing, and it was very clear that they would be very happy to have something that actually illustrated and gave some guidance. It sounded like the couple of people who managed to take a quick look at the brochure felt very comfortable, and even with the concept of it being at a 6th grade level, I think they were concerned about the readability for their patients, but also from the standpoint that this is something that would help facilitate any future discussion about specific genetic testing. That's all I wanted to say.

DR. CHARACHE: Two comments, one pertaining to your question, and then two little thoughts for the brochure. On your last question, who should develop such brochures, I would probably change the word "develop." I think this has had a lot of thought and has a lot of strength, but maybe it should be who should review and disseminate such brochures. But I think it's already had so much thought and so much strength that I'm not sure I would imply that it has to be started over again.

DR. KOENIG: Although I think that was meant to address also the issue of in subsequent brochures in the future, because that was one of the main -- in particular, Sharon Terry, maybe you can speak to that. It's really about the issue of if something is really focused to the public, have we come up with the right process? Was our model too much of a top-down model? Do we need a different sort of model to do this?

MS. DAVIDSON: Well, at the risk of misinterpreting Sharon, my understanding of it was that we're really looking at this brochure and its utility at the point of service, and at that point then it's not the general public. It's somebody who has a real generalized situation and they're looking at a specific test, a specific potential disorder. So we were thinking about the ability of using this more generic brochure, which I think is really excellent, it's really evolved over the period. But using this as a template, then, that could be used, kind of pasted, to create a very specific brochure that would be helpful for somebody at the point of service.

DR. KOENIG: But one of the things that we could do is make a recommendation in our recommendations to the Secretary of how subsequent specific brochures that should be developed for particular tests. Sarah, does that capture, do you think, one of the issues, the issue in terms of future brochures?

DR. CHARACHE: I'm going to suggest, then, that you consider rather than saying "you should develop," but "who should advance and maintain such brochures."

DR. KOENIG: Right.

DR. CHARACHE: Then there are two minor questions, thoughts, that I could tell you later. Every time I read it, I see something else.

DR. KOENIG: Me, too. But we agreed that we weren't going to do wordsmithing on it as the full Committee. So if it's a substantive concern, that's great.

DR. CHARACHE: Well, two are wordsmithing, but under "Limitations of Genetic Testing," you might add the importance of ethnicity. There's nothing in here about that, that a test that's good for one ethnic group is not appropriate for others. That is a concept that becomes important as testers select it.

DR. KOENIG: Okay, we will take that under consideration.

MS. DAVIDSON: Just one more comment or observation about how this might be used to force more specific genetic tests, and that is, again from the consumer perspective, what we're seeing is that there are parallel developments in some cases of genetic testing brochures or informed consent. So part of this question that we generated is that we should just be collecting our resources and being sure that we're not duplicating. So that's where we were coming from.

DR. KOENIG: Great.

DR. MANN: This is just an observation that in newborn screening communities, that some of the lay advocacy organizations, and certainly many of the states, have developed their own similar type of brochures on newborn screening, and certainly as to how this can be used as a template, what is the information that needs to be included and will allow flexibility at the local level to adapt it to their specific needs and to reflect their community needs.

DR. KOENIG: Well taken.

DR. KHOURY: This is a great effort. Thank you for doing it. Just a related observation. I know this process was done with the idea of the use of genetic tests in either a clinical or public health setting. My first question is whether or not there was any differentiation between these two settings, because I never really found that out. The other observation is that many of these processes -- I mean, there is a fine line between research and testing, and especially in the rare disease community, sometimes you use genetic testing to gather additional data on genotype-phenotype correlation and advance the state of research. A lot of groups are developing parallel processes, including what we recently did as a group on the research aspect of things. So I wonder, maybe in the next iteration of this, whether some group can take on -- what you have right now is a one-liner that says what will you do with the residual samples, to expand on that and inform people that maybe we'll want to use your samples for additional research on genotype-phenotype correlation. If you give this right now to people, it might be a bit misleading, because for most conditions you still want to collect data along the way, and you

want to marry a testing protocol with a research protocol. At least that's my reading, because there is rarely enough information, and it is an iterative process, as our friend keeps telling us.

DR. KOENIG: To respond to both of your points, first, we definitely did mean it to be applied to both the public health and the clinical context, so I think that was our intention for the generic brochure, because obviously it includes newborn screening as an example, for example, which I would consider sort of the primary public health intervention. But on the second issue, we're acutely aware of this problem of the complex boundary between research and clinical applications of testing, and that is one of the charges of our group. We specifically were directed by the rest of SACGT to begin with clinical, because that was sort of a black hole and because there was so little guidance in that area. So that, I think, I'm going to turn to that topic now if there are no additional comments on the brochure.

MS. UHLMANN: Hi, this is Wendy Uhlmann. I just wanted to say it was certainly very much a challenge to pull this all together to try to address all different types of genetic testing in one brochure. I hope that it actually can be really perceived as a stop-gap measure at this point in time and that we can go on to develop more brochures that would be specific to predictive genetic testing, for example, or, as others have brought up, to pediatric genetic testing, because I think that would also help in terms of not having a lot of extraneous information all in one brochure.

MS. CARR: I just wanted to ask Muin a question to clarify your point. Are you suggesting that we add something more to this? Because I do think that there was some sense that we didn't want to look as if we were promoting people getting -- you know. So I think that's why it

doesn't speak to that in any greater depth. But if you're suggesting that it should, then we should talk about that.

DR. KHOURY: I'm not sure what I'm suggesting. I'm suggesting that this group has done a marvelous job in this initial phase, and as we move on to the next phases, whether this group or other groups want to tackle it, it's very rare in this current climate that genetic testing will be offered alone in the absence of a research protocol. So somehow those principles might have to be discussed and further elaborated on. I think you've done the task at hand. I was posing this as a question to the group as to what you want to do with it. I mean, I'm not advocating one way or another.

DR. KOENIG: I think your point is well taken, that perhaps one of the questions we should urge consumers to ask is is this part of research. I don't think that's part of the document now. I don't have every word in my head, but that might be useful, just as a flag.

DR. PENCHASZADEH: Just to follow up on Muin, I'm not certain that your statement reflects what is going on today with genetic testing. I think the issue is offering genetic testing to patients without any regard to -- essentially for clinical practice. You might be thinking about the things we've discussed here about predictive testing and the many tests that still don't have a clear clinical utility or clinical validity. But for the most part, in many clinical settings, the general public is confronted with genetic testing for a practical situation and completely outside of the research setting or for any research user, whatever that information will mean.

DR. KHOURY: I guess I'm thinking of the new genetic tests that are likely to come our way in the next 10 years.

DR. KOENIG: Exactly.

DR. CHARACHE: I'm going to agree with Victor. I think there's a lot of testing that's unassociated with research, and this whole concept of saving specimens for advancing research and controls and all the rest of it is so laden, burdened with an awful lot of superstructures. So I probably would not add it in this particular brochure.

MS. CARR: I just wanted to get the Committee's sense of the point Judy made about when we actually commission somebody to work on the readability of the document. I think our rationale in doing it after the public comment process was that we thought we may get comments that require some modification of the brochure, and then we'd have to go back and work on the reading level then again. So I think we had some hope that the public would understand that we had not achieved the right reading level, and I think it was a cost-saving thing.

DR. LEWIS: My only point is that if we're trying to get this at the reading level that will be useable for patients, we're going to exclude an awful lot of people from being able to give us intelligent comments if the brochure is above their reading level. So we should be producing something and sharing something that we think is at the level that people are going to use it. So I hear what you're saying about the cost, but I think that the cost of not doing it may be greater, even if it's not perfect. The cost of not doing it, you're going to exclude a whole lot of people. If our goal is to reach out -- I see Mary shaking her head. I can hear the rattling. But if the goal is to make sure that this is sensitive to a bunch of groups and not just to middle- and upper-class educated folk that are not representative of the population, that was my concern. It was just an

advocacy access issue.

DR. McCABE: I don't know if staff would want to take a shot at that. I used to do things for patient brochures, and the key is making the sentences short, the paragraphs short, and the words short.

DR. KOENIG: Perhaps we can just make a staff effort at it at this point to try to get the readability down. I think that's a good suggestion.

DR. McCABE: You can see if it is possible to do.

DR. KOENIG: Right. Ann, and this is the last comment on this, because the other topic is actually much more difficult in some ways.

MS. BOLDT: I would also like to have the full SACGT Committee make comments on it before it goes out to the public, because I do have some others. I mean, I think a lot of us do, if we could just have a few weeks to do that before you sign off on the public, to consult on.

DR. McCABE: You want to move on?

DR. KOENIG: Do we want to do another modification, though, before we send it out for public comment?

MS. CARR: Ann, can you clarify that? I mean, is it extensive? Just a few words here and

there?

MS. BOLDT: Right.

MS. CARR: Because I think that's certainly doable.

DR. KOENIG: Our last meeting was scheduled for September 12th, so our group sort of got a little bit out of sync in terms of the pace of our work. So I want to make sure that we're producing things as we need to. I'm going to move to our second task. Points to consider in some ways is not the best title for this. What we're really trying to do is figure out how to -- one of our main tasks -- originally in our oversight report, the full SACGT recommended that one of the key issues in genetic testing in the future was going to be to make sure that there was adequate informed consent for particular tests as they moved into clinical practice. So with that as background, what we've been thinking about is a mechanism for accomplishing that. These are the things I'm going to talk about. I'm going to talk about the purpose of what we're doing, the principles behind it, objectives, again audience, test dimensions, characteristics, consent considerations, informed consent models, and then issues that we have come up with in our very extensive series of meetings on this.

So why is informed consent so important for genetic testing? I'll just do a little bit of history. The first bullet point, limitations regarding clinical validity, clinical utility, is basically meant to address our general strategy of the Committee, which is that we don't want the new FDA process to be overly restrictive in terms of allowing tests out on the market, so we actually feel as a principle that we're asking informed consent to do a lot of work out there in the real world

in terms of making sure that tests get used appropriately. It's not going to be dictated by the FDA in terms of when a new test is released, and also tests will be released and have multiple uses. There also is going to be, as I was just saying, a gap between diagnostic and therapeutic capability. That will continue. Information is complex, and there are implications for family members. So the issue of informed consent for genetic testing just has this element of being different than informed consent for other kinds of procedures and tests. Benefits and risks, or we might say the pluses and minuses, which might be a less technical way of saying it, are not well defined and can differ for each individual, and assessments may be based on personal values. So when there are no therapeutic interventions available after a test, it's really the value dimensions that become the most important. Also, in spite of all of our best efforts, in some ways there is still limited patient and provider education available on genetic testing.

So why do we need a points to consider for genetic testing? The informed consent decision-making process can help assure appropriate test use. We're hoping to make sure that somehow in the informed consent process there will be an appropriate consideration of is this test the right thing to do at this point in time. We think it enhances patient participation in the testing process. As we've looked over the issue of what are the current standards for informed consent for clinical use of genetic testing, there are no national standards, and there's quite variable practice. Even in things like in prenatal testing, for example, you might have informed consent for the invasive part of doing an amnio, but not for the genetic testing element of it. So the practices are extremely variable. We think that this provides a framework that tailors the consent process to the nature of genetic tests and patient needs, or that's what we would hope, that we could provide a framework.

The principles that we're working under, the first is that informed consent is necessary, and this is important. We're basically not asking a yes/no question about informed consent. We're beginning with the idea that informed consent is essential in all clinical work. So informed consent is necessary for genetic testing performed in a clinical setting, but the nature of the consent process will vary depending on the characteristics of the test and the implications of the results. There must be good sources of information about tests for patients and consumers to support the consent process.

So our objective really has been to develop a framework for determining the degree of informed consent needed, or you might want to say the level of informed consent or the type or the ideal model of informed consent needed for new genetic tests as they're introduced into clinical practice and public health. So what we've been trying to think through is something that's pragmatic and that facilitates decision making -- and we really mean the word pragmatic; we don't necessarily want to be burdensome in terms of just extra paperwork and extra signatures, those kinds of things -- based on a rational relationship between specific characteristics of genetic testing dimensions and consent practices. From the beginning, we've been looking for some sort of a model where the consent requirements would be modest in clear-cut situations when there really were few risks, for example, but that the informed consent process would be much more robust in situations where it was a very complicated genetic testing setting.

One of the issues we've been dealing with as we've been having a series of meetings about these issues is if we create a process for assigning categories to new genetic tests in terms of what level of informed consent should go with a new test -- a new test comes on the market, what kind of informed consent will we want to see applied in clinical practice with that? Who

really will be the audience for this mechanism that we've been developing? We came up at our last meeting with a whole series of a number of different audiences. Our main goal was to inform and make recommendations to the Secretary of HHS and possibly to FDA as well, because, for example, you might imagine that there would be certain tests where we would want to -- and I'll come back to this -- actually make a recommendation about what kind of informed consent would need to be associated with a new test as it was coming on the market. So policymakers is an important audience, test developers, professional societies, again disease and patient advocacy groups, and providers and consumers. What we've been trying to imagine is a system where we would have one overall framework but then have different versions of this overall framework for assigning informed consent levels that could be used in different situations. So especially in terms of providers and patients and consumers, you don't want to, for example, have a physician in their office go through the same sort of process about what level of informed consent is required as you would have someone in a professional society trying to make a recommendation about genetic testing in general for a specific procedure. So we're hoping to try to target this to particular groups, and I hope that's clear. Please feel free to ask questions if there are some points that don't make sense.

So what are the dimensions of the test itself that may influence the model level of informed consent that we would recommend? Well, obviously, the purpose of the test is important, the characteristics of the test, the disease characteristics, and what we're calling collateral implications, and I'll go through each of those.

The purpose of the test, this is essentially the same sort of material that was in our generic brochure. Is it diagnostic, predictive, presymptomatic, pharmacogenomic, et cetera. We're very

sensitive to the issue that there are certain kinds of tests that don't need the same level of scrutiny as something like a predictive Huntington's test. So, for example, certain kinds of pharmacogenetic tests might not require that same level of scrutiny or oversight or issues in terms of required signatures, et cetera.

So in terms of test characteristics, the key issues that we talk about continually are validity and utility. In terms of disease characteristics, severity, effectiveness of therapeutic interventions, availability and accessibility of treatment are the kinds of characteristics you would sort of put into the pot as you're trying to stir this up and decide that on the other side we want to come up with some ideas about informed consent levels.

Collateral implications. The sorts of issues that are important are psychological and social consequences, potential for stigmatization, family implications, potential for employment and insurance discrimination, and pleiotropic potential of results, which basically means tests that might predict more than one thing. I think that's the best way to think about it.

In terms of test considerations, I want to go through a couple of issues. First, in terms of the purpose, does the purpose of the test influence the consent process? So, for example, you might have the same test that has been approved, but does a prenatal or a predictive test warrant a more in-depth consent process than a diagnostic or therapeutic test? Often it will, so we have to find a way that the model is tied to the purpose of the test rather than just the fact that you're looking for a particular mutation. Then test characteristics. What aspects of the test influence the consent process? For example, if the clinical validity of the test for the patient's population is uncertain, should the consent process be more in-depth than if it is low or high? Disease

characteristics. What aspects of the disease influence the consent process? If it's not treatable, should the consent process be more in-depth than if there are treatments? Collateral implications. What are the non-medical issues that must be considered? If a test has significant personal or familial significance, should the consent process be more in-depth?

Let me now move on. Traditionally, people who have thought about informed consent, it includes four dimensions. There's a dimension of disclosure, comprehension, the decisional capacity of the individual, as well as voluntariness. That gets translated into four specific practices. These are information disclosure or the process of actually disclosing information. A few people are nodding. Ann is nodding. This is good. It sounds like this makes sense. Assessment of comprehension. You need to make sure that in the consent process, the person understands what you're talking about. Then the third area is what actually happens. We started off by calling it decision-making process, but then we added this idea of continuum, because in some situations we don't want to presuppose the idea that there's necessarily going to be a very big-ticket decision process. In some situations, certain tests, like newborn screening, it may be more a routine recommendation, as opposed to an elaborate process. Finally, there's usually some element of documenting consent. Again, remember that we're talking about informed consent in the clinical context exclusively, not in the research context at this point.

So in terms of information disclosure, the key issues are what information is necessary, how should the information be presented -- and we've had some idea earlier of some of the potential for technology in terms of making all of this different kind of information and presentation better in the future perhaps for potential patients, as well as for clinicians -- are there are issues of assessment of comprehension. Is it necessary to assess comprehension, or is it so routine you

don't need to? And what if the patient really doesn't understand? What do you do?

Finally, or third, the decision-making process and continuum. This has been the issue we've spoken about that we've had the most debate about. What we have come up with is a sense that there's sort of a dimension of this, that there might be certain kinds of tests where, if you think of this almost as a scalar kind of quality, at one extreme you have an idea that a provider might make a very directive recommendation about a test because the benefits are very clear-cut and the risks are low. In the middle you have a model of shared decision making with clinician guidance. We didn't want to have a model that didn't have some element of clinician guidance because we think that's appropriate. Then finally at the other extreme, you might have shared decision making governed more by personal choice or values. So in that situation you would have a less directive approach because the issues associated with taking a test are perhaps more to be governed by personal choice and values.

Then there's the issue of documentation, and we've talked about some of these things. But when in clinical care do you want a signature to be necessary? We were pretty clear in terms of our principles at the beginning that we didn't want to require signatures so often that they would lose their meaning. We wanted to reserve it for when it was a really meaningful event. When should a check-off be required; for example, in terms of a laboratory not doing a test unless they have a check-off? You also might ask what really does the signature connote? Is it comprehension, voluntariness? In some ways, it can be both.

Wendy Uhlmann actually helped think through this slide, which I think is useful. This isn't a complete view of everything that we're doing, but this is an attempt to summarize what I was

just talking about in terms of the consent continuum in clinical practice. You can see at your right, corresponding to a minimal level of consent would be the idea that the clinician might perhaps be somewhat directive or perhaps feel comfortable making a recommendation, and there might be a low degree of personal choice. A newborn screening was one example we came to at one extreme. Then at the other extreme, in the non-directive situation, we have a high degree of personal choice; for example, in the situation of a predictive genetic test with no treatment. That's an idea of the consent.

I should also say that we've worked very hard to try to think through all the background steps of this, and we basically have the same set of problems in dealing with this as the full SACGT did in terms of coming up with a classification mechanism for genetic tests. So we re-created a lot of the discussions. But we had at the moment in terms of how do you think through classifying tests in terms of level of scrutiny required, it's fundamentally the same tasks that we've been dealing with. It's a very, very difficult task.

This is fundamentally one of the first things we came up with, and I'll have to talk you through this and explain it. Across the top axis here -- I, II, III, IV -- these are the different possible models of informed consent in clinical genetic testing. We're not necessarily calling them levels, but in a way there is a sense of intensity that this is the highest level of procedure in terms of documentation, and this would be the lowest. So across the top is the different kinds of consent models, and across this dimension are the four elements of consent that we talked about or the four kinds of practices that go along with informed consent, the information disclosure piece, the assessment of comprehension piece, the decision-making process and continuum, what actually goes on there, and then the whole issue of documentation.

We came up with the idea of four levels because it seemed that, again, because of the issue of wanting to -- if we had just two or three, it seemed that we would be too often requiring a high level of documentation and, for example, signatures, and that would then become meaningless. I'm not exactly sure about the best way to talk this through. One might, for example, if you think about this in terms of an example of newborn screening or a routine diagnostic test -- diagnostic probably isn't a good example, but the information disclosure might be very basic and routine, and the consent required of the individual being tested could just be a verbal assent, basically, like in a situation of newborn screening. In terms of the decision-making continuum and this issue of directiveness, direct recommendations versus more values focused, this is the dimension where there would be a strong provider recommendation, and there might not necessarily be a particular requirement that there be documentation at any level.

But let's take the other extreme so you can perhaps see the extremes first, and then we can work back into the different levels. For IV, this would be the highest level of very complex information to explain. So we call this an expanded model where perhaps you would want to give the person information in writing, as well as in some kind of clinical interaction. Then also the other issue in informed consent at a theoretical level is that there are two models in the law in terms of how you provide information in an informed consent. One is do you just need to give information that the average person would understand, or do you actually need to provide information tailored to a particular individual? We think that there might be some situations where you have to tailor the information disclosure to the needs of a particular patient or family, and the focus of some of the information disclosure might be on these values and choice issues, as well as the clinical issues. Something like Huntington's and possibly certain kinds of breast cancer, genetic testing might fall in this model. Then again, the assessment of comprehension

would perhaps be individually tailored, and there might even be situations where you would want to require some kind of a test or an informal test. For example, in a counseling setting, that's one of the main things the counselors do, to actually make sure that people understand what you're telling them. The decision-making process piece would be, again, based on this notion that choice, as opposed to directiveness, on the part of the provider, would be highlighted, and possibly this might be a situation at the highest level of scrutiny where you actually would recommend that the process of consent be phased, as opposed to just a one-time encounter. That's the case with certain kinds of testing now. Is that built into the Huntington's protocol, that there's a phased decision making? Then finally, in terms of documentation, this should be documented somehow in the record, that there be signed consent, and that possibly there would actually be a checkbox on the laboratory recommendation. So this would be the highest level of scrutiny so that the test would not actually be run at the lab unless there was documentation on the part of the person ordering it that the informed consent process had actually been done appropriately.

Then you can see levels II and III are meant to be in some ways intermediate. I think I don't have time to go through this. We can come back to this if people have specific questions. Let me move to the questions, and then we can come back. But you can see that on all these dimensions -- for example, on II, it would just be a simple documentation, if it was a clinical encounter, in the person's medical record, and the only situation where there would actually be a requirement for signed informed consent would be at the highest level. Obviously, we would want a very good process in all of these levels, but the documentation of signed consent would only be at the highest level.

So basically, what we've been trying to do is to fill in this black box in the middle in terms of a classification methodology. So imagining a new test coming on the market, or we could think about doing this for all old tests too, but that's fairly daunting, what happens and who should do it in terms of assignment of a test to a particular consent model, assuming that a four-part model like I just presented would be some version of what eventually we would recommend?

So the questions that I want to ask the Committee to address today are, first, I showed you a slide of the audiences in terms of the Secretary for HHS and professional organizations, so are these the right audiences for this document that really fills in that black box? Should the report be targeted to the FDA as well as professionals and consumers? Second, does the SACGT wish to recommend that FDA mandate types of consent for certain tests or types of information that test developers must provide? Do we want to make recommendations about process? Should we recommend that deemed organizations be employed? For example, could we recommend to the Secretary that some of this work about the level of consent for a particular kind of test might be done by a professional association, for example, as opposed to throwing it all on FDA? Then what form of consumer involvement should we have at this point in terms of understanding the genetic tests?

We've talked a lot, and Ginette Michaud has been very helpful from FDA in terms of helping us think this through. For those of you who haven't been part of that conversation, at the moment, on the device side, there really are no precedents, or there is possibly one precedent for a product being released with a requirement that informed consent be done. It sort of comes as part of the package insert. So basically what we've been encouraged to do is to simply think outside of the box in terms of what would be the ideal situation, and then to make that

recommendation and we'll see what the issues are. But it may be complicated because, for those of you that know the FDA, it gets into the issue of would this be considered, for example, too much infringement on the practice of medicine if you actually made specific suggestions about informed consent?

MS. BARR: Ed, can I say something? I just want to say that this was a topic of a lot of discussion, and even some confusion, I would say, on our part as we tackled it. But where I come down is a slightly different approach, which is that FDA does require labels with drugs and devices, and there are review panels that make recommendations to FDA. So it seemed to me that part of what a panel review would do would be to look at informed consent information that should be included in a very readable form, an appropriate readable form with the approval of the test, and that that then would be available to providers. We have to find a way to make it available to providers and consumers. But it's building on the notion of the labeling to get the appropriate information attached to the appropriate test. I recognize that that only solves the problem once and does not address off-label use, but it is a way to move forward.

DR. KOENIG: Thanks, Pat. That's a helpful comment. So, just to conclude, this is the last slide I think. We've been working very hard, but we've discovered that this is an incredibly complex conceptual task. Basically, what we're doing to try to take all those different dimensions of testing is taking multiple dimensions, some of which are -- it's like creating this model in multi-dimensional space to see how all these things interact. It's been very challenging.

So have we appropriately identified the different models or levels of intensity for informed consent for genetic testing in clinical practice? Back to those four models I showed you. And

what approach should the work group take to developing a classification process to determine the appropriate model of consent for particular tests; i.e., what's inside the black box that I showed? We've worked through two different ways. One is a more narrative kind of thought in terms of that we wouldn't actually try to have a specific formula of how to get from point A to point B, but that rather -- and this gets back to Pat's issue. For example, a test developer might have to work through a list of points to consider, and then actually when a new test is presented to FDA for approval, they would then recommend a level of informed consent to be put in the package insert associated with that test, which I think is what Pat was just describing. A second idea which we've played with and we actually developed about four or six different models of this -- I mean, we've just spent an enormous amount of time on it -- would be a more formal decision tree that would be used by either regulatory groups. We've been having some disagreements -- not really disagreements, but we've just been struggling with the issue of which is the best approach at this point in time in terms of figuring out. So the issue is what kind of an approach, and to FDA and other groups, what sort of approach, a points to consider approach versus a more decision tree approach.

So let me go back to the questions and open the floor up for discussion. I realize that this is very complicated and we really have been struggling. We have 15 minutes or so to talk about it.

DR. BOUGHMAN: I still have a major disconnect here, that vis-a-vis Pat Barr's comment on labeling and the test going to market and the FDA process. If you take it through that route, that makes sense to the point that you understand that the labeling and the purchaser of what is being marketed is the laboratory. My question is how does that relate to this consent process, which in fact occurs at the point of ordering the test? So far you've only said that there was a check box

that informed consent had been obtained in the laboratory. That was the only connection between those two. But most of these points to consider, the real challenges, the complexities are in fact disconnected from the marketing performance.

DR. KOENIG: Right, and we've struggled with that issue of not wanting to make the lab do more than they can do, because that doesn't make any sense. Pat is a member of our committee. Do you want to address that?

DR. CHARACHE: Yes. Theoretically, there is not a disconnect, but it would have to be made clear that there's not, and I think it would be burdensome to the laboratory. The reason there's not a disconnect is because under CLIA, the laboratory has to establish their criteria for declining to do a test when a test is not acceptable. So if the test is, in fact, not acceptable unless you have informed consent, it is theoretically the laboratory's job to notify in whatever their dissemination is of what tests are available to indicate what the requirements are to obtain that test. So between CLIA and the FDA, theoretically it would be there. It would be a difficult thing for the laboratory, particularly a reference lab like LabCorp or Quest, to be sure that all the doctors knew how to do that. But every lab who first gets the specimen that they're then going to send on to LabCorp or Quest would have the responsibility to get back to their users and tell them that it's required to obtain this test. So theoretically it could work. In fact, it would be not easy to achieve.

DR. BOUGHMAN: And it may indeed be ideal under that theoretical scenario. I'm actually looking at it more from, if you will, even the bigger picture that our real goal here is protection of the patient or the consumer. From the consumer's point of view, not only from the laboratory's

point of view or from the physician training point of view, are we making great expectations. But it seems to me that we are not facilitating protection of the consumer, except by making this very, very complicated. But I realize how dense an issue it is.

DR. KOENIG: Let's get all the comments out. Sarah, can you keep track in terms of who wants to speak?

DR. LEWIS: I guess the disconnect I'm having is the disconnect at the level of the individual. It seems to me that the model predisposes that we know what individual values are. I mean, I'm looking at the same thing, that there might be the exact same scenario that might have a totally different meaning for two different individuals. So I think that by pre-imposing a top-down model, we might be putting something into minimal consent that for a particular family is a big deal, and we might be putting something into maximum consent that for a family who has been dealing with this problem for three or four generations it's now become pretty routine and they really do understand the implications. So I worry a little bit about a model where those of us who are "experts" are, in a somewhat paternalistic way, deciding what the level of meaning or the level of risk is for a family, because having dealt with people where something that seems pretty routine is a really big deal for some people, and for other people something that seems really complex to us is pretty routine because they're highly sophisticated consumers. So I just want to make sure that as we put a model together, it seems to me that it's sort of like being pregnant. It's hard to be a little bit pregnant. It's hard to be just a little bit informed. So I guess what I want to make sure is that we've got some kind of a model that takes the variation of meaning for an individual family into consent, as opposed to saying there can be a fair amount of provider direction in something that's pretty routine, because you may think it's pretty routine, but

your consumer may not.

DR. McCABE: Do you want to answer that?

DR. KOENIG: Well, I think it's an important question. Would you suggest, though, to use the Huntington's example, that you would want -- if you're coming up with a model that regulatory agencies and other groups should use in terms of setting out a set of principles, there would be nothing that wouldn't make it possible for you to do a higher level of consent with someone who had some concerns even though it was technically considered routine.

DR. LEWIS: I guess I'm much more worried about the lower level of consent than I am about the higher level of consent. In my own practice, for example, I see women who have "routine" triple screening early in pregnancy with minimal consent because it's the standard of care, and here are women who don't even realize they're starting down a slippery slope, and had they known what the outcome could be, they may never have consented. But because it was a pretty routine test and there was a minimal degree of providers presuming it was good. I guess I'm erring on the side more of -- I'm more concerned about the times that we consider something routine than the times when we consider something extraordinary.

DR. KOENIG: But we weren't making an argument about routine versus non-routine, exactly the opposite, because in all of our discussions, actually, the tests that are prenatal, by definition, are going to move up into the higher levels.

DR. LEWIS: Well, even newborn screening is an example. I mean, somebody who started

down a slippery slope didn't even know that they were starting down the slippery slope. So I'm much more worried about that side. I know it's a really dense issue. I'm just putting that on the table to make sure that we don't get too paternalistic.

MS. CARR: Could I just speak to that? Because I think there have been conversations about that in the work group, and I think one of the struggles has been not locking things into place and being too formulaic. In one of the decision trees we developed, we actually had a step in it that sort of recognized the concept that the recommendation that came out of it would be a minimal level of consent. If there were issues with the consumer or patient in front of the provider, then they would have to sort of do the higher level of consent. So it had built in it some flexibility, but I think this could be a principle that we adopt, that it has to be flexible and it has to be tailored in all cases to the needs of the patient.

DR. LEWIS: It's just something I worry about a whole lot.

DR. KOENIG: We worried about it enormously, but we really also, though, have been trying to apply this principle, especially in terms of what is low and high -- we're concerned that anything that's too cumbersome is just never going to be workable. So that's the other side of this. We've had a lot of discussions about the issue of paternalism and directiveness but still want to reserve the idea that there might be some things -- and the example that we used in our last discussion was at the height of the anthrax. You'd want someone to be pretty directive, like four weeks ago, of testing a postal worker for anthrax. That wouldn't be a huge values discussion about whether it was the right thing for them to do at that point. I mean, you would just do it. So there are certain things where directiveness is going to be appropriate and even if it's

paternalistic, it's not a problem.

DR. KHOURY: Barbara, can you go back to that slide with the four models?

DR. KOENIG: Sure.

DR. KHOURY: I think part of the disconnect here in tackling a complex subject postprandially is the amount of oxygen in our brains.

DR. KOENIG: Right, we're all tired.

DR. KHOURY: I think this should be a morning conversation rather than an afternoon conversation. However, I want to try to step back a little bit, since I was not part of the discussion here. I think what the group is trying to do here in the transition of, let's say, genetic tests from research to practice and this amount of oversight, we're trying to protect the public, trying to inform the public, and we're trying to collect more data as these tests make it out. So if we step back to our meetings three or four years ago, when we started trying to put together a classification scheme for genetic tests as far as high versus low scrutiny, and capitalizing on that experience, we hit brick walls and dead-end streets, et cetera. Just looking at this, and maybe you can guide us through it, I don't know whether four groups or four different models is necessarily a better thing than a binary classification. I'm not sure that a binary classification is at all needed. So I guess what I'm trying to say here is I think we should try to avoid going down blind alleys as we tried to do with the previous aborted effort with trying to do a classification scheme. Maybe you can walk us through this a bit more, because I think there is

some stuff here. In conclusion, what I want to say is that you have already pointed out the points to consider. I think that the group has done a wonderful job in outlining the issues in the informed consent process. Whether you want to take it to the next level and tell FDA what to do or tell HHS what to do, I'm not entirely sure. But maybe you can give us more guidance.

DR. KOENIG: I can. I'll say briefly something about this side of it, and then I'd like to ask also other members of the working group who want to comment on this to try to perhaps clarify a little more if they could too. We basically realized you could start from either side on this. You could either start sort of pragmatically and empirically with what really might work out there in the world in terms of what are the different levels of informed consent practiced that would be feasible to suggest to implement. We know what exists now. We have an example from research. There's the idea that there's an informed consent form that gets signed. We know that that can just become a meaningless routine, and so we didn't want that. There's the example of just information brochures in which newborn screening or MSAFP or triple marker screening is a good example, where it probably shouldn't just be done in a routine way. There should be some consent associated with it. There isn't, because there hasn't been any uniform practice about informed consent for genetics. That's exactly the problem.

So you could start on that one side by looking at what pragmatically might be different levels, and then imagining what the future is going to bring in terms of preventive testing for risk susceptibility, pharmacogenetics, all those kinds of things, as well as single-gene disorders. So that's where we started. Then on the other hand you could start with what we did before, the classification. So which test will you want to then end up at different levels of scrutiny? So we basically have been working from both ends, and then also as well as in the middle in terms of thinking about who should be the group, how should we then establish a process to figure out the

right level of consent for a particular test.

Does that help conceptually? We sort of started working on both ends and then also in the middle. Then again, Ben Wilfond has done a lot of background work on this.

Judy was concerned about this whole issue of the decision-making continuum. This dimension here was really what I tried to explain in that we had this idea that there were going to be some tests, and it's really a continuous variable if you think of it that way, some tests where it's going to be driven by a directive recommendation because it's of high utility, and some where there is not less clinical utility, and so therefore it's going to be more a matter of personal choice and values. So each one of these is meant to have one of those dimensions associated with it, too.

DR. KHOURY: Are there examples that fit neatly in the box?

DR. KOENIG: Examples. Well, that's one of the things that we did with this, was to try and then go back to particular examples and use a gestalt to see if they work. I think we were thinking that some pharmacogenetic tests would be in the second column, in that you wouldn't necessarily need to have signed informed consent, you wouldn't require laboratory sign-off, that you would want a decision-making process that would involve a verbal discussion with a provider, and that they would then provide some guidance about that; that there might be verbal consent, that it would be a totally verbal consent process as opposed to a requirement for a signature, as I said; and that it would be expanded, meaning that the information disclosure would be really focused primarily on the clinical domain as opposed to a complicated values domain; whereas in prenatal testing, it's always going to have a values component. So prenatal testing would probably always end up in III, in how we're imagining it, and then some of the very

predictive late-onset diseases would probably end up in IV. Does that help? We've really struggled with this.

MS. CARR: I'm sorry to step in here, but I just want to make one point about this. What you see in those boxes, this really is a straw man. I don't think the working group is in any --

DR. KOENIG: Right, we're not tied to this.

MS. CARR: Right, at all, in terms of what's in those boxes. I think what we'd like the full Committee to focus on is the concept of the models and the intensity growing and so on, and the idea of outlining these levels of models, but not what they look like right now.

DR. KOENIG: And give us feedback on what is a reasonable way of recommending oversight for particular tests.

DR. McCABE: I'll ask that comments be very brief or we won't even stay on the schedule and we won't have time for the education. So please be brief or there will be no break.

MS. BOLDT: This really goes back to an issue I think Joann brought up about the provider-patient relationship. One of our overarching principles that we put forth was genetic education and counseling would be tied to the level of scrutiny. So I guess I would like to see -- I mean, informed consent and education counseling go hand in hand.

DR. KOENIG: Precisely.

MS. BOLDT: I think it's this wording, but I'd like to get that wording in there.

DR. KOENIG: Well, the tailored, that is basically a gloss for counseling, some kind of counseling is required, that it requires a process.

MS. BOLDT: I just want to see more.

DR. KOENIG: That was implicit. We should have made it explicit.

DR. CHARACHE: One strength, two cautions. The strength is that this is very powerful in communicating that there's a gradient, and the gradient should be skewed towards the left because it should be the least burdensome. So we should reserve what is very deliberate, and particularly where the laboratory has to check the boxes, to those things in which it's really warranted. I think that's the strength of this. It emphasizes that.

Two cautions. Number one is that as FDA decides on their labeling and what have you, it's my understanding that by law they can only consider the use of the test that has been put forth by the sponsor of the test, by the manufacturer. So they're always going to come in with the fact that it's diagnostic. They're never going to come in with the fact that it's predictive. Part of working this through is going to have to address likely uses of the test, and then we're going to have to figure out how to make that legal.

The last comment has to do with the fact that there are other groups that are also looking at

informed consent. Joe Boone was pointing this out to me earlier today, that it may be helpful to get some of those groups together, just as we were talking this morning about getting groups together with common interests, to take advantage of each other's thinking, and also to communicate some of this elegant work.

MS. BEARDSLEY: I was just going to go back to Pat Barr's suggestion and the disconnect. I was going to say that I was going to go back to Pat Barr's suggestion and Joann's disconnect, because I agree that there's a disconnect here, but I can't see that we're ever going to be able to be telling providers and counselors and nurses what to do, but I think the disconnect may be useful because I do think there's some value in having test developers have to be thinking about this when they develop a test and having to be giving it to FDA. I know FDA may say we don't have the expertise for this, but maybe they could develop it. Even if there's a disconnect as to whether people have to use it, it might be valuable to have the test developers have to develop it.

DR. ZULLO: I think this is great. I think the grading approach is very nice. You're trying to get a very difficult task into something we can work with. My concern echoes Judy's in having some flexibility, which sounds like you were trying to work that in. But if FDA is to choose which scheme each test has to be in, how will we maintain that flexibility? That's my concern. Once they decide which scheme it has to fall in.

DR. KOENIG: Well, it will always just be a recommendation for clinical practice, and then hopefully if professional associations become involved in doing guidelines, at the highest level at the right, which we want to reserve for very rare occasions, then presumably there would be the usual sorts of legal requirements if you weren't adhering to the standards of practice in your profession. But other than that, if ACOG makes a recommendation that this level of consent is

required when you're doing MSAFP or triple marker screening, and then if you don't do that, then that can be problematic. It's a good practice issue.

MR. HILLBACK: I go back to the principles, which is about 15 slides ago, and think the principles make a lot of sense, that informed consent is required. We all agree with that. I don't understand why we're trying to codify what I think is an educational process. The people that are providing this informed consent I thought were physicians and counselors and nurses, people that are there talking to the patient. They need to understand how to do this. But to try to codify it and create a whole set of rules, a set of boxes, it's pick one from column 3, one from column 2, one from column 4. At this point in the life of this test, unfortunately, Muin, this is iterative. I just think we're trying to codify something that isn't codifiable. What we really ought to be doing with this, because there's a lot of good thinking here, is this ought to be the education process going back to -- and you just said it. It's ACOG or whatever group of practitioners who are using that test in their practice, and say, well, how do I fit this into my practice, and therefore what informed consent do I need to give them? I'm not sure it's up to the genetics community to define all this. Whether that's the lab, which I don't think can, or any other part of the genetics community. But I don't think this is the right outcome.

DR. KOENIG: Well, remember that this isn't what would go to the clinician. This process would be something that a professional group and a consumer group would go through to think through what might be an ideal recommendation about informed consent for this test, and then there would have to be another whole educational piece for the community of people who are actually doing the informed consent.

MR. HILLBACK: But you make it sound like that's some formal process. Is it a formal process?

DR. KOENIG: Well, that's one of the things that we're talking about recommending.

MR. HILLBACK: In the real world?

DR. KOENIG: Yes.

MR. HILLBACK: In the changing world that happens that we really live in? I don't know how you make it a formal process.

MS. CARR: I was just thinking, Elliott, that what it could be is a tool that professional societies make use of in thinking about what consent should be like for a particular test or tests that are important in their practice. So I think it could be used that way. But the question of whether we make a recommendation about FDA using it as a tool I think is a really critical point, and that's why Barbara is raising it as an issue.

MR. HILLBACK: I guess my point is I think it's a great thought process to get practitioners to go through to think about what do I have to say in each case, and it's going to change. It's going to change for lots of reasons. That's great. To put it into a regulatory process, you start regulating the practitioner as well as the lab, and I'm not sure that we're ready to do that.

DR. KOENIG: The problem is that we made a general recommendation about the need for

enforcing informed consent for certain categories of tests that require high scrutiny. So we're struggling with trying to find a way of doing that in a flexible way. It's a very hard problem.

DR. PENCHASZADEH: I think that the reality is really very complex. But if you think about it, it all boils down to what happens between the health provider and the patient in the office, what will happen there. I would agree with some of the speakers who preceded me, that I think this is great to show anyone who wants to look into this, and that the reality is complex, that there is a gradient, but I would agree with Elliott that it's almost impossible to categorize any particular test in theory in any box, because as Judy said earlier, a particular test in a given setting may require a higher degree of informed consent than others, and so on and so forth. So it all eventually boils down, I think, into standards of practice and into the clinical judgment of the health provider. I would not get away with this. This type of process is useful, but I think that probably one should focus more on issues of, for instance, what is really needed according to the different types of purposes of tests. But in a diagnostic test, the type of information needed is this and that, and in a predictive test you have to consider this and that and that, so on and so forth. But the bottom line is the provider, at the end of the session with the patient, should be confident that he or she gave the patient all the information that the patient needed, and from the other end as well. The patient should leave the office having all his or her questions answered. I realize the complexity of enforcing. The enforcement issue is still the one that I cannot see clearly in the real practice.

DR. McCABE: Pat and Elliott, very briefly, because we're beginning to encroach upon the public comment time.

DR. CHARACHE: I think it's critical to realize that unless there is some type of check, and the only way you can do it is to have this checkmark on the requisition, that the laboratory has to be sure that a consent has been obtained at whatever level is considered necessary, unless that's there, it won't happen. I think it's very difficult to over-state the lack of knowledge of those who ordered these tests, and we actually do this for our colon cancer test. We decline to do it if it's not the right population. The number that we reject is high, and it's because the patient wants it done and the physician therefore orders it, even though it's going to have a false positive. So I think it's critical that we find a non-burdensome way of achieving this goal.

MR. HILLBACK: I was just going to ask, did the combination of ACOG and the American College do this on the CF test that they just made all the announcements and pro-announcements about CF screening? Did they go and take these steps?

DR. McCABE: I don't recall that it was a major part of that.

MR. HILLBACK: I don't remember. I should, but I don't. I'm just asking about it.

DR. PENCHASZADEH: The statement does state that information and counseling --

MR. HILLBACK: -- should be done, but it doesn't go through and codify it, even for their members, which would have been a great opportunity to put it out to all the members of those organizations.

DR. PENCHASZADEH: All labs are required I think nationwide, at least in New York, to

have a statement putting in the requisition that the patient was informed and agreed to the test. But that is one of the easiest things to get routinized in the practice of medicine.

DR. McCABE: Barbara, I hope that this discussion has been helpful and that you can take some of these issues back to your committee.

DR. KOENIG: Can I just get one sense, though, in just 30 seconds? The issue of do we want to move toward just suggesting that certain tests should only be released to the market with a labeling requirement that informed consent be done. Is that a principle that we would want for certain very rare tests, or not?

DR. McCABE: I think it's one of those things that sounds good, but the implementation is the issue. So I think it's beyond the discussion that we can have in 30 seconds here.

DR. KOENIG: Thanks. Thank you very much. This is helpful.

DR. McCABE: Thanks. Thank you very much. We're now going to move on to the public comment. We have two individuals who wish to provide public comment. The first is Russ Enns from Vysis, who wishes to make a brief comment.

PARTICIPANT: He's not here at the moment.

DR. McCABE: Let's go with Cecil Bykerk, then. Mr. Bykerk has been a member of the Access Work Group and has been very active in that arena. He's here representing Mutual of

Omaha today with a comment to us. Mr. Bykerk, please.

MR. BYKERK: I appreciate the opportunity to come and present a few thoughts to you. I know that later on in the session you're going to hear from some Hill staffers on proposed legislation that is sitting in Congress both on the Senate and House side. I wanted to give some thoughts to this group either before or after. In this case it's before. As they make their presentations, you can observe some of the things that I've tried to bring out in my discussion here. The handouts that you have are two items: one is a copy of the slides that I going to use but that I'm going to cut through and jump ahead on some of them, and then the second thing is a four-page, somewhat more technical sum-up of the language. I'm going to jump over the insurance slides on the assumption that, given the time, I'll go by those.

I want to talk just a second about current practices and laws. I'm here focused more on the privacy issues. Each state has privacy regulations and fair trade practice laws. I know there's a lot of concern about insurers keeping information, but historically insurers have had an excellent track record in handling personal information. There are currently Federal privacy requirements already in place, and I'll come back to that at the end here.

HIPAA provides two things with respect to genetic information. First, it prevents group coverage from using genetic information in issuing, pricing, and renewing coverage; and HIPAA also provides for guaranteed renewability of individual major medical coverage in general. That's not specifically genetically related, but it's important because one of the issues that continues to come up and part of the momentum for the legislation is concern that people are going to lose their health insurance coverage if they have a genetic test or some other item like

that. Currently, there's no way that we can cancel them for that or for any other health reason, unless we get out of the business.

Areas of concern. We feel like the definitions are very broad. We're concerned about unintended consequences. We're very concerned about the destruction of the ability to underwrite even using our current tools, and we're focused here on our current tools, not future tools. We constantly are and have over the last 10 years been faced with balancing access with affordability, and that comes into play very importantly in the issue of underwriting. In the end, the concern is that the result will be even higher costs and more uninsured.

I'll talk about the three primary pieces of legislation, actually the first two, Senate Bill 318, sponsored by Senator Daschle, and a companion bill, H.R. 602, sponsored by Representative Louise Slaughter, and then the Snowe-Frist Senate Bill 382, and then there is an Ensign amendment, but I won't spend that much time on that. In the Daschle bill and Slaughter bill, if you will, there are two definitions. There's a definition for genetic test; there's also a definition for protected genetic information. Genetic test includes in the definition analysis of proteins, metabolites, and mutations, in addition to RNA and DNA and so forth. Our concern here is that that definition basically covers any routine medical exam that we could use today. So that's the concern here.

We understand why they were drafted this broadly, so that things like BRCA1 and BRCA2 get included. We understand that, but we're also concerned about the impact that it will have on our ability to underwrite. I might come back and say again that we're focused here on the individual major medical market. Group coverage can't do this anyway. The individual market is very

small, and it's also very fragile.

Also, 318 protects inadvertent discovery of genetic information, and all that says is if we happen to cross something, we aren't going to get in trouble, but we still can't use it. We understand that, and we need to protect it and so forth.

Now we get into the definition of protected genetic information. This provides for exceptions. This is the safe harbor, in effect. It provides exceptions for chemical, blood and urine analysis, but then it says unless the analyses are genetic tests. This circularity loops you back up to the definition of genetic test, and our concern is that the overly broad definition of genetic test takes away the safe harbor. So there was a clear attempt to provide a safe harbor for current underwriting practices, but the current language does not do that. In another bill, Snowe-Frist, again the initial definitions of genetic test and information are similarly broad. However, there are clear exceptions that seem to be provided, and the safe harbor allows for current underwriting tools. We still have some concerns here with the overly broad definitions, but we feel like this is a reasonable balance among all parties. Finally, the Ensign amendment, which was involved with the patient bill of rights, is similar to Snowe-Frist, but there is again some circularity.

Why is this all important? Looking ahead, there's going to be an inevitable extension to other forms of insurance in which the one-sided knowledge of genetic information is more important: life insurance, long-term care, the first part of the overheads talk about, and it's important as we craft legislation to think about what the legislation is attempting to do. It will attempt to do two things. It will attempt to provide real protection and eliminate clearly certain things that cannot

be looked at. But the second element of it, it wants to deal with a perception. It wants to deal with a perception so that people are not inhibited to go get genetic tests and get treatment or change their lifestyles or whatever they need to do to try and react to that. So the question is will any law prevent the concerns or the perceptions and the fears that are being reported today? What can we do to solve the problem? I just throw that out there, because we can pass the legislation, we can pass it the way it is now in the Daschle bill, but in the end, when that's all done, will the public believe that it's still okay to get a genetic test? HIPAA provides for insurers not being able to cancel, and yet there is still the perception out there that we're doing that.

The next thing I want to just throw out, and I'll finish up here in just a second, is what the dividing line is. Is someone with a given genetic flaw healthy? Down the road this will become a very difficult issue, something maybe that all of you will try to deal with, but when is it that someone is considered unhealthy? Does it happen at the moment that they're born?

So to sum it up, we suggest or I suggest any possible legislation regarding major medical should have processes and standards for protecting the confidentiality of genetic information, but it should be consistent with the privacy requirements that are already there. We would suggest a potentially narrower definition than is there now. We feel that there should be some safe harbor that would clearly define what is not a genetic test. We are comfortable with legislation that would prohibit health insurers from requiring an applicant to take a genetic test. Perhaps that will give some comfort. We are also comfortable with some limitations on the use of genetic information, again in an attempt to attack the perception that people have. In any case, we must take extreme care to prevent unintended consequences now and in the future. We're in a very dynamic area, evolving very quickly. The legislation that gets passed will be locked in place

today. The science will change tomorrow and a year from now and five years from now, and you have to think about any legislation in that context. Thank you very much.

DR. McCABE: Thank you very much, Mr. Bykerk, and thank you also for the work you've done to help this Committee.

Let's move on. The next is Russ Enns, who will make a very brief comment. Russ is from Vysis.

DR. ENNS: Thank you. The comment I want to make is on the consent form in the previous presentation. One thing we need to consider is well controlled, prospective studies, like in solid tumor cancer studies where you have excess storage specimens that are preserved as formal and fixed paraffin-embedded tissues, to consider the prospect that the tumor markers or genes that we are evaluating today may not be sufficient, and we may find newer and better markers tomorrow; the ability to have access for translational research to these well controlled studies and specimens from many patients who may be deceased. It's very difficult to get consent and follow-up in those circumstances. So it's just something to consider to try to make these valuable national treasures available for further research. Thanks.

DR. McCABE: Thank you, Russ. Maybe, Dr. Zullo, I don't know if you'd like to comment on this. My understanding is that informed consent is very different once an individual is deceased compared to consent for living individuals. Do you want to comment on that, Susan?

DR. ZULLO: I will comment on it, and it is true what you're saying, once someone is deceased, but this is a hot issue and I don't know if Kathy has any information on it either. But I know that

they're rescheduling with Dr. Carome in our office a meeting with some other folks to discuss this issue exactly on tissue banking.

DR. McCABE: So perhaps in your role as liaison, you could take this issue back and note that it was raised here.

DR. ZULLO: Definitely.

DR. McCABE: And perhaps get clarification from Russ.

DR. ZULLO: I will do that.

DR. McCABE: Thank you very much.

(Recess.)

DR. McCABE: Okay, let's go ahead and get started. Given the momentous changes that have taken place in the last several months, I think we're all aware that the Congressional and governmental priorities have shifted, and understandably so. Yet we believe that the enactment of Federal protections against the misuse of genetic information remains an important public information and certainly a high priority for SACGT. We've urged the Secretary of Health and Human Services to work toward the achievement of this important goal, and we continue to monitor developments closely and do our part to keep the issue in the public eye. To this end, we are extremely pleased that two key Congressional staffers, Ms. Kim Monk and Ms. Cynthia Pellegrini, optimistically will both be with us. Ms. Pellegrini is with us now, and Ms. Monk is

braving the Washington traffic -- oh, is here. Great. They're going to report to us first-hand on the status of genetic discrimination legislation in Congress.

Ms. Monk is a member of the minority staff of the Senate Committee on Health Education, Labor and Pensions, or the HELP Committee, and in this capacity works for the ranking minority member of the committee, Senator Judd Gregg from New Hampshire. She focuses on private-sector health issues, including employer-sponsored health benefits and ERISA, retiree health, the uninsured, the Health Insurance Portability and Accountability Act, or HIPAA, medical records privacy, patients bill of rights, genetics, and quality issues. Prior to her current appointment, Ms. Monk served as minority health policy advisor to the Senate Health Committee under Senator Jeffords' chairmanship. She also worked at the Pension and Welfare Benefits Administration in the Department of Labor and in the private sector for the Washington Business Group on Health and the William M. Mercer Benefits Consulting Firm. Ms. Monk holds a Master's degree in health services administration from George Washington University.

Ms. Cynthia Pellegrini is chief of staff and legislative director for Representative Louise Slaughter. Representative Slaughter is the sponsor of H.R. 602, the Genetic Non-Discrimination in Health Insurance and Employment Act. In a reflection of the bipartisan national nature of this issue, Representative Slaughter, a Democrat from New York's 28th Congressional district, is joined in her efforts by a Republican colleague, Representative Constance Morella from Maryland's 8th district. Ms. Pellegrini is responsible for, among other things, developing and implementing strategies to advance Representative Slaughter's legislative agenda. She also covers all health issues in addition to the genetic discrimination issue. Prior to joining Representative Slaughter's staff in 1996, Ms. Pellegrini worked for two other members of Congress, handling a broad range of legislative issues, including welfare, labor, education,

banking judiciary, agriculture, consumer affairs, and the environment. Ms. Pellegrini holds a Bachelor's degree in political science from the College of the Holy Cross.

We've also invited your colleague from the Senate, David Bowen, majority staff of the Senate HELP Committee. Unfortunately, he is not able to be with us today. In any case, we're very grateful that you are both able to be with us here today. Thank you very much.

We'll begin with Ms. Monk and then hear from Ms. Pellegrini. Ms. Monk, thank you.

MS. MONK: Thank you very much. I got here with maybe 30 seconds to spare. I understand we have 15 minutes each? Okay. Probably what I'll do is give a brief history of the key pieces of legislation in the Senate, a little bit of a forecast of where it will go and when, and then save the majority of my time for a discussion of the substantive issues, and in particular where my current boss is on some of the key issues.

I started with the committee under Chairman Jeffords in January of 1999, so that's my starting point, but there had been a number of activities. There had been legislation drafted prior to my arriving there. When I got there, there were efforts underway to work, I believe, with Senator Daschle and your boss to work out a bipartisan bill. That sort of fell apart, and that might have happened just before I got there or about the time I arrived. We decided to kind of go our separate ways. When I say we, on our side Senator Daschle introduced his bill which covered both health insurance and employment, and Senator Snowe, along with Senator Jeffords, Frist, and a few others from the HELP Committee, introduced the health insurance bill. That bill basically closes the gaps in existing health insurance laws, in particular HIPAA, and also in

particular the individual market, which when HIPAA was passed didn't really address the non-discrimination issues in that particular market; then also further expanded on what we mean by genetic definitions, fleshes out some of the definitions and so on. That particular bill -- and it's had different numbers; in this Congress it's S.382 -- has passed the Senate three times now. Through most of its history it was included as part of the Republican version of patients bill of rights, so it passed in that context I think twice, and then also once as a stand-alone bill when there was a floor debate basically between the Daschle bill and the Snowe bill.

Throughout the past couple of years there's been a fair amount of discussion about the degree to which we also need to do some genetic non-discrimination legislation on the employment side or the labor side. There's been a real learning curve on the issue, and when Jeffords was chairman we held a number of hearings to explore that issue. One of the things I learned was in addition to the science evolving very rapidly and our understanding of the science and our ability to put terms and definitions around those that worked, the law was also moving and there were some Supreme Court cases and so on.

So I think that when the debate first came up of whether or not we should do something on the employment side, there were some questions as to whether or not that was necessary, and I think through the HELP Committee process we heard from a number of experts. We heard from Dr. Collins many times. We heard from ADA experts and the EEOC. We did establish that there are a lot of laws out there and some of them touch on these areas and they are evolving, but there are also some gaps.

So I think, unlike even perhaps a year ago, we're in a place now where there's not a question of

whether or not we need to do something on the employment side, but it's how that ought to be structured and how that fits within our existing laws and exactly where the gaps are. So although we haven't passed anything, there has been progress in terms of the knowledge level out there and the acceptance that there needs to be something also on the employment side.

So that's kind of where my current boss is. That's about where my former boss was. Still very supportive of the Snowe efforts. In the past six months or so we've been looking at that legislation, at the health insurance side. It's not a perfect piece of legislation. We've been trying to refine that, work on the definitions and clean that up some, and at the same time trying to flesh out exactly what the employment piece ought to look like. Whether or not Senator Snowe and that coalition introduces their own piece of legislation or they work with Senator Daschle and Senator Kennedy to try to work out a bipartisan bill, I think obviously that would be the ideal. I think where my boss is coming from is we should get a package that meets all of our principles that should address both health insurance and employment, and he's not particularly wed to whether it's working with Daschle to address his concerns or doing a separate piece of legislation. So that's still an open question, but he is very interested in moving forward.

Prior to September 11th, actually we were moving quite rapidly in the area of genetics. If you had asked me on September 10th whether or not I thought we could enact something, I think I would have said there's a really strong chance, we're getting very close. Things obviously have changed since then. Number one, all the people who were working on that legislation -- I'm down to two pieces of paper on genetics. But we're also very busy working on bioterrorism and some other issues that are high priority. So I don't think it will happen this year, but I do think that it's got very good prospects for early next year, and I'm actually very hopeful that this thing

can be worked out.

In terms of the substantive issues, as I indicated before, there are basically two pieces of legislation, major pieces of legislation on the Senate side. In terms of the substantive issues, I think that there are a few issues with the Snowe bill, some things around the definitions that ought to be cleaned up. Some of the kind of overarching issues that we would want to address with Senator Daschle, and perhaps with your boss as well, there are really about three, and I don't think any of them are insurmountable. Some of it is just some of us coming up to speed.

I think the first issue really is everybody wants to include and everybody agrees there ought to be some privacy protections in the genetic legislation. When folks first sat down to draft the legislation, we didn't have privacy laws, we didn't have regulations, and since then we have 1,600 pages of privacy legislation through HHS. But that's also been an evolving process, and we're not exactly sure what those rules, final final, are going to look like. So I think one of the concerns my boss has, at least with the Daschle bill, is it's got a whole set of privacy protections in there that appear to duplicate the rules that HHS has put out, which according to their preamble are meant to cover all health information, including genetic information, and we would just want to make sure that we're not recreating the wheel, that we're not duplicating those requirements, we're not creating separate rules for providers to somehow isolate genetic information on the medical record or have a different medical record. That's something my boss cares about, and the committee was going to have a hearing on that issue prior to September 10th to actually look at the rules and try to figure out what the interaction is between genetic legislation and the privacy rules. So that's one concern we have. We don't want to duplicate or conflict with those rules. We think we can set the genetic piece within it, and then if there are

any gaps we would obviously be willing to address those.

The other piece has to do with, on the health insurance side, we feel very strongly that the genetics legislation ought to deal with predictive information. The way that the Daschle bill is drafted, it appears to encompass current health status, so the restrictions are also applied to current health status. While I think there are very valid concerns -- and this is really an individual market issue, it's not so much a group market issue. But while there are some real issue about underwriting and rate-setting based on current health status, those have pretty much always been regulated by the states, and it's separate and apart from a genetics issue. So we just want to make sure that we're focusing on the genetics issue and not getting into the whole morass of reforming the individual market, which is, as you know, very difficult to do.

The final category of concerns is the remedies concerns. The way the Daschle bill is structured, you have to look at it in the context of the existing laws that are out there and the remedies that are in those laws, and some of those laws have limits on remedies and all kinds of requirements. But the way the Daschle bill is structured, people who are currently disabled or sick would have greater remedies than people who are not, who have a genetic marker and may or may not someday become sick. So we think that might be an equity issue, and we'd want to make sure that that's kind of fair for all those people. Those are my broad categories, and I think I've taken up my time.

DR. McCABE: Thank you very much. I think we'll hold discussion until we've heard from both of you.

MS. PELLEGRINI: I have just a simple handout that I'm going to send around which, since I'm going to talk a little bit about definitions and what-not, I thought it would be helpful to have a side-by-side chart of what's in the various proposals that have been out there.

First, I'd like to really thank the Committee for inviting me to be here today. It's a privilege to address such a distinguished group of scientists and experts in the field, and I'm very grateful for the opportunity. I've been working for Congresswoman Slaughter for five and a half years now and have spent the vast majority of my time on her staff on this issue. Every time I make this presentation, that number goes up a little bit and I wince, and like Kim I'm very hopeful that soon we'll be able to say that we have this law done and I can move on to a new project.

Mrs. Slaughter introduced her first genetic non-discrimination bill in December 1996, and at that time most people thought she was day-dreaming about a problem that wasn't there and wouldn't be for quite some time, that we were thinking about something that was very interesting in theory but really not particularly relevant to the Congress or policymaking. Unfortunately, in the intervening five years, we have seen that this is actually an extremely relevant issue as genetic science has rocketed forward in a way that few of us would have believed possible in 1995 or 1996. Maybe Dr. Collins believed it, but he was ahead of all of us anyway. At this point now, we are at a stage where our nation has very few laws on the books, comprehensive laws, addressing genetic discrimination. What we have are states addressing these issues in a piecemeal fashion, some of them looking at discrimination in health insurance, some of them looking at employment, some of them looking at genetic testing, some of them looking at privacy, and as often as not, each one reinventing the wheel over and over and over. So you end up with a mismatched patchwork of laws all across the country. On the Federal level, we have only one

law that addresses this issue in a meaningful way, which is the Health Insurance Portability and Accountability Act of 1996. That law was really written to talk about allowing employees to carry coverage or to obtain coverage as they moved between jobs. They didn't carry the same policy from job to job, but to ensure access as they moved from position to position. Genetic information was really added to the protections of that bill at a very late hour almost as an afterthought, to the point even that genetic information is not actually defined in statute. It's defined in the report, the non-binding report that accompanied the law. So in the past several years, we've seen an acceleration in the states taking up this issue simply because the Federal Government hasn't moved beyond HIPAA.

Now, my boss has been working strenuously, along with Connie Morella, who of course represents this area of Maryland, right here, with Senator Daschle. We now have 256 co-sponsors in the House of Representatives for her bill, H.R. 602, the Genetic Non-Discrimination in Health Insurance and Employment Act. We've been delighted to work with Senator Daschle, Senators Kennedy, Dodd, and Harkin, who have been absolutely wonderful allies in this effort, and we truly look forward to working with the majority in the House and the minority in the Senate to come together and pass a strong, enforceable genetic non-discrimination law.

Now, I'd just like to review, in case there's anyone here who may be doubting our premise here at the outset of the discussion, that genetic discrimination is wrong, it's a bad thing. That's where we start. But I'll give you four reasons why we think that's true. First of all, genetic science is not fully understood today. Genetics is really in its infancy. We have a very elementary knowledge of how genes work, how they interact with each other, how they interact with environmental factors, and so using this information to discriminate is really often using bad

information from the outset. Second, having a gene almost never means that you will necessarily get sick. There's only one gene that we're aware of for an adult-onset disorder where, if you have the gene, you're 100 percent certain to get the disease, and that's Huntington's disease. Every other disease with a genetic factor only confers upon you a higher or lower level of risk. Third, we all have genetic flaws. There is no perfect genetic specimen, and by allowing discrimination to continue right now, what we're essentially doing is punishing people who have the bad luck to carry the genes we've discovered first. Sooner or later, we're all going to be unemployable and uninsurable if discrimination is allowed to persist. Finally, it's my boss' firm opinion that both employers and insurance companies have managed to do very well, survive in a very healthy way, without genetic information for the past many, many years. In the insurance market today, only a very small percentage of policies are issued using medical information, using medical underwriting. The vast majority of individuals in the United States with private insurance have group policies, where the policy is issued to all comers regardless of your health status. So when we're talking about genetic discrimination in health insurance, we're mostly focused on the individual market where people engage in medical underwriting. So on the basis of all of these factors, Mrs. Slaughter believes and Mrs. Morella believes that we should err on the side of caution and ban discrimination rather than allow it to move forward and wait and see what happens. We should be forward-looking here and progressive.

I will not take the time to go over Mrs. Slaughter's bill in any detail. If someone would like me to review its provisions at the end, I'd be happy to do that. But as the title implies, it would ban discrimination in health insurance and in employment on the basis of a genetic predisposition to develop a disease in the future. It is written not to affect current health status. So if a person is currently sick or has been in the past, that information is not protected by our legislation, and I'll

talk a little bit more about that in a moment, because as far as the language on that goes, there is some discussion.

As Kim stated, we had been very, very hopeful earlier this year that this legislation was going to move forward to a vote at least in one chamber, if not both, before the Congress adjourned. The events of September 11th changed the whole calculus on Capitol Hill, not just for this bill, of course, but for every piece of legislation that the chambers were considering, that Congress was considering. So we're not taking it personally that this bill has dropped off the agenda temporarily, but we are working to keep this on a lower level on the members' radar screens. We are still doing educational events. We are still sending out "Dear Colleague" notices to the House of Representatives. We're still soliciting co-sponsors for the bill and talking, on a staff level, to the committees and other members. It is not necessarily very appropriate for us to be pushing right now and trying to get this legislation passed ahead of anti-terrorism bills or appropriations legislation, and so we will be patient, as we have been for the last five-plus years, and continue working behind the scenes.

Just a couple of comments, because I know you all heard from Mr. Bykerk on the definitions in our legislation. I believe his presentation focused on definitions. Am I right? Okay. There are a couple of things that I'd like you to take a quick look at, and this is where the side-by-side summary comes in useful. The main discussions that we've had with folks have centered on the definitions of genetic test and predictive or protected genetic information, depending on the bill you're looking at. First we need to look at the definition of a genetic test. If anyone here has looked at the various state bills that have been passed, you'll find that the definition of genetic test varies widely and often determines the scope of the coverage of the law. Here's what I

mean by that. There are states that have what look like excellent, comprehensive genetic non-discrimination laws on the books. But when you look at their definition of a genetic test, it is limited to DNA sequencing. Now, it's a pleasure to talk to a group with some scientific background so I don't have to explain what a genetic test is and what DNA is and the fact that we all have genes, so I know that you all understand right off the bat that when you limit a definition to DNA testing, you are leaving out the vast majority of genetic tests that are administered today. These tests are performed on proteins, on metabolites, on the downstream products of DNA, not on the DNA itself. So you'll see that the definitions between the Daschle, Slaughter and Snowe bills look very similar, and in many places they are. They both cover DNA, RNA, chromosomes, proteins or metabolites. You'll see the Snowe bill says "certain metabolites." The last version of the Daschle-Slaughter bill said "certain metabolites" as well, until we looked at it and said, well, from a legal perspective, if we say "certain metabolites," some judge is going to come out and say, well, they must have meant not to include other ones, but which ones do they mean by "certain" metabolites? So we just took the word out and said, all right, we're going to cover all of them up front.

In the Snowe bill, however, that definition is then qualified by the phrase "for the purpose of predicting risk of disease in asymptomatic or undiagnosed individuals." From our office's point of view, the key problem there is the word "asymptomatic." How do we define an asymptomatic individual? If I have migraines and in two years I'm diagnosed with a brain tumor, were my migraines a symptom or was I just in a very stressful job? If I have indigestion and a year or two later I'm diagnosed with colon cancer, was that indigestion a symptom or was it not? Many times, we won't know. Until science progresses far beyond where it is right now, we often won't be able to make those connections. It's my boss' belief that having that kind of

qualification in there leaves open far too many circumstances where someone who might be engaging in testing can say, well, we're going to go on a fishing expedition. You say you have migraines, so we are going to conduct some tests, and it's going to be connected, we think it's connected. The connection will probably never be provable.

Our office and Mr. Daschle's and our other co-sponsors are also, however, very sensitive to the arguments that have been raised by Mutual of Omaha and by some others that they sometimes come into the possession of genetic information through no fault of their own. A good example is that if an employer needs to do blood work for a person, let's say they're testing for anemia, they may run a CBC. A CBC, a complete blood count, is a package of tests. You can't really usually pull them apart when you send it to a lab. You just get back 15 or 20 results, and some of them may contain genetic information. Now, the employer didn't necessarily seek that information, or the insurer, whoever ordered the test, but now they're in possession of it. Under the Daschle-Slaughter bill, they would not be penalized for coming into possession of that information, but they still couldn't use it to discriminate. We think that the way this concept is set out in our bill is somewhat better than the way it's set out in the Snowe bill. We just think from a legal perspective, the language is tighter, if you will.

The other definition that gets a lot of attention, the most attention perhaps, is protected or predictive information, and I apologize for the typo in the left-hand column. It should say "protected," not "protective," genetic information. That's me not paying enough attention. When Congresswoman Slaughter and Mr. Daschle reintroduced their legislation in this Congress, we changed the term "predictive genetic information" to "protected genetic information" in our legislation, and we've had a lot of people come to us and ask why. I think some of them have

thought that there was some trick here, we were doing something clever and special, or sneaky or something. What happened here is that in discussing this over a very long period of time, we came to the conclusion that the term "predictive genetic information" had taken on a life of its own. It had a meaning out in the world, outside of the strict meaning that we wanted the term to have in our bill. To a lot of people, and even to some doctors in practice, "predictive genetic information" means you will get sick. If you have a gene, you will develop a disorder. For the purposes of drafting a law, we wanted to be able to define a term to mean exactly what we wanted it to mean, not what a judge might think it means or a juror might think it means, but something that they would have to follow very strictly in the law, and so we changed the word. That's the first major distinction between our two definitions.

The other really major one, and you will see many similarities in the language between the two definitions, is that in the Snowe bill the term means what it means, qualified by the phrase "in the absence of symptoms, clinical signs or a diagnosis," and that's where we run into the same difficulty with defining symptoms. What is a symptom? When is it a symptom? How do we know? And in what cases do we want to allow discrimination potentially to take place based on a questionable factor like that?

I'd like to make just a couple of closing comments about this new legislation and where the major differences are with the Daschle-Slaughter bill, what we see as the points to be worked out or the main issues, echoing what Kim said. The first is employment. As we stated, the Snowe bill doesn't address employment discrimination at all, which we think is crucial. The second is a philosophical approach to the issue of collection and disclosure of genetic information. Under the Daschle-Slaughter bill, we take the approach that the collection of information must be

limited, not completely restricted, not shut off, but limited to some extent, because if information cannot be collected, then it certainly cannot be used to discriminate. So the collection provisions of the Daschle-Slaughter bill we think are stronger, and that's why, and the same goes for disclosure.

Now, this is where we get into the issue, as Kim stated, of the overlap with the privacy bill. As she said, we still don't know exactly what the HHS privacy regulation is going to look like. We know there are going to be changes to the draft as it stands right now, but we don't have a clear idea of what they are. In fact, our staff and the Commerce Committee majority in the House of Representatives have been trying since early August to get an HHS official to come and brief us about the medical records privacy regulation and what exactly it means, so that we can start thinking about substantive changes to our bill, and we can't get them to send someone to talk to us. So we're hoping that as soon as things die down a little bit more from the events of September 11th and anthrax and everything else, hopefully HHS will be able to spare a human being to be able to come and talk to us for a couple of hours about this issue.

We do agree with our colleagues that the bill should be limited to genetic information that predicts a risk for the future. We're not interested in covering current health status. We don't think our bill, as written, includes any information related to current health status. We're not interested in overhauling the individual insurance market. So I think there we're just dealing with a question of exactly how our language is drafted.

Finally, the classic hang-up on so many bills outside of this one is remedies and enforcement, are you going to let people sue, are you not going to let people sue, are you going to let the Secretary

levy penalties, aren't you. While we do want to look at other laws and see what they are, what they do, what kind of structures they set up, we also have to ask ourselves the question are those laws a good yardstick, or are you just taking a lousy set of penalties and applying them to another law? So we're going to be asking that question as we move along. Just as an example, under HIPAA, the penalty for most violations is $100 per violation per day. Now, if you're going to choose between denying someone potentially tens of thousands of dollars in care if you think they're going to develop a genetic disorder or taking that penalty, frankly it's cheaper to take the penalty. So we don't want to perpetuate penalties that we think are ineffective.

With that, I think I've used up my time as well, and I thank you again for having me here today.

DR. McCABE: Thank you very much. I had hoped that you'd have a few minutes for us to address some questions to you. Thank you.

DR. COLLINS: I'd like to thank both of you for the hard work you've put into getting us to this point, because I know what an up and down and all-around rollercoaster experience it has been over these past several years. I would share what each of you has pointed out in terms of the momentum that has built over this past year, and I think that's a testimony to the hard work and the bipartisan support that has arisen for this enterprise, and you and your bosses, as you call them, deserve a lot of credit for making this very strong effort to see this come to pass after it's been around for a while and we hadn't seen nearly as much motion until this year. We'd been hearing several of them to discuss this. The President's statement, in his Saturday radio address back in June, was also I think a very important signal that the administration is prepared to support a legislative solution to genetic discrimination in both the workplace and in health

insurance. So all of the pieces seem to be in place, and it's gratifying indeed to hear the discussion now coming down to the nitty-gritty details about definitions and clauses and precise provisions. It does sound as if there is a real determination here to see this happen.

I guess I wanted to ask, Cindy, from your perspective, the one place where I think it's a little harder to see how this is going to come to this happy endpoint at the moment seems to be in the majority on the House side. We have heard and seen evidence that on the Senate side both Republicans and Democrats are engaged and interested in seeing this happen. Clearly, Mrs. Slaughter has been a wonderful champion in the House, but what are your current impressions of the prospects of seeing this kind of legislation embraced sufficiently by the appropriate chairpeople and leadership on the House side to get the job done?

MS. PELLEGRINI: We are currently in negotiations -- well, maybe that's too strong a word -- discussions with both the Energy and Commerce Committee majority staff and the Education and Workforce. So while we continue talking to both of these committees, I would not say that they have the level of enthusiasm that the Senate staff do. Education and Workforce is, to their credit, committed. We're still talking very actively to them, but it's a very slow process. They're going up and back right now with some very basic draft language, but they're starting from points much farther apart than we had hoped. Energy and Commerce, their enthusiasm pretty much disappeared after September 11th, but they have told us they will come back to it over the recess, whenever Congress decides to adjourn for the first session.

MS. MONK: If.

MS. PELLEGRINI: No, don't say if. They said that they're committed to coming back at some

point, so they're not abandoning the effort, and we continue to make ourselves difficult and poke and prod and, like I said, send out notices, have briefings, forward interesting newspaper clips and things like that to the staff, so that they don't forget about us.

DR. McCABE: Ms. Monk, do you wish to make a comment?

MS. MONK: I would like to make a comment because I think you can probably gather from our comments that there's a lot of agreement in principle, particularly around what we're trying to achieve, what exactly we're trying to do our end product, and I think you hear a fair amount of discussion about the exact words that we need to put into law to achieve our mutual goals. I think in the end it will all boil down to exactly as you said, probably a disagreement over what are the adequate remedies once we are able to work through the details on the definitions. I look at the Slaughter-Daschle bill and I think it's a bit circular. I think it does present problems for current health status, but obviously the intent is not to do that. I think you point out very valid problems with the definition in the Snowe bill, and we've been talking to that office and trying to work through those. So I think we will get there. There are some people who need to come up to speed. This is further complicated in the House by the fact that they have multiple committee jurisdictions, because we're talking about employment practices and we're talking about health insurance, and that's really complicated to begin with because there are already about five statutes out there, and then we're creating new statutes or expanding upon those. One example of the challenge there is the HIPAA non-discrimination rules, the privacy rules apply to group health plans, and in ERISA that applies basically to the employers who sponsor them. There's really not much of a difference. It's kind of a legal firewall between the employer and the group health plan, and in those regs they try to kind of separate out the employer as a plan sponsor and

the employer as a plan. But how those issues get resolved in the privacy regs has great meaning for what we do on the employment side and how directly we need to regulate how employers handle information. So there are a lot of legal complexities, and some of them we're kind of dealing with moving parts. But I think that there is obviously a lot of promise in that we're in agreement on what we're trying to accomplish, and I think we're actually pretty close to getting there.

I guess I'll just leave it at that. But it's very promising to me, unlike other issues I've worked on, like patients bill of rights and some of these others. I think once people look at this there will be agreement that we obviously have some goals to achieve here. We want people to be able to take advantage of the science and the promise that the science holds, and we obviously want to put the protections in place, and those need to be fair and workable. So I really think that we can get there.

MS. PELLEGRINI: Let me just add one point because Kim makes an excellent one on remedies. Our real problem on remedies is going to end up being the fact that any compromise that we try to negotiate is going to have implications for many other health bills that are out in limbo right now, most prominently patients bill of rights. If the folks on patients bill of rights could come to an agreeable compromise on remedies, I think that would solve our remedies problems.

MS. MONK: But please don't hold genetics up for patients bill of rights.

MS. PELLEGRINI: Right. We don't want to hold this one hostage to that, either.

MS. MONK: And one other point on the remedies. This is another area where we get into complex legal areas, because you had mentioned the insufficiency of penalties on HIPAA when we're talking about somebody who is denied coverage, and that really gets to the crux of it. We are trying to, within the genetics bill, deal with both the privacy elements, and that has to do with the flow of information, as well as the discriminatory elements, where somebody is actually treated wrong, they're denied coverage or employment or something, and in my mind there's a big difference between a penalty for, oops, I faxed this information to the wrong person, but it didn't get used and nobody got hurt, versus this information got into the wrong hands and the person used it in a discriminatory fashion. So right now, at least the Daschle bill has sort of the same set of penalties for all those things, and obviously there are degrees of offenses here, because we are trying to accomplish both the privacy and the discrimination piece. But again, this is some of the stuff that we're facing in sorting out the legalities of this issue.

DR. McCABE: This was a very important issue for us. We have written letters to both Secretaries of Health and Human Services during our tenure. The reason it's such a big issue for us is because we were charged by Surgeon General Satcher, when he was Assistant Secretary of Health, with identifying what the concerns of the public were about genetic testing, and clearly genetic discrimination is a major concern. People told us, the public told us that this would interfere with the translation of the science into practice if we did not get this under control, and we heard stories of people losing jobs, especially in the small companies where the insurer is also the employer. That was a big issue. So this has been a major concern. We very much appreciate the work that you're putting in on this, because it is critical to taking the information from the Human Genome Project and having it come back to benefit individuals and

not to hurt them.

MS. PELLEGRINI: I just want to make sure you know, Dr. McCabe, we've used excerpts of your letter, as well as comments the committee received, in publicizing this to the House of Representatives.

DR. McCABE: Thank you. Thank you very much. Are there other comments or questions? If not, we thank you both for coming and speaking to us today. If our Committee can be of any help to you in the future, please let us know, because this is a very important issue to us.

MS. MONK: We might take you up on that.

DR. McCABE: Thank you.

MS. MONK: If the administration is busy.

DR. McCABE: Thank you. With that, I think we're going to now -- we've got about a half-hour before Steve Gutman was to speak to us. So, Joann, if you would, we can address the issue on the education subcommittee. I think Joann didn't expect us to get to this, and therefore, despite her usual high level of organization --.

While Joann is looking for that, I'll make a comment. I was on a panel this weekend at Cal Tech called the technology and law panel. Interestingly enough, it was a number of lawyers, and they took a very forensic approach to what is genetic discrimination. They argued that there is rational and irrational discrimination, and argued that rational discrimination would be if two

individuals were identical by all other criteria, then it was appropriate to use genetic information to discriminate. That was rational discrimination. I pointed out the same thing that Ms. Pellegrini did, and that is that it's incomplete information, so it is irrational discrimination because you have information on one. You simply don't have information on the other. The other was the argument that there is not discrimination if there is not a history of discrimination, which I had not heard before. The argument there was that remedies were made against racial and gender discrimination because of the history. Again I pointed out there, just in case anyone else faces these arguments, I pointed out there that there was, in fact, a recognition that there was a history of discrimination, and it was remedied through the Americans with Disabilities Act. In fact, many of my patients with genetic disease also have disabilities. So there was a history, and, in fact, this was recognized by the Congress. But I can tell you there were strong debates and very forceful papers saying that there is no such thing as genetic discrimination, and we need to be aware of that, despite all we've heard from the public.

You found your overheads? Great. Thank you.

DR. BOUGHMAN: Yes, in my clearly organized way. What I'd like to do in just a couple of minutes is put forward to the group as a whole what we will use as an initial outline in the conference call for the Education Work Group in planning the upcoming education summit after the morning session and so on. As Dr. McCabe reminded us why we need this kind of thing, we need to have the public, we need to have the stakeholders inform our own Committee process so that we might recommend to the Secretary actions that the Secretary might take to improve, to enhance genetics education, but also to inform the Secretary of the status of genetics education at this point in time. As unique as it might be, there may be some things that we could actually

say to the Secretary that there are some programs out there that are working, and keep up the good work.

We also are trying to facilitate the process of the integration of genetics into the broad sense of health care practice. We talked a little bit about when, and there have been a few sidebar discussions that have gone on since this morning, and we are now thinking that the May timeframe associated with the Secretary's Advisory Committee might be the best time. That would be in the timeframe of May 13, 14, 15. We've been putting calendars together, calling back to offices to see if there might be a little bit of wiggle room. But, in fact, that is what we are shooting for right now.

The who. Of course, we would want the public involved, consumer groups, health care providers in the broadest sense, practitioners, organizations representing providers, health care educators. This would include the education system in its broadest sense, not only those that are involved in development of curriculum but the accreditation process. When I say health care agencies, that is trying to broaden the scope to include the AHECs coordinators, state health departments and so on, as well as other policymakers that might be interested.

Then we get into the how, and this is the straw man that I'm going to be proposing. The reason I'm presenting it now is so people can give me feedback so by the time we even get to the conference call we've come a long way. You remember the message that we got is that we have to make the message very clear, to define the desired changes in behaviors or outcomes. What I'm going to put forward is that in the morning there be a plenary session around this concept of the importance of family history. This has not been fleshed out at all, but there are a

lot of ideas floating around out there. There are some standardized methods that are already underway by some organizations, including working with NCHPEG and the genetic counselors. We have some unique models coming out of some of the GPCs. There are a variety of things that we might look at.

Then we thought that the concepts of defining the roles of various people and promoting the team approach to patient care might be addressed by some panels, and in this situation we might capitalize on the development of case scenarios, thinking that if a case were presented, then we could have a combination of specialists or generalists, non-physician providers, a variety of allied health professionals, for example, and/or consumers approach an individual case. The idea here is to erase the possibility of absolute denial in the people in the audience that are not already converted. So if we use the stroke example that was used yesterday in some of our discussions, that the importance of genetics as it related to that case from a variety of perspectives might be the kind of thing we could do there.

Then, not unlike the meeting in Baltimore but a little bit different, the idea of some focus groups and the three areas that got expanded from two, actually, representing the columns. If you remember our conversation yesterday, first we looked at practitioners, providers, active, current professionals, and then we had the second area focus on curriculum itself. But if we expand that slightly and talk about pre-degree or the actual degree curricular process, advanced training -- in other words, the residencies, the post-degree kinds of things -- and then individuals in current practice, we might start each one of those tracks or focus groups with a short presentation or two that might give some examples, things that are working or processes that are in place, things that are the challenges to those. For example, in degree curriculum, this idea that

there's no more time. How do you address that issue? In advanced training, the discussion of the challenges or the steps in the process to bring into the process the boards and the accreditation or the certification processes. For examples across here, there are some great programs out there that have curricula infused already with genetics. In advanced training, some of the GPC models that were mentioned yesterday were terrific. Then in the current practice, there are a variety of software kinds of things, some ideas that are coming forward.

If we talk about discussion points, this is where some of those other items that floated up yesterday. In the degree curriculum, the accreditation process, the ownership of the curriculum. It can't be just one geneticist or one person who is an advocate of genetics. We have to create better ways that there be a group ownership of infusing this into the curriculum, and we need to figure out better ways to train the faculty that are going to be doing the teaching and the curriculum. If you think back, we're suggesting that it be the leaders in the education areas, it might be deans, it might be chairs of curriculum committees or whatever, those points will be major points in their day to day lives that we would hope to have addressed.

In the advanced training, it's a variety of workforce issues, not just the genetics workforce but, in fact, how do we get all these services provided and how do we distribute the workload. In the current practice, for example, the idea of a team approach, that not everybody has to become a geneticist instantaneously and there are ways that we can capitalize on that.
When we come down to recommendations, resources, resources, resources. I think that to inform the SACGT process, what we could learn from this kind of approach is certainly get a much better idea for ourselves and to try and prioritize and/or define in time or in amount those kinds of things that we think would be some immediate possible fixes or implementations versus

ways that we would suggest, not unlike some of the things that we've suggested with various agencies working together that would be a longer-term kind of thing, but this group that represents a broader constituency might be able to inform the process and make that kind of recommendation, too.

So that's where we are. This is kind of a straw man that we'll start with, and I will be happy to take any and all comers and suggestions now or in the next day or whatever, knowing that this is evolving.

MR. HILLBACK: Are you going to hand those out? Those slides?

DR. BOUGHMAN: Do you want one?

MR. HILLBACK: Yes.

DR. BOUGHMAN: Yes, we'll get them.

MR. HILLBACK: That would be good.

DR. BOUGHMAN: I just drew it on here.

MR. HILLBACK: I think to the full Committee, not just to the education subcommittee, so everybody can see it, because I thought those were a useful way to start.

DR. BOUGHMAN: Sure.

DR. McCABE: A couple of comments. You mentioned that one conclusion might be just keep up the good work. We certainly heard that yesterday in the roundtable about Title VII and GPC and other things, and also given the pressures on our government today, it's worthwhile restating what is working and keeping up the good work is not necessarily a bad thing and may be effective.

The other thing you mentioned -- deans, curricula, those sorts of individuals -- the AAMC might be a group that you might want to seek representation from. While we're going to be searching offline for an appropriate time, I think if we can make it contiguous with SACGT, that's great. But also I'd point out to everyone the University of Maryland meeting, which was highly successful, was free-standing, independent of other meetings. So we'll be working on the timing, but I think we'll try to find the best time that doesn't conflict with other meetings that could distract people.

Other comments for Joann?

DR. LANIER: Just two comments, Joann. I'm having a little problem with calling this an education summit, because although education is clearly a necessary component of it, it doesn't seem to be sufficient to get us where we want to go. I mean, what I think we're really trying to do is to improve clinical behavior, which is the ultimate thing, which leads to my second point, that we haven't really talked about the quality measurement improvement end of this, and I think there are some other organizations we might want to think about, NCQA or the Joint Commission on Accreditation of Hospitals, or people that are just involved in quality

improvement efforts across the country. One thing to think about within the group would be whether we really wanted to move this beyond a passive learning thing that is clearly necessary, but it seems to me we want to move beyond that to something else, and whether that becomes a hang-up for other people, as it is for me as I'm sitting here listening to education, that's one issue, and the other is whether to expand this to quality improvement issues.

DR. BOUGHMAN: Well, I would say to you that under the rubric of education, in fact, those issues were mentioned certainly more than once yesterday, and I'm embarrassed that I'm blanking on his name, but he was sitting in the same seat that I'm sitting in.

MS. BOLDT: Gene Rich.

DR. BOUGHMAN: Gene Rich pointed out two or three times the way that especially the infusion into practice, the change in behavior, the measurement of the behavior, and that's one of the reasons that we need to clarify the message. So I think starting from the broad-based concept of education certainly did not keep that from coming out, and I think we could be more focused on addressing some of those issues.

DR. McCABE: I think David has an important point, though, and that is that education may draw a big yawn from people. As an educator, I can say that. I think the name will be important. A topic that came up a lot yesterday was translation, but I think that it'll be important to come up with the right title for this to get the right individuals actively involved.

DR. CHARACHE: It seems to me it's more knowledge than education. The education is how

do we expand the knowledge base of everybody on genetics and genetic testing.

DR. SHORT: This is a moment to plug a meeting that we're actually hosting next month, which I think will help inform the summit process, which is the convergence of genetics and performance measures. Obviously, the hospitals and health plans have moved forward in the development of quality measures, and the physicians are somewhat behind that. But in the performance measure work that's gone forward in prenatal and coronary artery disease, just to mention two, we've not been able to carry the day with regards to family history. So the goal of this meeting next month is to really begin to look at that perhaps family history as a performance measure, informed consent as a performance measure can begin to be discussed and be a focus of education in genetics.

DR. BOUGHMAN: Yes, and I have the pleasure of attending that meeting. So it will, in fact, inform the summit process. I will be happy to hear other comments that people have and so on. I think especially ideas to get the message out that "gene" is a four-letter word, "genetics" is not. So we don't want them to avoid genetics. But we will be continuing and I'll get copies of these overheads made for anybody, and then you can red-pencil them to your heart's content.

DR. McCABE: We've been talking over the last two days about family history and how important family history is. I didn't ask you about this ahead of time, Dr. Zullo, but could you inform us about where OHRP and the advisory committee are going with this whole issue of whether we'll be able to ask a family history? If you can't say at this time, that's perfectly fine.

DR. ZULLO: Well, I can tell you it's still an issue of great interest. NHRPAC, the National

Human Research Protections Advisory Committee, just met a couple of weeks ago, and both that committee and the committee that I'm involved with, the Human Subjects Research Subcommittee, which is part of the National Committee on Science and Technology -- say that a few times -- both have working groups on third parties, which is what came out of the VCU case, and we're looking at if we take a family history, are those folks human subjects now that we have information about them? What's considered something that would be detrimental and hurtful to them? Is it that they'll be embarrassed or is it something more? They're not clear cut. In our working group in NHRPAC, there was a 5-4 vote on whether they were human subjects. So it continues to be a point of discussion, and I hope by the next NHRPAC meeting they'll have some guidance out, as well as the Human Research Subjects Subcommittee.

DR. McCABE: Can you tell us which way the vote went? If you can't, that's fine.

DR. ZULLO: I think it depended on the context that you put them in. They would go back and forth, and then they met for the breakfast, and then they'd go the other way. But it never really went to a clear majority. So it is, as you can see, a pretty contentious issue, but I think they're trying to be thoughtful and not make changes that will impact something that we don't want to. I think they're trying to be very thoughtful in making a decision.

DR. McCABE: I think that yesterday the consensus was that perhaps the most effective genetic test that we have right now is the family history. So it is very important. Any other comments before we move on?

DR. McCABE: Thank you very much, Joann. So we're next going to have an update from Dr.

Gutman. Dr. Gutman will provide us with an update on developments at FDA. He will focus on the premarket review template and the guidance on the use of data from clinical literature. So, Dr. Gutman.

DR. GUTMAN: Good afternoon. On the table for discussion this afternoon is a discussion of the FDA review process. I'm going to talk about the process in general, consideration in caveats for use of the genetic test template as a proposed tool to substitute for our usual review process, a description of a template pilot to actually test this review tool, and then a very brief discussion of guidance on the use of clinical literature, which frankly has broad use but was specifically engineered as an accompaniment to the template. What is not on the table, off the table, are actual details on the specifics of an FDA regulatory plan, and the reason for that is because there is ongoing discussion of options and legal authorities for the plan that actually has, at least in draft form, been discussed in at least two or three of the last SACGT meetings, and FDA is never known for lightning speed; glacier speed perhaps, but not lightning speed.

I'd like to recap the fact that there has been previous discussion about premarket review and that there are four established types of submission, the premarket notification or 510(k), the premarket approval application or PMA, the investigational device exemption application or IDE, and the humanitarian device exemption or HDE. For better or for worse, probably for better, I'm not going to go into detail on those four choices, although you will have an opportunity to hear from one of my co-workers, Joanne Less, tomorrow, who will talk about the unique strengths and weaknesses of the HDE as it might apply to this testing arena. I raise those four types of submission because I fear that perhaps in previous discussions Dr. Feigal and I have not impressed you with two important points in the evolution of our review program.

The first is that there is actually significant overlap between various parts of the review program, and although there are important administrative differences in these products, in fact there is a blur between the science that can be applied to any of the four products, certainly a blur between the science that can be applied to high-octane 510(k)s versus me-too or run of the mill PMAs. That blur has, in my estimation, perhaps in a beneficial way, been abetted by the passage of the Modernization Act of 1997, which created new classification opportunities in which substantial equivalents became less germane to some 510(k)s in establishing safety and effectiveness in the context of the risk profile of a device became a classification option for us.

The second point I want to stress is that over the last four or five years, there have been a number of very innovative management initiatives in my center which have created some fairly flexible programmatic forms, and although I appreciate the fact that these are somewhat arcane and perhaps indecipherable names -- special 510(k), abbreviated 510(k), third-party reviews or replacement reagent reviews -- they have a common message, that message being that the agency has found ways to develop review tools which lend themselves to novel review approaches, and the template in fact is nothing more than another tool that fits into a mosaic that the center has been interested in over a while. While it would be fair to say there are striking differences in endpoints which can be chosen for different programs, the 510(k) program is one that has historically been based on substantial equivalence and actually modified in 1990 by making that substantial equivalent determination one that would suggest that the new version of the old device is as safe and effective as the old device. The PMA program has historically been based on a de novo estimation or assessment of safety and effectiveness. The objectives of all of the review programs converge, and the objective is always to characterize performance and to label devices appropriately. So there is an underlying common theme, frankly, to all of

our work products. I want to describe that theme to you and try to bring you into the life of what review means to us, and then take that into the context of the template and what its strengths or weaknesses might be. Does anyone have a question?

Our work is framed in two parts of the regulations, I suppose framed in the statutes. I don't know the statutes as well as the regulations. In 860.7, it talks about both safety and effectiveness. This is a little bit condensed, but it states that for safety, "There is reasonable assurance that the device is safe when it can be determined that the probable benefits to health from use of its intended uses and conditions of use, when accompanied by adequate directions and warnings of unsafe use, outweigh any probable risks." Effectiveness from the same section, it states, "There is reasonable assurance that the device is effective when it can be determined that in a significant portion of the target population the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results." So our review process always returns to these same two parameters that are codified in the Code of Federal Regulations. As you can appreciate by looking at both of those, our review process always starts and ends with intended use or the claims made for a particular product. I might note that for in vitro diagnostic devices, for medical tests, there's a unique, sometimes problematic but challenging synergy between safety and effectiveness, because our device product line impacts people not because of contact or direct impact with patients, but because of the informational content of the signal that's generated and the benefits of true negatives and positives and the banes of false negatives and positives.

In the day-to-day life of our reviewers, what is of key interest are many of the things that are of

key interest to SACGT and that have been the subject of repetitive, sort of a leitmotif of discussion across many meetings of SACGT, and for us, always the key life of the device begins in analytical data. So for us, as a routine to look at a new device, we're anxious to understand the analytical performance. We want to understand the accuracy or the bias if accuracy is not possible, the precision and repeatability of the assay, the analytical specificity of the assay, and the analytical sensitivity of the assay. If truth be told, the data requirements do, in fact, largely parallel what CLIA seeks in its oversight program, but our review process allows for a product-specific rather than a process general type of review, and for accountability on a product by product basis, although the endpoints are, frankly, the same. The data for the analytical part is certainly the same. The process is sufficiently different that it really does result in a different work product and a different outcome.

For us, clinical data is sought when it's needed. In fact, when there is an obvious analytical and clinical bridge, when knowing the analytical performance of an assay tells you the whole story, we don't try to reinvent the wheel and we don't seek clinical data. So when we get a me-too device for sodium or for hemoglobin or for IgG or for amylase, we don't start asking for clinical studies to demonstrate that hemoglobin levels are associated with anemia. But what we find irresistible is that when the analytical to clinical bridge is missing, we will in the course of review try to build it, and we'll try to build it always in the least burdensome way, and we'll try if possible to understand the performance using cross-sectional studies, we'll try to use surrogate endpoints when they make sense, and what we will try to avoid, what we will generally avoid, for better or for worse, is actual outcome-oriented studies. So depending on where you slice clinical utility, we'll certainly assume that we know enough to suppose that this test is effective, but in terms of looking at the big picture of impact on morbidity or mortality or health care systems or health

care costs, we don't venture there.

We have a long history, even without this pharmacogenomics group's guidance document on use of literature, even without the page in our guidance document on the use of literature, a long and treasured history of revering and using the literature, albeit -- because I'm an honest man, I'll tell you -- our approach to literature has historically been reserved and conservative, and that's in spite of the fact that I love the medical literature.

I grapple with trying to explain what FDA review process actually is. You have to come and live with us for a day or a week or a month to actually understand what the FDA review process is. The closest terms I can come is it's akin to manuscript reviews, perhaps it's akin to being on a study section for NIH, although again, I'm an honest guy, so I'll tell you it's akin to pretty intense manuscript reviews. We expect in the preparation of submission a lot of attention to detail. When we review products, we provide comprehensive review with a lot of attention to detail. I guess what we would argue and what we would worry about in the context of this template pilot is that in life generally, you get what you pay for. So you get a lot when we sit down and look at every page and every table and every word in every submission.

The FDA review process, as I already perhaps implied, always starts with an evaluation of claims. Intended use is everything. It's kind of the hypothesis of the study. We are limited, as Dr. Charache suggested before, by the fact that we can only look at what's claimed in the context of the four corners of the label, but we take those four corners of the label pretty seriously. We look at the data. We frequently differ from manuscript review in that we will actually evaluate the line data. We'll look at the quality control that's in place, and we may

actually autonomously re-analyze the data as per a statistical consult, check the numbers out and do things that you might not do when you were doing a usual review for a journal.

Then, last but certainly not least, we look at the labeling and, without doubt, we spend more attention looking at methods and methodologies and instructions for use and limitations and warnings than probably would be concocted as part of a normal manuscript review. So you could call our work kind of a manuscript review plus, or king size.

But what we're looking for is not particular arcane or opaque. For quantitative tests we are seeking accuracy. We will try to identify a yardstick. We prefer, if possible, to have a reference method or reference material as that yardstick. We're enthused about the movement in the IVD directive, and in Europe in particular, that moves in that direction. We think that will be a good influence on the U.S. Frankly, the state of medical art, and certainly the state of our law, does not always allow us to find reference methods as yardsticks. We often look for comparisons to predicates. When we do that, we try to encourage the best predicate around, the working predicate, a market leader, something that people will understand and know and love, and we will try to strive for an enunciation of either accuracy, if possible, or when accuracy is not possible, then we try to establish bias for a new method. The most common technique we apply for quantitative techniques is regression analysis. The scope of regression analysis that we see in submissions, or the scope that we call for, is dazzling. We've seen every regression analysis you can ever imagine, ranging from the most simplistic linear regressions to complex Demings regressions, and in its greatest glory we'll sometimes even see Bland-Altman displays of data. Some of you may be familiar with the NCCLS document coming out on total error, which I think will tremendously improve American laboratory evaluation science and will

have a beneficial impact on our review process.

As a leitmotif, we're always concerned with precision. There is a pretty decent document on precision that we constantly refer back to or try to convince sponsors to refer back to. That's an NCCLS document called EP5. That document, in all honesty, is mainly directed at laboratories, so I guess it would be perfect for a home-brewed template. For manufacturers we will sometimes push the limits and ask for components of error that go beyond EP5, in particular for new technologies interested in translation across sites and for high-octane products interested in translation across lots or across instruments or across operators, when appropriate.

We quite regularly would expect to see information on the analytical specificity of an analyte. We try to ensure that the sponsor identifies and studies known cross-reacting substances and characterizes whether those substances can cause either false elevation or false depression in results. We encourage sponsors to pick relevant ranges, and analytical specificity, particularly for new analytes, can often be problematic in challenging because, in fact, you may not know the spectrum of cross-reacting materials. In fact, if you look at the FDA review process, for that matter if you simply look at the literature and watch as tests move from initial studies or pilot studies to broad-scale use, probably the most common and significant failure you see are failures in specificity as the test becomes challenged by larger and broader populations.

The division like the medical community in general will grapple with analytical sensitivity and will generally pick the parameter that works. Sometimes it's the lowest detection level, sometimes it's a change in signal per change in analyte, and sometimes that's the functional sensitivity of the assay. We don't have a rule of thumb or a rule of one.

For quantitative tests, we're generally interested in linearity. We have a light touch with linearity, usually looking at visual models. We've not come to terms with any of the more complicated statistical models that float around in the laboratory literature, but we do look at linearity in the context of important elements, like the reportable range of the assay -- that's kind of critical -- and also the reference range of the assay, which also influences the way we look at linearity in reportable range.

The models for review of qualitative tests are, frankly, less well defined. As you've grappled with some of the SACGT issues, you've probably appreciated that. For accuracy, we look at the relative performance of the assay, very much akin to what you've defined in the SACGT template itself. In the SACGT definitions itself, we're looking at performance again against a defined yardstick, and we perversely submerge what the SACGT documents refer to as analytical sensitivity and specificity. We submerge that into our accuracy determinations, and actually efficiency is probably a better term than accuracy to define that. There is a nomenclature problem that actually popped out with one of our relatively newer reviewers who has been playing around with the templates and sitting in the room there, when he and I were talking about some of the template cases that we've been playing around with. When you compare a new device to a non-gold standard reference technique, to an old device or a non-credentialed device, you have not established the sensitivity or specificity of the device, and in our own examples we appreciate that we're probably using the wrong semantic. What we're really doing is establishing percent agreement, not sensitivity and specificity, even using the generous SACGT definition.

There are poor models for precision with qualitative tests. We do ask that repeatability be studied and that percent agreement be reported. We ask for specificity studies to look for interfering substances with the same caveats that you see in quantitative tests. For analytical sensitivity with a qualitative test, we're more interested, frankly, in the readings of the cut-off zone than at the lower level of detection.

What reviewers examine is each feature in the claimed analytical performance of the test. They check for the results, they evaluate the methodologies leading to the results, they evaluate the statistics that have been applied to create the data, and they follow that to the label to make sure the label correctly and appropriately reflects what is in the submission. Reviews tend to be meticulous. They tend to be driven by literature, by past review experience, by collaborative interactive approach, sometimes by outside input. We can have panel meetings, we can have homework assignments assigned to panel members. We turn to NIH, to CDC, to CMS and other government agencies when we're stumped, and there's great attention to the detail in our work.

As I've already suggested -- well, I haven't actually already suggested -- clinical correlates of tests appear all over the package insert and all over the label. They can appear in the explanation of the test, they can appear in the reporting of the results, and they can appear, in some cases, in the attention we pay to limitations and warnings. For a well-established test, we drive on well established parameters, textbooks or literature or the body of common knowledge. For poorly established tests or new tests, or an old test with new methodologies or new technologies, we will generally ask for clinical studies. Those studies, as I've already mentioned, tend to be cross-sectional, tied to surrogate endpoints, not outcome oriented, but need to provide

plausible constructs for use, otherwise we can't label the product. Those products that can't be labeled can, in fact, be sold, but instead of being sold as in vitro diagnostic products, they probably deserve a different name. That name is investigational use product.

We prefer, when possible, to strive for clinical sensitivity and clinical specificity in our clinical studies. It's not always possible. It is sometimes, in fact, as hard as hell for the sponsor and hard as hell for us. We prefer, when possible, that cut-offs be independently established prior to studies and then assessed or tested in the course of studies. We like to see data displayed by receiver or operating characteristic curves.

The division has become increasingly sophisticated in the last four or five years. Those of you who follow the methodological literature for reviewing lab tests will know that there's a reason why, and that's because the literature is increasingly sophisticated. We now understand the perils of discrepancy resolution. We understand the advantages to clearer semantics and defining performance. We even have one or two very intrepid statisticians who will help firms, or I suppose home-brew labs, bail themselves out when they've done studies that aren't perfect by using techniques like bootstrapping or Monte Carlo simulations to try to drive the data and get even blood from a rock.

Reviewers examine each feature related to clinical claims, checking for results, examining methodologies leading to results, evaluating the statistics applied, and trying to follow all of this to honest labeling.

Although for analytical me-too type reviews generally a single reviewer will address the assay

might ask for a statistical consult, might not, for clinical reviews we generally assemble teams. Our teams will usually have one or more senior scientists, they will have one or more medical review officers, will generally have a statistician, and will call on other scientists as need, software engineers or other types of engineers, whatever seems to hit the spot for that particular device.

Where we are in the context of template development is that we continue to work on refining the template. We're now at version number 20. I think it's better than ever because we've gotten broader feedback from our own work group. We've created new examples which we're still grappling with, because our own examples don't exactly follow our instructions. I was too embarrassed to share this with you today. We do plan to put all of this out under our good guidance practice procedures so that it will go out as a Level 1 guidance and will be publicly available, not only to this group but to any group that would like to weigh in and give us advice on how to make this document all that it can be.

In terms of template use, the good news, as I hope I've already alluded to, is that there really are precedents for thinking out of the box and applying new review processes to our work, and the bad news is that the truth of the matter is that even if I was more wedded to come to you and tell you how it was going to work today, I actually don't know how it's going to work today because we've never reviewed using that template. We've not had any experience or any extensive experience with real submissions. We've not had any extensive experience, any real experience reviewing submissions, but we're going to take care of that. The solution to that is to pilot this tool, and that idea actually surfaced after the last SACGT meeting. There were multiple authors who probably get credit, but one of the authors of that idea is sitting at the table.

I don't want to pick on her, but actually Pat Charache at the end of the meeting was one of the people who came up to me and said, "You really ought to try this out, and Hopkins is willing to help," and I'll be damned, they are.

The result was we had a discussion of the template at the Professional Roundtable. To remind you all, the Professional Roundtable is an activity which FDA sort of created but runs under the auspices of any professional association that wants to participate. So the College of American Pathologists, the American College of Medical Genetics, the Association of Molecular Pathologists, AACC, CAP, ASM, AAB, COLA -- I'm sure I've left some out -- it has everybody. It even has a trade association that was suing us. We deliberately invited them to participate to show how inclusive we were. The bottom line is that at the fall meeting the Professional Roundtable decided to adopt this as a work product. Talk about leveraging and getting other people to do your work for you. They created a working subgroup, and poor Debra Leonard, having done good work in expanding the template -- it shows that there is no reward for good work -- actually ended up being the chair of that group. Steve Gutman and Joe Hackett ended up being the partners in crime for the subgroup to kick off this pilot. Clara Sliva is working as sort of the executive secretary for that, and AMP has indicated that if there are further work products, they are willing to sponsor future roundtables to try to either address loose ends or wrap up loose ends. We've drafted a letter, we've solicited volunteers, and the intent was quite deliberate, we wanted to get a spectrum of labs. We wanted big labs and small labs, we wanted commercial labs and academic labs. There's a fascinating discussion about which one has the best work product.

We wanted to evaluate the ease on the part of labs in preparing and submitting templates, and

we also wanted to evaluate the ease and quality on behalf of FDA in actually reviewing these templates. The nine labs that have been selected, that threw their hats into the rink, are the Midwest Hemostasis and Thrombosis Lab, the New York State Department of Health, LabCorp, GeneDiagnostics, Nichols, Hartford Hospital, Johns Hopkins Hospital, University of Pennsylvania, and I really apologize to Larry Silverman, I left the University of North Carolina out, but please write it in. I don't want him to tell me he's not going to submit examples because I left him off this slide. In fact, there was more enthusiasm than we had room for. There were a couple of back-up labs so that if some of the first-rung labs turn out to be laggards, we probably will enlist a substitute lab or two.

What we did was -- and this is through both the help of my group and the help of Debra Leonard -- we created work assignments in six categories. We have 14 submissions, and I'll go through both the categories and submissions, albeit I will be mercifully brief. We have two biochemical tests, homocysteine and 17 hydroxy progesterone; two cytogenetics tests, XY fish and postnatal chromosome analysis; three diagnostic tests, one for Peutz Jeghers, cystic fibrosis, and Fragile X. We have two prenatal tests, a spinal muscular atrophy and a Fragile X. You will note that Fragile X appears twice, because from our regulatory review perspective, two different intended uses from our perspective makes it two separate tests, and we wanted to have the fun of seeing the same test at two labs with two different intended uses. We have three presymptomatic tests. We picked really low-profile ones, the Factor V Leiden, BRCA 1 and 2, and hereditary hemochromatosis; and then two somatic tests, 1p and 10q LOH, and bone marrow engraftment analysis.

We developed metrics for allowing the labs to evaluate this word product, so they're going to

record who completed the template. Was it the head of the lab? Was it a first-year resident? Was it the senior tech? Was it the senior tech's mother-in-law? We're going to look at the time for each section and the total time to create a template, the sources of information -- are they getting them out of their procedure manual, out of their latest manuscript off of the American College of Medical Genetics website? Where are they getting this information? Questions that arise as they create the templates, and overall comments from the process.

FDA also gets metrics, time per section for review, overall time for review, the utility and importance of each section to the review process. Are there parts of this review process we really don't want to review? What kinds of questions we encounter, and then overall comments, and then we'll end up with -- it will be mock, it won't have any real meaning, but would we clear this product, would we reject this product, would we create a deficiency letter on this product.

DR. COLLINS: Is each lab submitting on each test?

DR. GUTMAN: No, each is submitting two. I didn't identify the lab with the test so that if I am able to share with you results, nobody gets credit or blame for good or bad submissions. That wasn't inadvertent. I just didn't want to identify the labs.

DR. COLLINS: I would think you'd probably learn something by having different labs that are performing the same test submit independently and comparing the two submissions to see how they're similar and how they're different.

DR. GUTMAN: We could go back and revisit that. Again, I don't want to put too much

pressure, but we'll take that to heart. You'll see that the pilot isn't quite off the ground yet. It's in progress. We think this is real work, by the way. It's real work, and we're grateful to the professional roundtable for sponsoring it. We're particularly grateful to the participating labs, and either Debra or I will have to be their conscience to be sure that they do follow through, and I'm grateful to a wide variety, too many people to name, in our own FDA work group who are really the brains behind this. I just get to make the Power Points the night before.

The deadlines. We have a deadline to actually create the rules of the game. Our deadline is the Friday after -- not the Friday after Thanksgiving, but Friday a week after Thanksgiving, and we're going to at that point electronically generate rules of the game and timetables, and perhaps charts for recording data on use of the templates. Our tentative deadline for submission of the template is January 18th, so we're hoping to give people enough time given the holidays to still be able to generate some, if not all, of these. Our internal deadline would be to review these templates in approximately a month so that we have some information to bring back to SACGT and tell you that this is a success, that this is a failure, that this is something in-between.

It's worth noting that there's a parallel, albeit unconnected, work product that's also been leveraged out, so FDA doesn't have to do this work either, and it's been leveraged to the pharmacogenomics roundtable, which is a group of drug and device manufacturers that has been largely the brain child of Joseph Hackett. They've been very instrumental in helping us with educational programming and considering how the template might be used in the context of pharmacogenomics submissions and making sure we have a broad view. This is a document to assist in the use of literature to support clinical use. It's based on an ISO outline. I was informed this morning that the actual ISO document to which it's attached has a controversial

life of its own. I never got to that document. I only saw the outline, and the outline resulted in four working subgroups to look at general principles and objectives in use of clinical literature, to select criteria for selecting documents to be used in support of clinical literature, to help with test performance, and then two groups looking at the various parts of the assessment of documents and description of methods. Three of the four groups actually have delivered products, and one of the four groups has suggested that their delivery may not be necessary because FDA was so clever in the drafting of its own insights in version 17 or 19 of the template instructions that we might have already answered some of the questions. The challenge at this point is trying to stitch this together and then to decide whether this is too much, too little, or just right in terms of helping us create a base for carrying clinical literature over into the support of tests.

So one thing that we're certain of is that, frankly, for home-brew genetics tests, and frankly for all tests, we shouldn't be reviewing the same clinical data dozens and hundreds of times, that once something is established, we probably should develop some level of comfort with it and find an analytical bridge to what is already well known.

So where you see FDA at this point in time is exploring a variety of regulatory options, certainly exploring in a very active manner a new regulatory tool, looking for mechanisms to leverage our resources, to obtain outputs, to meet issues identified by SACGT. We've been fortunate to assemble a working group. We've been able to recruit a couple of new people to the division, so we have both an old and a new working group. As you might guess, the devil is in the detail, and for better or for worse at this point in time, the story has not been told.

DR. McCABE: Thank you very much, Steve. Questions, comments for Dr. Gutman?

DR. CHARACHE: I'd like to make one comment, which I've made before but perhaps not as clearly. One of the templates from Johns Hopkins was highly successful on the part of getting the support of the person who did it, because it was given to the investigator prior to the completion of their study. In fact, it was very early in the course of their study. So they could use the template to ensure as they went along that they had all the data recorded that was required. The comments I got were highly positive because it served as a model for the information they needed and made it very simple to record the data that was necessary. The person who was so enthusiastic was from an organization -- namely, AMP -- that's been highly critical of these templates. But in using it to develop the test for patient care in a translational manner, she changed her mind. I suggested this be pointed out at the AMP meeting, which is today and tomorrow.

My recommendation has been that we also perhaps consider piloting this through an IRB, because that's where the template should be given out, to those who are thinking of perhaps having a test that ends up as a patient care test. So I would love to have one or more IRBs, and in this case not Hopkins at the moment, try out this and see if they can understand it or explain it to an investigator who may be setting up a test in any discipline for which this would be extremely helpful.

DR. McCABE: Thank you. Steve, I guess I'd like clarification on the point that Francis raised. One of the criticisms of this approach would be that if there are 100 laboratories in this country doing a test for a disease, but all doing it by independent home brews, that that would require 100 submissions and 100 reviews. You implied that you were seeking a way that that would not

happen, and I guess I'd like you to expand on that and also, if it's possible, give a judgment as to whether you think that could be successful.

DR. GUTMAN: I didn't mean to imply anything terribly definitive. There are a variety of options that are being considered and we're looking at legal authorities and trying to also figure out the practicalities of handling work. If I did imply, I meant to imply that we don't want to reinvent the wheel. So there would certainly not be the notion of bringing in 100 of the same products at 100 labs and necessarily reviewing them all from soup to nuts. That would be interesting, but that would also be quite challenging. There are models. We've talked about models. I'm not sure that I actually understand the models, but there are models for trying to build on existing information so you don't keep reviewing the same stuff over and over again. The trick would be to decide whether there are unique pieces. The analytical bridge, for example, might be unique and different in every lab, and if that's the case, then does FDA need to see that? Is that something that can be accomplished through the inspection and accreditation program? So I don't have an absolute idea on how that would work. I wouldn't say we wouldn't get 100 submissions, but I certainly would say we wouldn't want to review 100 submissions from soup to nuts unless we really had to.

DR. McCABE: Even the laboratories are concerned about the 100 submissions and whether there might be some standardization. If they're using something that's very similar, can they then piggyback on that as long as there is some assurance that --

DR. GUTMAN: Yes, this might be a really good area. I realize that in the device industry in general, there's a certain competitive flair to the nature of it. This might be a very good area for

collaborative work or professional groups to establish templates or standards so people, in fact, can sort of fill in the blanks. That would be a very desired outcome because, if nothing else, it would standardize things.

DR. McCABE: Yes, and also it would fit with our recommendations, which were for a flexible approach that did not begin to be a bottleneck for translation of the technology.

DR. CHARACHE: I think probably the key difference that one would have to understand is this concept of percent agreement or sensitivity and specificity, because that would vary with the master mix or whatever. The rest of the submission perhaps would not. So if there were a professional group that focused on what really mattered, this might be a very reasonable answer.

DR. McCABE: Kate, I see you shaking your head yes, and you're more knowledgeable than most of us in this area.

MS. BEARDSLEY: What Steve is saying makes a lot of sense to me. You all know I've been very worried about the number of applications that are going to be involved here and the standard of review, and it seems to me that what Steve is saying is if we can deal with the clinical validity and utility sections en masse, maybe we can just deal with the analytical validity sections individually. That makes sense to me.

DR. McCABE: And I think it's important to recollect that there were some discussions, some very explicit discussions when we made our recommendations that we placed into the record so that should there be problems as FDA progressed, we could revisit the recommendations.

Other issues?

DR. COLLINS: Just thinking this through for a second, is it likely that in this format the information that's supplied in the template would be publicly accessible, or not?

DR. McCABE: Well, I will respond to that before Steve does. Again, I think that the evolution of this Committee has been that the labeling, that the template is important for the labeling. So to the extent that at some point it becomes public information I think is critical to our ability to educate both the public and the health professionals through the process. But now, having said that --

DR. GUTMAN: Well, certainly it would be highly desirable, so it would certainly be our objective. Again, there is a lot of background discussion about where to go with this. But that would certainly be our first choice.

DR. COLLINS: Yes, it makes sense.

DR. BOUGHMAN: Steve, you started out by making a comment about lightning speed and glacial speed. Are there any ways or suggestions that you might have that SACGT might be supportive of movement of the jurisdictional and/or authority issue, knowing that that's being looked at by other people within FDA or other agencies? We haven't addressed other groups. We've been talking to you.

DR. GUTMAN: Well, I actually think the deliberations of the Committee have come to the

attention of the right folks, so I can't think of anything you could -- it's being reviewed by the right people.

DR. CHARACHE: I really think that -- and congratulations to Steve -- this has not moved with glacial speed, and I think that it has moved with precision, and that's also thanks to some excellent people in the professional group.

DR. McCABE: Which we had also included in our recommendations, that you draw on the professional groups in order to help bring the expertise to bear. We're also pleased that you are hiring in-house expertise to address some of these issues, but I don't think you'll be able to do that in sufficiently large numbers to move it forward without the help of individuals outside of FDA. Other questions or comments?

DR. McCABE: If not, I want to thank you, Steve, for informing us and moving it forward. I also have a very important housekeeping point, and that is that we will start sharply at 8:10 tomorrow morning. That's because it was to be an 8:30 start, and we tacked 20 minutes on before that. But it will be a very sharp 8:10 beginning to tomorrow morning. Thank you very much.

(Whereupon, at 4:53 p.m., the meeting was recessed, to reconvene at 8:10 a.m. on Friday, November 16, 2001.)