DEPARTMENT OF HEALTH AND HUMAN SERVICES

SECRETARY'S ADVISORY COMMITTEE
ON GENETICS, HEALTH, AND SOCIETY

Third Meeting

Monday,
March 1, 2004

Congressional Ballroom I-III
Bethesda Marriott
5151 Pooks Hill Road
Bethesda, Maryland

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C O N T E N T S

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P R O C E E D I N G S (8:40 a.m.)

DR. McCABE: Good morning, everyone, and welcome to the third meeting of the Secretary's Advisory Committee on Genetics, Health, and Society.

The public was made aware of this meeting through notices in the Federal Register, as well as announcements on the SACGHS website and listserv.

First I'd like to take note of two new ex officio appointments to the committee. We're extremely pleased to welcome Mr. Matthew Daynard, senior attorney for the Federal Trade Commission. Mr. Daynard briefed us in October about the FTC's mission; and also Dr. Ellen Fox, director of the National Center for Ethics at the Department of Veterans Affairs. Thank you both for participating.

We're extremely pleased that your agencies regard the work of SACGHS as important and relevant to their missions. As with all of our ex officio members, we very much appreciate the time and effort that you make to participate in the work of the committee and the expertise and perspective that you all bring to our deliberations.

Before I review today's agenda, I'd like to remind everyone that at the end of the October meeting, the committee decided that it was important to engage in a systematic process to determine the priority issues that should be the focus of our work during the next year. An inter-meeting task force was formed to guide the issue identification process and help plan this meeting.

During the past four months, the task force has been hard at work on this important project. I'd like to take this opportunity to thank the members of the task force for your efforts on the committee's behalf. Emily Winn-Deen, who chaired the group; Cindy Berry; Barbara Harrison; Debra Leonard; Reed Tuckson; and Hunt Willard, all members of the task force.

In a moment we will hear more about the activities of the task force from Emily Winn-Deen.

I also want to say a word about the 12 issue briefs in Tab 4 of your briefing books. They were prepared by SACGHS staff under the direction of the task force. The briefs have provided us with precise background information about the issues, given us deeper understanding of their policy implications, and helped prepare us for our deliberations. I'd like to thank the SACGHS staff for your hard work and dedication in preparing the briefs. Our thanks and compliments especially to the principal authors, Amanda Sarata, Fay Shamanski, Suzanne Goodwin, and Krista Crider. Of course, since Sarah prepared these remarks for me, she did not give herself credit for having supervised all of that work, so thank you because we know how much, Sarah, you put into this as well.

Actually, Hunt Willard and I were commenting that before the session this morning, that we think these are such excellent documents at framing these issues that we really think that there ought to be an exploration of publication in some forum to get this work out so even more of the public could see this.

The primary goals of this meeting are, one to identify the top one to three issues that will be our focus for the coming year; two, to develop a work plan, and three, to begin deliberations on the first issue. The first half of today's agenda will be devoted to hearing about the work of the task force and advancing our priority-setting process. In order to organize the forthcoming discussion and engage the committee's current views on the prioritization of issues, we will take a straw vote before today's first break. Then, with the

benefit of today's discussion, we will take a second straw vote at the end of the day. You'll find in your table folders two ballots to use for these straw votes. These are in the white briefing folders, this one, so that you can find them and be prepared for those straw votes.

In the afternoon we will hear a series of presentations and will hold a roundtable discussion on coverage and reimbursement of genetic technologies and services. Questions about coverage and reimbursement were raised in the October meeting, and a number of members suggested that an in-depth briefing might be in order. In addition, coverage and reimbursement is one of the 12 priority issues under consideration, and during the inter-meeting process it was ranked among the top three issues.

This afternoon's session will explore public and private health insurance coverage and payment policies for genetic technologies, the perspectives of service providers and the financing and economic considerations with respect to these technologies.

Tomorrow, after we make our final determinations about the top three priority issues, we will develop a long-range work plan for accomplishing the three projects. Then we will begin deliberations on the top priority issues. We hope to make enough progress on the first issue to be able to outline preliminary recommendations to the Secretary.

Let me also point out that we have public comment sessions each day. We will hear testimony immediately following lunch today and first thing tomorrow morning. We have a number of individuals, five, who have registered to address us. If there are others here who wish to provide comments, please inform the individuals at the registration desk so that you can get onto the list.

I'll now turn to Sarah Carr for an important reminder about the conflict of interest rules.

Sarah?

MR. CARR: Thank you, Ed.

Being a member of this committee makes you a special government employee -- I'm speaking to the members of the committee now -- and thereby subject to rules of conduct that apply to government employees. The rules and regulations are explained in a report called "Standards of Ethical Conduct for Employees of the Executive Branch." This is a report that each of you received when you were appointed to the committee. I'm just going to review one of the rules in that document.

Before every meeting, you provide us with information about your personal, professional, and financial interests, information that we use to determine 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. We waive conflicts of interest for general matters because we believe your ability to be objective will not be affected by your interest in such matters; but we also rely to a great degree on you to be attentive during our meeting to the possibility that an issue will arise that could affect or appear to affect your interest in a specific way.

In addition, we have provided each of you with a list of your financial interests and covered relationships that would pose a conflict for you if they became a focal point of committee deliberations. If this happens, we ask that you recuse yourself from the meeting and leave the room.

If you have any questions about these rules and your interests, our committee management officers can help address those questions. David Alperin and Claire

Harris are this committee's committee management officers, and David at least is here today, and I think Claire will be here later.

Thank you.

DR. WILLARD: Ed, could I ask Sarah a question on that issue?

Could you address explicitly how we are supposed to behave in discussing issues in which either we or colleagues at our institutions either have grant applications in to the federal government or are anticipating those applications? So as we prioritize issues, there is at least an indirect potential for conflict of interest in leaning the deck in areas where we have our own expertise or institutional expertise.

MS. CARR: I would still say those are general matters. The discussions that we have about those things, and if the committee decided to make something a priority where you are doing research -- let's say pharmacogenomics -- the fact that the committee made that a high priority isn't going to, in my estimation -- and we can talk to our committee management officers about this more specifically. But in my estimation, you would not be favoring yourself in any specific way. So as long as the discussions are about general issues and you will not benefit specifically from decisions of the committee, I think you'll be okay.

But if you ever have any doubt about it, and I know what you're trying to do is get clarification, but if you have any doubt, just come up to me and we'll try to take care of it. I think if you ever have a doubt, the best thing to do is to leave.

David, go ahead.

MR. ALPERIN: Hi. I'm David Alperin with NCI's committee management office. We do all your ethics clearance.

In relation to your question, the specifics of ethics clearance is for you as an individual and the holdings that you have that you would receive a direct benefit if you had insider knowledge of a decision to be made by this committee. If your colleagues have grant applications, that is not a specific issue for you. That is an issue for your institution, and you are not here representing your institution. You are in here for your specific professional expertise. So I don't feel that anything related to a colleague that may or may not have a grant application in process or a grant application for your institution would be an issue that would require you as an individual to recuse yourself from the discussions.

Does that help?

DR. WILLARD: Sort of. I mean, I guess the issue, without hammering this too deeply, is if I had a grant application in on genetic non-discrimination, it seems to me to be in my best interest to have this committee decide that genetic non-discrimination is one of the big issues that we want to have the Secretary put his weight behind. So would you consider that to be a direct conflict or not a direct conflict?

MR. ALPERIN: I would say that that is not a direct conflict. However, it may be a potential conflict. If this becomes an issue of a very focussed discussion, it would probably be the best course of action for you to recuse yourself from that specific section of the discussion.

DR. WILLARD: Okay. Thank you.

DR. McCABE: The other thing that I will remind everyone is that as a special federal employee, you should not engage in any lobbying of the government agencies or on the Hill while you're here on this visit. Similarly, I think it would not be wise to be involved in any discussions with any companies or relevant to any private holdings that one might have

involvement with.

I think that the discussion that we just had is that if you feel uncomfortable about it, then there's a perception of a conflict of interest and it's probably best to recuse yourself at that point, since it's frequently perception as well as reality.

Thank you for that discussion and for pursuing it further.

Emily Winn-Deen will now review the process and outcome of the inter-meeting priority-setting project.

Emily, let me thank you very much for chairing the task force. I know how much time and effort you put into advancing this during the interim and in the issue identification process and planning and organizing the meeting.

Let me also remind the committee that as Emily reviews the process and issues, you should be thinking again about your rankings. We will take a straw vote after Emily's presentation before the break so that Sarah and her staff can have time to tally that vote over the break.

Thank you.

Emily?

DR. WINN-DEEN: Well, first I want to thank everybody who worked on the committee, and that includes all the people who provided input both from our SACGHS committee, the ex officios, and all the staff support that we got. It was really a group effort.

As Ed mentioned, these are the individuals from the main committee that participated, but we did have, when we sent out things for votes to the whole committee, everyone had a chance to vote and participate.

The goal of the task force was to conduct a systematic identification of issues that might be appropriate for this committee to address, with the goal of prioritizing some very specific issues that we could and should address; and then as a result of that to try and develop an agenda for this meeting, and that work product is the agenda you see before you.

It was a multi-step process. We first identified a number of issues, and this came from feedback that was obtained at the very formation of this committee on what issues were of interest to both the ex officios as well as the members. We then reviewed the top ten issues and assessed how to frame those as short phrases. Then we surveyed the members and asked them to pick their top three to five priority issues. So they got a list of 19 issues that were identified as potentially relevant to this committee's work, and then everyone was asked to vote on which they ranked as the top priority.

Then Sarah and her staff organized the results of that first vote based on the frequency, and 12 top issues emerged. Then the full committee went out and worked on that.

So again, we surveyed all the members and the ex officios to rank the top 12 issues, and that guided the development of the position papers or background paper I should say, issue briefs that you find in your binders. We also identified that coverage and reimbursement was a fairly highly ranked issue among both the ex officios and the members of the committee proper, and arranged to have this as one of the sort of deep issues on the agenda for today.

So we went through and tallied all the votes, and these votes were from the committee, and this is sort of the result. The top-ranking issue was large population studies and education and training. They both received a total of seven votes. Coverage and

reimbursement and access received six votes each. Then the next group was patents and access, nature of genetic information, oversight and public awareness. Next came the vision statement, direct-to-consumer testing, and pharmacogenomics. And then at the bottom -- and these were the issues that we ultimately decided we would drop, with one exception -- were enhancement versus treatment, bioterrorism, new health-related applications, genetic discrimination, scope of genetic technologies, informed consent, forensics, privacy and confidentiality. The one that we kept on the agenda as sort of an ongoing issue that we're monitoring is genetic discrimination.

As I mentioned, 11 issues rose to the top, and the genetic issue was retained because we had already identified this at our very first meeting as an issue that we wanted to at least keep some vision on, make sure that things were happening to take care of that. So the bottom seven were dropped and the rest went on to the next round.

In the next round we asked the committee and the ex officios to think about the following questions in terms of trying to prioritize these issues. How urgent is the issue? That is, is there some lurking thing that we have to act on right now? Does the issue warrant the committee's attention? Is it an important issue but maybe not really within our scope? Is there other media attention or some event that's happened that precipitated a need for us to react to that? Of course, does the government have jurisdiction and authority? Because it doesn't do us too much good to work on topics which Health and Human Services can't really take action on.

Then the other issues are is there actually already some activity in the federal government addressing this issue? Is the issue of a nature such that the best place to address it is through the government, or are there already other agencies and private sector mechanisms happening to take care of that? Are there any particular moral and ethical concerns that warrant government intervention or leadership on an issue? And then finally, it's the "so what" stuff. Will the committee's policy advice on the issue significantly benefit society, or will the failure to address cause some harm? Does there exist a sufficient body of data from which we can actually deliberate and make a recommendation?

So again, we surveyed the members and the ex officios, and there were some differences that emerged between what the members thought and what the ex officios thought, and we'll look at that in a minute. Access was ranked first by members but only tenth by ex officios, so there's some difference in priorities or viewpoints there. Coverage and reimbursement was ranked second by the members and ninth by the ex officios. On the other hand, public awareness was ranked seventh by the members but number one by the ex officios. So I think we need, even within our own extended committee, there's some open issues and need for debate about really what are the priorities.

So this is the overall ranking, and I'll let you have a look at that. I highlighted the ones where there was sort of significant differences. I think there were not too many where there was obvious ranked number one by both, so we still I think have some sorting out to do at this meeting.

What we did then was we asked Sarah and the support staff to develop an issue brief on each of these topics to sort of flesh them out a little bit more. What people were voting on were these one or two or three-word titles. So it was clear that maybe as we had our task force discussion, not everybody's interpretation of what that title meant was quite the same. So we went through to try and really flesh out what we believe the issues are surrounding this

word in relationship to the SACGHS charter, and we'll be going through that in a little bit.

I'll give you sort of the highlights of each of these areas on the issue statement, and then we'll come back and have some deliberations. Under access, the key issues that were identified were barriers to access to genetic services that might prevent the realization of the full benefit of advances in genetics, and the fact that access can be impeded in several ways. It can be impeded during the test development and marketing process, through the use of intellectual property patents that might be used in a way that would limit research in an area or increase the cost of tests through licensing royalties.

In genetic research, the choice of populations that are available to study might impact ultimately the access of individuals who would benefit from testing to that. So if we never do the studies to determine what the genotype/phenotype correlations are, we're not going to have genetic tests that would benefit, and how do we deal with the rare disease issues.

The issue of clinical integration, how do we move from a research level into the practice of medicine; and finally, the sort of standard players in terms of financial barriers, lack of insurance, lack of coverage, inadequate reimbursement, and the cost of the test.

From the societal point of view, we also felt that access could be impeded if there was any fear from genetic discrimination or some kind of stigmatization that would create unwillingness for someone, even if it was paid for and available, to have a test, and that this could then, if there are specific groups that feel more likely to be stigmatized, that they might as a group have some disparity in access. Finally, the relevant policy question is are there specific things which the federal government could do to intervene which would minimize the barriers to access.

For coverage and reimbursement, we all know that health insurance affects both the cost of the overall health care system and the quality that's delivered, and as a result the access to care. So coverage and reimbursement decisions, particularly for new technologies, new markers, are still very difficult in this country. We're a multiple payer system and we have multiple payer disparities in terms of what's covered, how it's covered, when it's covered, and that all has an impact on who actually is able to get testing done.

Some of the coverage and reimbursement decisions are not made because there's felt to be insufficient data to support that something really is medically relevant. There's some misunderstandings about the costs associated with genetic technologies, and there's some new challenges that genetic technologies pose in the paradigm of health insurance, that sometimes it's necessary to test family members in order to get a specific result for a proband, as well as the fact that we now will be potentially able to do testing for diseases that would develop much later in life but are currently asymptomatic.

So again, coverage and reimbursement. The policy questions are basically focused on is it a barrier to allowing people to get access to the genetic technologies, what specific actions would facilitate coverage and reimbursement decisions, and are there any unique characteristics that impact these coverage and reimbursement decisions, or are these really just like any new biomarker that comes out and has to establish itself on the basis of clinical utility.

We heard at a previous meeting about concerns in direct-to-consumer marketing, and this is basically focused on the marketing of medical services and products to consumers. It's common practice now with all the television and print advertisement for pharmaceuticals, so there's some concern that genetic testing might not be quite ready for that

level of consumer interaction. So the risks really are who is regulating the claims that are made in a direct-to-consumer situation, and the potential harm that could be done to this field if the public's first interaction with these kind of tests is through sort of junk science.

The average consumer we felt doesn't really have the background and experience to judge for themselves what's good science and what's junk science, and there might be some need for "experts" to weigh in on that. Then there's the whole issue of how many results do you want going directly back to a consumer without the intervention of a health professional, and which kinds of tests might be okay to have results go directly back to a patient and which ones you would definitely want to have a health care professional and potentially a counselor involved with.

So the benefits of having some kind of intervention would be to enable the consumers to be better informed and to participate more fully in their health care. We all know that the first thing anybody does today when they're diagnosed with Disease X is log on to the Internet and find out what Disease X is really all about. So in terms of being an informed consumer, that's a good thing. We do have oversight both from FDA and FTC to protect consumers from false and misleading advertisements, but unfortunately right now we've heard from both FDA and FTC that neither agency has the bandwidth on their staff to be actually monitoring this.

So the policy questions come down to basically do the risks of direct-to-consumer advertising outweigh its benefits? Does direct-to-consumer advertising in this particular field raise any greater concern or warrant more attention than any other area of medicine? And is there anything that this committee can do to sort of facilitate the right kind of consumer interaction with genetic testing?

The next area was genetic discrimination. We've talked about this a fair amount. We know that genetic technologies have been sold on the promise of the future of medicine being positively impacted. We have just completed a really huge publicly financed program to sequence the human genome, and now we're working on the next phase of understanding the variation among individuals in the human genome. But we're not at the point where it has yet been integrated into the practice of medicine in a routine way.

So what are the barriers? Is there a fear that patients would not either utilize genetic services or participate in the basic research that's needed to move from a research setting into a medical practice setting?

There's still a perception that genetic discrimination exists, although there are actually not that many documented cases, and the ones that have been documented are ones we trot out on a regular basis. So the question is is this a real fear based on facts, or is this a sort of fear of the unknown or fear of worst case scenario and we just haven't seen the worst case scenario?

The policy questions are will a federal law, such as the Senate bill that passed last fall, be effective in preventing discrimination? Are there other areas beyond health insurance and employment that we should also be thinking about? There is a moratorium in the U.K., for example, on life insurance, using genetics to make any risk assessment for the purpose of life insurance. But there are also areas, like adoption and immigration policy, that we really haven't discussed or gotten into at all yet. Then again, what further steps should this committee take to deal with this issue?

We also heard at the last meeting a lot about the status of genetic education

and training. The goal, of course, is to make sure there's a better understanding of the role of genetics in health and disease. We are I think well acquainted with the fact that we need to involve a wide variety of health professionals and make sure that they have the right education and training to facilitate the integration of genetics, and I think currently there is still a perception that health professionals are not sufficiently trained and educated to meet the goals of having this just as a standard part of your medical care.

So what are the gaps and how can we fill those gaps? Is there a role that the federal government should play, or is this a role that should be played, for example, by the AMA and other professional groups? So that was the training and education section.

Genetic exceptionalism is sort of a philosophical issue. It basically comes down to do we believe that genetic information is different than any other medical information, so should it be treated with some special additional considerations beyond the confidentiality and other things that are in place with which all medical information is treated.

The critics say that genetic information is just another part of your overall medical history and that there's no real compelling reason to separate it from other information in your history that might be just as damaging or difficult to deal with, such as HIV status or the fact that you'd had cancer five years ago, those kinds of things. The advocates say that genetic information is unique because it is a unique identifier. It does allow you to, with the exception of identical twins, a unique personal identifier. Because it's inherited, anything that you find out about an individual could have implications for family members, and it can be predictive, and therefore it can be used to stigmatize and discriminate.

So this is sort of one of those ongoing debates, whether we want to make it an issue, and what, if anything, this committee can do about coming down on one side or the other, whether we believe genetics is exceptional or not. Clearly, the fact that we have a committee focused on genetics says that we at least think we need to talk about this issue.

So in terms of policy questions, I think I already mentioned the issue of does the fact that genetic information is individually unique warrant special attention. Should our public policies be based on the premise of genetic exceptionalism, and is there an alternative concept that would allow the special features of genetic information to be acknowledged without necessarily creating a whole separate and parallel set of rules and regulations for genetics?

The next issue is large population studies. This basically is focused on the concept of translational research, that we need to understand better the genetic variability within populations and across populations and the impact that that has on the way individuals develop disease or react to drugs used to treat disease. The federal government has been funding a number of studies aimed at understanding the extent of variability and creating haplotype maps to help us with the research tools. I think we've been doing a good job of funding the research tools, but do we need to do the next step of actually initiating a large population-based study, such as is being done in some of the other countries?

One of the reasons to think about this is because for some of the kinds of genetic effects that we might look at in the broad practice of medicine, we are going to see effects that need a large number of people to actually get the statistical power just to properly power the clinical trial, and this might be beyond the realm of individual grant applications or clinical trials that might be funded by a company.

So the policy questions really are how important it is to mount large

population cohort studies in the U.S., how would we deal with the heterogeneity of the U.S. population. Most genetic studies that have been done in the early phases went to very homogeneous populations to try and find effect. How do you extend that to heterogeneous populations? What should the role of the federal government be, and what obstacles might there be in order to be able to actually conduct a study in the United States where we're a mobile society, we don't have centralized health records? I mean, there's a lot of sort of logistical issues that would come into play that would have to be dealt with.

In oversight, we were looking at basically sort of a follow-up of what SACGT did a lot of work on, our predecessor committee, and that is what kind of oversight is needed at the federal level to make sure that the tests that are developed meet all the criteria for being put into medical practice. So basically the issue is have we done enough or are there still some gaps? Clearly, a number of agencies are already actively involved in oversight of both genetic as well as other tests, and the question is is there a need to do more than what they're currently doing? So I guess that's really pretty much those things.

Patents and access. This was a pretty hot topic I'd say two years ago, and still I don't think has been completely resolved about what to do about the patent system. The pros, of course, are the basic premise under which the U.S. patent system was created, which was to promote innovation by granting exclusive rights for a limited period of time, basically so that you would invest in developing things and get some kind of assured reward, as market conditions permit.

The cons are that when patents are held in an exclusive manner and not promulgated across multiple sites, there's a perception that this can limit innovation or limit the ability to use innovation. Of course, the financial rewards that come from patents are basically through licensing fees. So those who need to take a license and pay fees almost always pass those extra costs directly on to the consumers of their products, including patients who are getting genetic tests.

The questions on a more basic level are is there any evidence that patents held in an exclusive manner have limited research or decrease the ability for tests to be out and utilized in terms of access to genetic testing services? So the policy question as it relates to genetics is is there really anything in the way U.S. patent law is interpreted and executed in the field of genetic diagnostics that is unique and requires some kind of special treatment or special consideration, and can we somehow balance the public good that comes from full dissemination of new innovative technologies with the financial rewards that are required to incentivize investors in actually developing those things to the point where they're commercially viable?

So again, a balancing act. Is there anything that this committee can or should do to sort of influence how that scale is tipped?

In the field of pharmacogenomics, I think it's fairly well recognized that there are individual differences in the way people respond to drugs or are susceptible to disease. There's some evidence that your genetic background also plays a role in your likelihood of developing an adverse event when treated with some drugs. So the question is how to make the best use of this sort of general knowledge and put it into the practice of medicine. So to what extent should we individualize the practice of medicine and use genetic determinants to target pharmaceutical interventions, or to what extent are we using genomics to identify new drug targets and evaluate them in the process of drug development through clinical trials?

So the relevant policy questions in pharmacogenomics are basically does the current evidence indicate that genomic technologies can improve health care outcomes? And the part that we haven't really dealt with too much as a society yet is the costs and quality issue. So do we need more health economic modeling of how a test might or might not benefit the overall practice of medicine? How will the clinical validity and utility of pharmacogenetic tests be established? How will pharmaceuticals already on the market be reassessed? We know that there are a number of drugs, for example, that already have in their labeling a statement that says, "By the way, this drug is metabolized by this enzyme, which we know to be polymorphic," but they don't really tell you what to do about that. So how do we develop that body of information that takes it to the next level? And then how will the integration of pharmacogenomics into clinical trials and drug marketing be optimized?

So the relevant policy questions in this area are basically what can the federal government do to improve the chance that this technology will be integrated and used to improve patient care? Are there sufficient research studies in place? Is there a role there for the federal government? There's always the fear that if you genetically subdivide diseases into enough groups, that you end up with genetic subsets of disease that might then be sort of orphaned diseases on their own, and do they qualify then somehow for orphan drug status or orphan disease status? And finally, what's the most efficient way to integrate this technology into the health care system?

On public awareness, I think we also have identified this and discussed this to some extent at previous committee meetings. The question is just I think focused on how to make informed consumers, how to make sure that the public, and the public being kids in school through elderly on social security, how do we make sure that they have enough knowledge to make good, informed decisions when presented with an opportunity to integrate genetics into their health care, and how to make sure that the public education that occurs through the media is accurate and not misleading.

So I guess the key things in terms of what this committee might do is what is the role of the federal government in assuring or improving genetic literacy, and if we can identify what the role is, is there more that the federal government should be doing or could be doing to improve public awareness in the right way?

The vision statement issue is really not an issue, more a mechanism to help this committee formulate its framework, and we have a very, very broad charter and basically are given a wide range of things that we could work on. The thought was that if we could create a vision statement, it might help us to describe where we want to get. What is the goal ultimately of integration of genetics into health care and into society? Then once we identify what the ultimate vision is, then you can take a step back and do a gap analysis and say really where are the gaps, what are the most critical gaps, and which ones do we have the ability in this group to influence?

So I guess the main policy questions are beyond just giving this committee a chance to get more focused and get a better internal vision for what we want to do, is there some role that such a vision statement could play in becoming a broader Health and Human Services vision statement or a federal government and public vision statement so that we really sort of start with the seed at this committee level and move it up to speak with one voice about where we as a people of the United States want to take this whole area?

So that's the overview, and now what we're going to do is we have different

committee members assigned to just give us a brief run-down on each of the areas.

DR. McCABE: Thank you, Emily.

We do have time now for a very brief discussion, probably about 15 minutes or so, before we take the straw vote right before the break. So if anybody would like -- Francis?

DR. COLLINS: Just a point of information. When it came to the discussion about patents and access, you may be interested in knowing the National Academy of Sciences has started a study on that, which met for the first time this past Friday, specifically looking at the impact of patents on genetics, genomics, biotechnology, and a distinguished panel, chaired by Shirley Tilghman, president of Princeton. This will be an 18-month study. They have a lot of expertise on that panel from both the public and the private sectors and will be collecting data in order to try to assess what the impact has been so far of patents in this arena, and then ultimately making recommendations about steps that might be taken to maximize the benefit to the public in the future.

DR. McCABE: Thank you. That is important information because, as we've discussed before, there's no point in us taking on issues that are actively being engaged by other groups. There are a lot of things to do, and we shouldn't duplicate efforts. That would not be efficient, nor probably effective.

Other comments? Yes, Emily.

DR. WINN-DEEN: Francis, can you tell us who would be the right person to contact to maybe have somebody come and just give this committee a briefing when they get to the point of having something?

DR. COLLINS: I can get you the name of the chief staff person, and I'm sure they'd be glad to come and make a presentation. They're just getting started with the first meeting, but perhaps in two or three months. I can get you the name.

DR. McCABE: Good. Thank you.

Other comments? Questions?

Yes, Brad?

MR. MARGUS: Just on the same lines, I remember at the last meeting someone mentioned that the IOM is looking at the population study idea. I was wondering how much redundancy there would be if we made that an important thing here.

DR. McCABE: Francis, can you help us?

DR. COLLINS: That has not gotten underway. It's been discussed. Actually, at the present time we're sort of deciding between whether that kind of analysis would be best done in a fashion organized by some of the HHS agencies -- NIH, CDC, and so on -- or whether the IOM would be a useful contributor. We're sort of leaning in the direction of doing that internally. But certainly from my perspective, having the input of this distinguished panel on the value of such a study would be quite helpful.

DR. McCABE: Is the IOM still pursuing it, or is the discussion moving toward the agencies?

DR. COLLINS: Well, you may be aware, the IOM pursues studies when somebody identifies a budget to support that. So they're looking to the NIH for whether there are funds available. Things are very tight right now, so at the present time the IOM has no plans to initiate such a study.

DR. McCABE: Thank you.

Other comments or questions? Point of clarification of anything that Emily raised?

(No response.)

DR. McCABE: Any thoughts about some of the discrepancies between the two lists, the list from the members versus from the ex officios?

Yes, Francis?

DR. COLLINS: I'm sorry to talk so much, but I'm curious, in the deliberations of the groups that met in-between meetings of SACGHS, there is this apparent potential for overlap between the topic called access and the topic called reimbursement. In fact, reimbursement appears as a subtopic under access. So how did you all come to grips with that in terms of deciding whether these are really different or whether these are two topics where the federal role in terms of what could be done as far as a policy decision is actually fairly similar?

DR. McCABE: Emily?

DR. WINN-DEEN: It was clear to us that among these 12 topics that you could easily create some subgroups that had common threads, such as access and coverage and reimbursement, whereas you say one of the key issues surrounding coverage and reimbursement is whether it does limit access. But we decided that since they had been ranked as important by enough individuals on their own that we would keep them for now as separate topics. But it is absolutely clear that -- I mean, you could put patents in there as patenting, limit access. So there are subgroups that one could construct and make a sort of coherent subset that might fit together.

DR. McCABE: Debra, did you want to make a comment?

DR. LEONARD: Well, in fact, there are four of the topics that are subsumed in access. There's discrimination, patents, coverage and reimbursement, and there's a fourth one. I forget what it is.

MS. HARRISON: There's large population studies and also --

DR. LEONARD: Education. That's the other one that was specifically included in access.

DR. McCABE: On one of the conference calls there was some discussion about one of the things that might be done is some lumping, though we wouldn't want to be so creative in our lumping that we ended up not narrowing the field at all, which given the creativity on this committee I'm sure we could probably do. But that would not be effective given the purpose of the process.

Barbara?

MS. HARRISON: I don't want to get too ahead of myself as the point person for discussion on access, as well as reimbursements. As I was going through information last night, I was trying to separate my thoughts, and it was becoming very difficult.

One of the propositions I have for the committee is a topic that was brought up before, if I'm not mistaken by Emily, to use access as a framework for whether or not a topic is worth our consideration or not. It's my bias that in serving the public, to make sure that people can even access these kinds of services, that maybe those are the kind of topics that we need to expand upon, the ones that fit under access. So maybe not identify access as a separate issue but really set it up as a framework in setting these subtopics and these are the ones that we're going to try to address in the next year, couple of years.

Again, it may be premature to bring that up, but I wanted to let the others outside of the committee know that that's a thought that's out there.

DR. McCABE: I think that was actually Cindy's idea, but thank you for reminding us of that.

Suzanne?

DR. FEETHAM: Just as a point of clarification, due to a communication in how HRSA scored it, their rankings were not added in, and as the access agency, that may have affected it also. So just to get that on the table.

DR. McCABE: As I looked at the discrepancies between the rankings by the members and the ex officios, and this is only my interpretation, but it looked like perhaps what we were seeing was the members just looking and ranking by their feeling of importance, but perhaps the agencies were looking at what could actually be accomplished by the agencies. I don't know if the ex officios would comment on that.

Francis?

DR. COLLINS: Yes, I think there is some truth to that summary, although that in no way should either imply that the agencies know what they're doing or that the members don't. It's just a different perspective.

(Laughter.)

DR. McCABE: Yes, Hunt, then Cindy.

DR. WILLARD: For the purposes at this point in the conversation, it may be useful to get some guidance before people go into the straw vote, because clearly there are issues of how people read this, or even react to what Emily presented, that we also saw in the task force. So genetic discrimination is a perfect example. Some people rated it number 1 because it's a critical issue. Some people rated it number 12 because it's a critical issue, but we already dealt with it because we wrote to the Secretary. So everyone meant the same thing, but the votes were completely opposite, and probably there are six other examples like that. So I don't know how you want to address that from the standpoint of either the first or the second straw vote.

DR. McCABE: Well, I think to some extent that will probably come up in the discussion between the first and the second straw vote. But I think it is important to recognize that that probably did influence -- I mean, genetic discrimination was the obvious one that everybody feels is important in the public to SACGT. You know, my first communication as chair of SACGT to both administrations, and our first communication as I was directed by this committee was on genetic discrimination. Clearly, everybody feels it's important.

There's the issue of how rampant is it, but the perception is that it's a concern to the public. But I think that will come out. What more can be done about it? If there is more, then that would influence the ranking. But that will probably be a matter of discussion between the first and the second straw votes.

Cindy?

MS. BERRY: And also, I'd put the genetic exceptionalism in that same category, because you'll remember when we first ranked it and then we looked at it and had a discussion on our conference call, we were all in the same boat in terms of our thinking, but we interpreted our duty to rank it in a different way. So it's the same exact thing, and that one might also merit some pretty intense discussion because it actually has the potential to dramatically affect how we rank our priorities overall and what the committee does.

DR. McCABE: Kaytura?

DR. FELIX-AARON: Thanks. I just wanted to comment on the apparent discrepancy between the members and ex officios' rankings. It appears that, at least from my perspective, I interpreted the mandate to be, one, what was uniquely the Department's role. So getting clarity and focusing on using that as a priority. So ranking, topics where I thought the Department had a unique role; and two, where action could be taken in the short term. So where there were opportunities for the Department to intervene on a short-term basis. Those were the two things that drove my ranking of the items, and not that the others weren't important. I recognized the importance of others, but I was driven by those two factors.

DR. McCABE: Thank you.

And I think it's also important to recognize the second point that you made about all of these being important issues. Certainly these are the 12 most important issues that the committee identified. So we recognize in our ranking that we're making some difficult calls, but we also recognize that if we're to be effective we have to have some prioritization. So I don't think we should consider that we don't think that the other points are important. We just have to identify what is the most important where we can be effective.

We will also be discussing process, and to the extent that we can come to some closure on one or more of these within this meeting and possibly the next meeting, then we can move on in the prioritization list. But the purpose of this was so that we didn't flounder around not getting our arms around anything, but trying to identify at least three items or three to begin with, and then move on.

Debra?

DR. LEONARD: There are also things the committee can do that are rather rapid, such as recommending an NIH/CDC study on how we would do a large population cohort that this committee wouldn't necessarily do, and then there are things that this committee would need to do work on. So doing the relative ranking of those types of things is also difficult.

DR. McCABE: Thank you.

Emily? And I think this will be the last comment, and then we'll take our straw vote and our break.

Oh, I'm sorry.

MS. MASNY: I was going to say something very similar to what Debra said, that I think if we could clarify what are the important priority issues that we have to address versus those areas where we could make more quick recommendations, because we would want to be able to focus most of our time on those areas where we want to set the priorities rather than spending time where we just need to make a quick recommendation.

DR. McCABE: Thank you.

Emily?

DR. WINN-DEEN: Well, I think we seem to be coming to a little bit of a consensus here in terms of what we might want to do, so I'm just going to try to reiterate for a moment what I think I've heard in this discussion. That is, when we vote this time on priorities, I think we should try and consider what issues are sort of burning issues, what issues the committee can actually do something about in the time frame that we have to work with it, and what are the issues that we believe are important but are either already dealt with or someone else is dealing with them in sort of an active mode. I mean, the goal of this exercise is to focus

on getting to a small subset, and we'll say three just as a guiding number, of things that we're actually going to specifically work on and push to take action, not that all of these things aren't important but to try and have some guidance on priority, sort of the "so what?" rule.

So if we do something with it, so what? That's just sort of my comment on maybe how we could think about prioritization.

DR. McCABE: Okay. So with that, we will vote. It is the blue sheet in your folder. The green is for the second straw vote. Please vote. Recognize that there was a lot of discussion about this on the conference call in terms of prioritization. They're just alphabetical here. That's the way they are listed here. There is no priority intended. It is merely alphabetical on the blue sheet.

Please vote, and then Sarah and the staff will pick up your votes and tally them during the break. We will resume at five after 10:00. For members, ex officios and presenters, there are refreshments here. For the members of the public, there is a gift shop out in the lobby of the hotel for refreshments.

We'll resume at five after 10:00. Thank you.

(Recess.)

DR. McCABE: Let's go ahead and get started, then. First of all, I want to just comment on the task force and what you will see is some very fancy footwork now, because each of the members of the task force had topics that they were responsible for. We did not know which were going to be prioritized, so they have all been prepared to lead the discussion.

Before we start to look at the screen, as everybody is watching and not really paying attention to my comments, but I just wanted to remind you that really the straw vote will organize the discussion, but there will be another straw vote that occurs later. Remember, the purpose of our discussion today is to help us think through the issues. It's not to resolve the issues, though with a subsequent discussion we're having there may be some that can be resolved very quickly.

We're not trying necessarily to address the substance of the issues, and we should not be endeavoring to resolve them, as I said. We want to discuss them in sufficient depth to allow us to weigh the relative significance, and again, problem solving will begin tomorrow, not necessarily today, though with some comments that Chris Hook is going to make, there may be some resolution that could occur to some of these today if the committee wishes to do so.

So can we go to the next slide, then? Chris had some ideas that some of these are yes/no. If we look back at the points, the guiding questions, Round 2, it's on page 2 of the handout, the PowerPoint from Emily's presentation. There are four of these points that Chris thought are probably fairly straightforward yes/no and that, in fact, some could be resolved fairly quickly, moved up and dealt with, or moved down and assist us with decreasing their priority.

So, Chris, do you want to comment on this, please?

DR. HOOK: Thank you, Ed.

My concern was that all of these issues are important or they wouldn't have made it onto the final list, and I think it's important that we acknowledge that and that subsequent rankings don't diminish the importance of a given issue by our choices. But we also have to recognize on a practical basis that the Tuckson questions are yes/no sorts of issues. Is

someone else working on it? Do we have jurisdiction in the first place? I think we should answer those simple questions first just to acknowledge or recognize those areas where we may be able to move on quickly and say it's not that we don't think the issue is important, but for these simple reasons, practically, we probably should move on to something else. So those were the four that I picked out of his list that seemed to be the easiest to answer in a straight yes or no fashion.

DR. McCABE: Thank you.

So everybody can see this, and just to comment -- I'll be saying more about this tomorrow -- but Reed is not here today. That's because Reed was picked to be a member of a blue ribbon panel that the NIH has looking at their conflict of interest policy, and that panel is meeting exactly at the same time as we are. But Reed will break away for a couple of hours tomorrow to join us because he has some additional rules that will be important for us to discuss. But I'll talk about those more tomorrow when Reed is here with us.

So basically, these are the four points that Chris picked out and mentioned briefly. Does the government have jurisdictional authority over the issue? Does the issue raise concerns that only the government can address, or would the government involvement be duplicative? We heard today about, for instance, the patent issue may fall into the second. Is there another body addressing the issue or better equipped to address the issue? Again, the same thing with patents. Have the policy solutions to the issue already been worked out?

So with that, any discussion of these four points? Do people agree that these are fairly straightforward and to some extent yes/no, or at least we can debate the yes/no nature of them on a point by point basis, issue by issue basis?

DR. WILLARD: Yes, I agree with Chris totally. I think at the end of the discussion, as you're leading up to straw vote 2, it may actually be better to vote on each of the 12 and put them into one of three categories. One is it's not a high priority, so we're not interested in dealing with that at all. A second category that says it is a high priority. We simply want to make a very short statement and pass that on to whoever else is better equipped to deal with it, but at least go on the record as saying it's high priority and this is what we recommend. And then the third class, the relatively small number of issues that are meaty and chewy and that we're going to really get into over the next year, and one of those, just to tip my hat -- I mean, genetic discrimination may be one of those second class issues, the second of the three classes --

DR. McCABE: A Class 2 issue.

DR. WILLARD: -- because I am very nervous about this committee not saying that genetic discrimination is absolutely a critical, burning issue for us. If we rank that number 10 out of 12, you can bet that will come back to haunt us someday, because the House in particular will look at it and say clearly this is not a burning issue or they would have addressed it number 1. Yet that's an issue that we in a half-hour could draft a quick statement, get it out, and then move on.

DR. McCABE: Yes, Joan?

DR. REEDE: Speaking against this issue, the genetic discrimination, I actually think among the 12, when we get through with this, there are some issues that are recurring, and when I think about something like genetic discrimination, it could be addressed in all of the other 11 issues that are mentioned. It should be a part of them. I think to pull out some of them that are overarching issues such that no matter what we did a component would

have to address something like genetic discrimination -- for example, if it was determined that a population study was important, clearly genetic discrimination would have to be a part of that. I think what that does, it stresses even more the importance. It's saying it's not something you can pull out, examine once and be done with, but rather it's a recurring theme, that no matter what area we go into, we have to look at what is the impact with regard to genetic discrimination. There may be a few others that fall into that same category of being so overarching that we need to look at them no matter what the topic.

DR. McCABE: Thank you.

With that, and just to reiterate Hunt's categories the way I have them down, number 1 was not high -- and I would say not high enough priority rather than not high priority. Number 2 is high enough priority but can be dealt with briefly, quickly. And number 3 was high enough priority and meaty enough to warrant further discussion. I think those are important points.

But with that background, now we will begin an in-depth discussion of the 12 issues with the highest ranked issue, which is access. Can we go back to the other slide? So here we can see that we have the members list on the left again, the ex officios on the right. We see that access was number 1 on the members' list, number 3 on the ex officios' list. Some of them moved up or moved down. Some of them moved sort of in both directions on the two lists, up on one, down on the other, to bring them a little closer together. I think it will be important to discuss some of these differences as we go through.

Having said that access is the number 1 on the members list, then I think, as I mentioned before, each of the members of the task force was prepared to now be called to action to begin to discuss these issues, and they will serve as our discussion leaders. The task force members will use the policy considerations outlined in the issue briefs with the expansion on those as we just heard. We want to keep the priority-setting criteria in mind. Emily reviewed these before, and as we begin to discuss the specific issues, I think we can go back to -- is it possible to put all of the priority-setting points on the screen? Would that be helpful to everyone? We've sort of separated them out now, so it may be hard. You have them accessible to you in the handout that represents Emily's PowerPoint.

So, Barbara, you will be the discussant for access.

MS. HARRISON: Okay. I think I just want to very, very quickly summarize the issue brief and explain again that within the issue brief of access, that there are several different subcategories within that that are also on our issue list. These included, as far as the development of genetic technologies, the importance of large population studies that involved diverse populations and pharmacogenetics, and the further development of those technologies, patents and oversight, and the accessibility of the public, coverage and reimbursement, public awareness and education of health professionals, and then finally discrimination so that people do not feel inhibited to pursue such technologies and fear that they will be stigmatized.

So I think we will just go right to the questions. I don't want to take more time than necessary. So the first question we have is does the government have jurisdiction or authority over this issue? I can field responses. Any thoughts about that?

DR. McCABE: So, access. Does the government have authority, jurisdiction over this?

I'll lead off the discussion, and I would say yes, to some extent. Does

anybody wish to comment?

MS. HARRISON: I guess I could further say that I think because access covers so many different topics, it's maybe difficult to even answer this question because some aspects we may feel government does have control over, while other aspects it does not.

DR. McCABE: Yes, David?

DR. FEIGAL: Just a quick comment. I think the access falls down into two categories. One is the regulatory category of how things come to market and move from being investigational and access to investigational tests. Some of that's government, but some is also local IRBs, which aren't government. Then there's the CLIA standards and the FDA standards and how they control access. Then there's the indirect government role in access that relates to coverage decisions that practically affects access by determining what you can actually get paid for.

MS. HARRISON: Okay, both of which we can have an effect on. So let's move on to the next question.

Does the issue raise concerns that only the government can address, or would government involvement be duplicative? Are these issues that if we put forth effort into researching them are things that other people are doing anyway, and so we'd be reinventing the wheel and we could better extend our efforts elsewhere?

Joan?

DR. REEDE: I think the answer I would have here falls under the same category as the last statement in that there are some things that the government really would be involved in addressing, such as the regulatory issues, the things that are under FDA, et cetera; and then there are some others that may fall under state or federal. I mean, I think it's broad in terms of the response here. So there's a general answer of yes, but it depends on what aspect of access you're looking at.

MS. HARRISON: Chris, did you have a comment?

DR. McCABE: Please use your mike just so that it can get on the record.

MS. HARRISON: Suzanne?

DR. FEETHAM: It's also important, I think, to frame this in thinking of the federal role as just by having voice and recognition of it, it may move these programs along, and I think that's a very important component of that. It's not duplicative. It's complementary in the light of its acknowledging the interest of the government.

MS. HARRISON: Brad?

MR. MARGUS: I absolutely think access is important, and I think this committee's composition, the people on this committee are able to give some really good insights to it. My problem is it seems like a very different word or a different category than everything else on our list because access is going to be discussed in every other area that we're going to vote on anyway. Then if we voted on this one, and let's say we were only going to do access and nothing else, based on what we just heard, then we're going to talk about all the things on the list. It's kind of a different category than the other categories. It's absolutely important, but it's not specific enough that when you say you're in favor of making access an important priority, that you really know what you're going to be talking about because there are so many things it covers.

So my vote is that as a category of one of the things to focus on for the committee, I would say we shouldn't make access really one of them. But when we pick our

three or whatever number of things we're going to really focus on, make sure access is clearly dealt with when we talk about them.

MS. HARRISON: Paul?

MR. MILLER: In thinking about the guiding questions, which I found really helpful, I read that a little differently than what's been put on the table. Instead of asking the question does the government have jurisdiction, my sense is this is an advisory committee to the Secretary of HHS, and so in a sense I'm reading it a little bit more narrowly and saying, well, does HHS have jurisdiction. If this committee is coming up with recommendations to the Secretary of HHS but ultimately HHS has nothing to do with FTC issues or patenting issues, then the government may have jurisdiction about it, but it may just not be appropriate for an HHS committee. That's the way that I've sort of been prioritizing these things.

It may, in a sense, explain more fully why there's a difference between ex officios and public members of the committee. Public members of the committee may think these are really important issues in terms of genetics health and society. The government being the government, the bureaucrats, may say, well, this is really not an HHS issue; this is my agency's issue. Why are we telling Secretary Thompson about that?

So if I am wrong in that this is a much broader mandate than just HHS, that's sort of a good point to discuss. If this is really an advisory to the Secretary of HHS, that may help focus some of these issues.

MS. HARRISON: Emily?

MS. CARR: I was just going to speak to that.

MS. HARRISON: Oh. I'm sorry, Sarah.

MS. CARR: One thing to consider about that -- Paul, you raised a very important point, and the committee should be aware that its main purpose is to advise the Secretary of Health and Human Services. But there is a reason why all of the other agencies are represented here. So if the committee decided that, let's say, patents was the highest priority issue, and obviously this is an issue that is handled principally by the PTO, and the Department of Commerce does sit on this committee, it could be that we would decide to write to the Secretary and ask the Secretary to recommend to the Secretary of Commerce that something be done.

So I think there is a little room. Obviously, unless the Secretary of Commerce wants advice on that issue, I don't think it would be necessarily appropriate for this committee to offer it. But there are other mechanisms, I think, where you can have some effect on issues that are not solely within the purview of the Department of Health and Human Services.

MS. HARRISON: Emily?

DR. WINN-DEEN: I think when we worked on this as the task force, we actually did have sort of in our heads a narrower discussion, that this was really what can we as Health and Human Services do. But I agree with Sarah that if there's something we see that needs doing, I think we could still refer it. We maybe shouldn't make it one of the things that we're going to deliberate on, but we should still at least be responsible as members of the community and the public making recommendations to our government to draw attention to it.

MS. HARRISON: Also, I'd like to add that under the subject of access, there are topics there such as coverage and reimbursement, Medicaid, et cetera, that do definitely fit under HHS. So I think it's valid for us to consider it.

Debra?

DR. LEONARD: I agree with Brad and with Joan that this is an overarching issue, that we really need to look at the individual components of access and consider whether those are high ranking or not.

MS. HARRISON: So perhaps going back to the suggestion, this can offer as a framework, as a way to look at other issues. It may be possible.

Cindy?

MS. BERRY: So am I safe to assume that the committee's judgment is that access should be afforded to everyone to genetic technologies, that that's a goal that we want to achieve? When we say access, what do we mean? Do we mean that all individuals, regardless of insurance coverage, regardless of race, regardless of socioeconomic background, whatever else, they should have access to these technologies and the health care benefits that they could produce? Is that kind of the statement that we want to make? Is that what we're saying when we rank it number 1?

MS. HARRISON: Emily?

DR. WINN-DEEN: Well, I guess I would go back to the Constitution, that our goal, our ideal is equality for all. So, yes, from that point of view, the ideal goal is equality for all. Are there gaps between that ideal goal and reality and practicality? Absolutely. So I think that's what we need to address. Maybe I'm just speaking for my personal voice, but I would say that the overall goal, as it is probably with all health care, is equality for everyone.

MS. HARRISON: Hunt?

DR. WILLARD: Then that goes to the issue of exceptionalism again. So we end up having to focus, within the general area of access, on which are the specific issues where one might want to tackle access to genetic or genomic services or tests different from the general statement that says everyone should have access to everything in the realm of health care? There's a thousand new technologies that people don't currently have open access to. Should we be saying that genetic technology is somehow different than all of the others, or they're just the same issues that have been dealt with and continue to be dealt with both on the political and scientific end?

MS. HARRISON: Joan?

DR. REEDE: I would like to suggest that at a minimum the committee take the issues of discrimination and access and say that these are issues that are going to have to be covered no matter which topic. As opposed to discussing is access important, be able to come back when we look at the other topics and see to what extent should access be addressed here, to what extent should discrimination be addressed in each one of them, because I think these are so overarching that if we pick them, basically what we're doing is just starting from ground zero again and saying everything. So I think being able to say when we look at a topic what are the areas of discrimination that we need to take into consideration, what are the areas of access that are relevant here, and making sure we look at them is a practical approach around this issue of can we resolve everything under the heading of access.

MS. HARRISON: Kaytura?

DR. FELIX-AARON: Yes, I have two points that I'd like to make. One is on the issue of access. I struggle with the scope of that issue because I find it's so broad. When we try to sort of operationalize it, like Emily and others did, I find that it's even more problematic, because what I hear in the statement that everybody should have it, because

equality is a value that everybody should have access, is that it can be interpreted as the fact that access to genetic technology is a human right; however, health care isn't a human right.

So I think we get quickly into trouble when we make such broad statements, and I just think they raise areas of conflict for us as a committee, but also for the Department when we make those types of statements.

MS. HARRISON: Robinsue?

DR. FROHBOESE: Hi. Good morning. I do think it's possible to use the construct of access, and I agree with those who have suggested having it as the overarching framework guidance for the committee's activities, and having it really more in keeping with a vision statement or the goal that we are trying to achieve. I think certainly we can support equal access as being fully consistent with the Secretary's initiatives around enhancing access to health care, Healthy People 2010. I think the concept of access without answering the ultimate question of whether everyone is entitled to health care is something that we can endorse and should endorse as equal access to opportunities within genetics.

MS. HARRISON: Ed?

DR. McCABE: Based on this discussion, we've actually added a fourth category to your three, Hunt, and that was added as a third, keeping the high enough priority and meeting topic as the final category but now a new third topic of an overarching framing topic that needs to be considered in the context of each of the other issues, because I think that's what this discussion is really telling us, that some of these are so important that they transcend through all of the other issues.

Is that acceptable to the committee, then, as we begin to think about these, to have that fourth category but we're calling it Category 3?

MS. HARRISON: Cindy?

MS. BERRY: Is there any other issue that falls under that new category, though? Because I was one of the ones early on that was sort of advocating for access as the framework, and I still think that's the way to go, and I posed the other question just a moment ago because I think we should really nail down what it is we're saying when we pick access as number 1. We could be saying everyone is entitled to it and making the big overarching, lofty statement; or we could be saying it's integral to everything, it's the framework under which we consider all these other issues. There may be another way, but I don't know if there's another issue besides access that falls into that category, that new third category.

DR. McCABE: I'd just speak to that point before we move on. I think the other point was made that discrimination really is the other of the categories that is integral to so many other things.

MS. BERRY: Do we think discrimination, for example in patents, does that have a role in there? Discrimination is one of those issues that we all care about and think is really a top priority, but I'm not sure it fits or is as pervasive in all the other categories.

MS. HARRISON: Martin?

MR. DANNENFELSER: I guess I have a question on access. By access, are we saying really coverage and reimbursement? Is it an economic issue we're talking about, or is it broader than economics? Are we saying that people have access by virtue of having the economic wherewithal to get these tests, and then if so, it seems that that's basically -- maybe that's a coverage and reimbursement issue. Or is it a broader question as to who will be allowed to have access to this service, and then the question of reimbursement is perhaps an

overlapping but not completely all-encompassing issue in that area.

I think just briefly on the genetic discrimination, I think that's a different issue in that I think that that relates very much to the individual, basically kind of the privacy of the individual and things of that nature. So I think that's a different issue. I think that's an issue unto itself largely, but to me it sounds like the way we're defining access sounds very similar to a debate, if you will, about coverage and reimbursement.

MS. HARRISON: Ed?

DR. McCABE: Yes, I agree. I think that access can be included in coverage and reimbursement, and I think that as an individual that's how I saw it early on. But I think, as I've thought about it more, I really do think it is pervasive. I think that in response to Cindy, is genetic discrimination as pervasive as access, I think they're the ying and the yang, as it were. I mean, lack of access by any individual or group becomes discrimination against that individual or group if an individual doesn't have access to this.

So that's why those two, I think, are integral to so many of the others. For instance, with patent and licensure, I think we heard in the Secretary's Advisory Committee on Genetic Testing the concern about Canavan disease families, that because of overly restrictive licensure, they felt that they had been discriminated against. Having supported the research with both their samples and their money, they then did not have access to that.

So I really do think it can fit, as I thought about it. It fits into all of the other categories.

MS. HARRISON: Joan?

DR. REEDE: I agree with that. I think the other part is it is such an important issue for the public that it needs to be seen and stated explicitly, just not implicitly. So I think if we're talking about overarching, to be able to say repeatedly as we look at various topics that discrimination is an important aspect. It sends a message that the committee really does take this seriously.

MS. HARRISON: Kim?

MS. ZELLMER: I think the other aspect of access is not only coverage and reimbursement but I think that physician education plays a large role in it as well, because if you don't have a physician who can diagnose the problem initially, you're not getting access to genetic technologies that may be beneficial as well. So I think that it does apply in a lot of different areas.

MS. HARRISON: So I guess true to form, we basically agree that access covers many, many different areas and maybe just needs to be placed in Class 4. I don't know if that's a decision we can come to at this point or if we need to wait to do that.

DR. McCABE: Well, certainly we can come to the decision. We can have these typed up so that people can see them, but the four categories again would be not high enough priority to pursue in the initial consideration; number 2 is high enough priority but can be dealt with in a brief statement or some other rapid approach; number 3 is that it's really important to every other topic, integral to each of the topics. So in that sense, it gets taken off the table because it will be included in the discussion of each of the high-priority topics. Then 4 would be high enough priority and meaty enough that it deserves substantive deliberation by the committee.

MS. HARRISON: Okay, I think Cindy had a comment.

MS. BERRY: Just a point of clarification on the genetic discrimination

issue because I'm hearing from folks now a broader definition or concept of genetic discrimination. When we initially looked at it or the scope of our letter, it was confined to the legislation which had to do with using genetic information against somebody for purposes of health care and also employment discrimination issues. It wasn't really discussed as broadly as we are now. We can do whatever we want, and I have no objection to the broader interpretation.

But talking about other issues, like if someone uses or volunteers their genetic material for research, are they being discriminated against if they can't get the benefit of that, that's a much broader concept of genetic discrimination than what we originally focused on and what we originally ranked, I think. I have no objection to the broader interpretation but just want to put that out on the table because it's different from what we originally looked at.

MS. HARRISON: I agree with you, Cindy. I had the same reaction.

I'm sorry, Sarah.

MS. CARR: What I was going to suggest is that perhaps you could put genetic discrimination into that transcendent category but also place it in the second one, which is that it's a very high-priority issue but can be dealt with rather swiftly, perhaps through another letter to the Secretary, and you can make an overarching statement as well, that it is one of your highest priority concerns.

MS. HARRISON: I don't want to get off on the genetic discrimination tangent too much right now, but I think staying on access -- I don't know if we can just take a quick vote to see if that goes into Class 3 -- is it Class 3 or 4? Class 3.

DR. McCABE: Is that fitting with the committee, then? So access, then, would fit into that new Class 3, which is pervasive and should be considered in the discussion of each of the other issues or in the deliberations of any issue that rose to the top in the priority.

MS. HARRISON: Is there any opposition?

DR. McCABE: Let's take a vote, and probably it's a vote of the membership. We can then take a straw vote of the ex officios.

How many individuals would agree that access should go into group 3? Can I see a show of hands?

(Show of hands.)

DR. McCABE: Anyone disagree?

(No response.)

DR. McCABE: I'm not seeing anyone who is a member who didn't vote, so it appears that that's unanimous. So then access would move into Category 3, which probably explains why it was number one, because everybody saw it as such a pervasive issue that needed to be considered.

Okay. Well, that was very quick, because we had planned to have all the discussion through the morning on that. But I think that was easily dispensed with as we got to the heart of what the real issue was. Thank you, Barbara.

So the next is coverage and reimbursement, and you're not off the hook, Barbara. You're still on to lead the discussion of coverage and reimbursement.

MS. HARRISON: Okay. Now, on this issue I do want to note that we'll be getting more detailed information this afternoon on this specific issue. However, I do appreciate that our purpose now is to see whether or not it's something that we feel we can have an effect on.

One thing I want to note that wasn't really highlighted I don't think in the overview this morning is that the Secretary's Advisory Committee on Genetic Testing had actually done some work on this topic, and I would argue that could offer us a springboard for us to continue. They had come up with two reports, "Coverage and Reimbursement for Genetic Education and Counseling Services," and also "Coverage and Reimbursement for Genetic Testing Services." Those reports, I believe, were not completed, but they were in development when that committee was ended. So one thing I want to offer is that we could possibly continue work on that.

They had also defined next steps as including drafting a letter to the Secretary expressing their urgent need for data on health on the economic value of genetic services, including genetic testing education, and had also proposed to convene a roundtable with individuals who have a role in and/or are affected by coverage and reimbursement decisions for genetic services as a way to assess the need for policymaking in this area.

So I just want to have those things in mind, again, as we go through these questions.

So the first would be does the government have jurisdiction and authority over this issue? I would say that we do.

Emily?

DR. WINN-DEEN: Well, I think the government does to the extent that there is a government insurance system. But there's also a huge private payer insurance system over which Health and Human Services doesn't have much authority. Maybe influence through where they set Medicare and Medicaid reimbursement levels and what criteria they use, but we do have to recognize that there is a third-party payer system out there. I don't know what the ratio is. Maybe someone from CMS knows what the ratio is between private payer and public payer in the U.S. I mean, it's a substantial contributor.

DR. REEDE: It's in our handout. There's a table that describes the relative percentages of coverage, and employment-based private insurance is about 60 percent, and a combination of Medicare and Medicaid is about 25 to 30 percent.

MS. HARRISON: Right. The combination I think is around 30.

DR. McCABE: I think it is important to point out that CMS establishes through Medicare reimbursement schedules, what is frequently picked up by the third-party payer. So while I agree that it's an influence rather than responsibility, but it is an important influence.

MS. HARRISON: So I guess there is agreement that we do have some jurisdiction.

Oh, I'm sorry. Debra?

DR. LEONARD: There are also upstream aspects to this, like billing codes that get created. That's what the reimbursement is set for, and sometimes the billing codes are inadequate to provide information to third-party payers in the area of genetics as to what is being performed, because the CPT, the billing codes are so generic that there's no real test information provided to payers to provide reimbursement.

MS. HARRISON: This is a particular issue with the genetic counseling and education portion.

So I think we'll move on to the next question. Does the issue raise concerns that only the government can address, or would efforts be duplicative? My feeling, from what I

reviewed, is that our input would be very useful. I don't know if anyone has any other views on that.

DR. McCABE: And I think your point in the preamble, your discussion that there were documents that had been prepared and were ready to be rolled out by SACGT, so using those as a springboard, perhaps revisiting them now a couple of years later, that they might serve as a way of getting our arms around this issue fairly quickly.

MS. HARRISON: Okay. So I guess I can feel agreement on that issue.

The next one is, is there another body addressing the issue or better equipped to handle this issue?

MS. MASNY: I still had a statement for the last one.

MS. HARRISON: I apologize.

MS. MASNY: I'm not in your line of sight.

Are there issues that are raised by this area of reimbursement? I think it is a big policy area because one of the things that has been brought out in the brief is that Medicaid itself does not cover screening, and that with the translational effect of the Human Genome Project, that much of the genetic technologies and services are going to move hopefully to the area of prevention and health promotion, where disease has not yet been identified.

So I think in this whole area of reimbursement issues, we could make a policy statement about the need to look further into actually better funding, and then of course access to prevention technologies.

MS. HARRISON: Emily?

DR. WINN-DEEN: I agree that this is definitely an area where we could make some very positive influence. There are also a number of professional group organizations that are taking up this issue, and I would say that if we decide it's something that we want to work on, we should also try and incorporate their expertise and work group products as well. AdvaMed I know has got a broader reimbursement overall of the CPT code system level task force working. So in the context of an overhaul of the whole system, I think we certainly could provide input on what things are missing, need to be there for the things that are inadequately described by current codes.

I mean, this is going to be a big issue of do we have to go to the House and the Senate every time we want to get a new screening test or predisposition test, because they don't cover any of that under the current system. In fact, just out of curiosity, I wrote to our reimbursement folks when the latest thing came out on cardiovascular screening, and I said, well, what if we had a genetic predisposition test, would this be covered. And they said, well, cholesterol, yes, but probably not ready for genetics.

So there's a mechanism with the U.S. Preventive Services Task Force, but that's where you have to go to get a recommendation. Maybe that's another group that would benefit from getting some guidance on integrating genetics into preventive medicine.

MS. HARRISON: Ed?

DR. McCABE: And Sarah reminded me that one of the conclusions of the SACGT work group was that there needed to be more of an evidence base, there needed to be development of an evidence base for some of these tests and the recommendations for tests. But again, we could visit that, and that might then intersect with the large population studies as well. I think these are not necessarily going to be independent issues as we go forward, and we can explore those intersections.

There may be some where there are groups working on them and it would be duplicative for us to do it. There may be issues like this one where there are a number of groups that are working, both federal and professional organizations working on them, and we can serve as a forum to bring those groups together. It sounds like this is one where that might be the case.

MS. HARRISON: So the last question as to whether policy solutions on the issue have already been worked out, I think for the fact that we're talking about this, the answer is no. I don't think there's any dissenting opinion about that.

(No response.)

MS. HARRISON: Okay. So were there other questions, or did we only want to get through these? I think there was another level of questions.

(No response.)

MS. HARRISON: How urgent is the issue? Is this something that if we didn't address today, or even within the next couple of months, it would not cause much harm, or is this something that we really do need to put effort toward now? My feeling is that this is something that we need to put effort toward now. We need people to be able to access these services, and already people are running into problems.

Any thoughts? Emily?

DR. WINN-DEEN: I think it's been pretty clearly identified that there are certainly some specific gaps with coding for services and testing modes that are just not there, and you're forced to use some sort of make-it-fit generic code which drives reimbursements. So I would say there's at least that level of need for some work, but I'm also very concerned if there's a sort of global overhaul, as is being discussed, of the whole reimbursement system, that we need to be active participants in that.

MS. HARRISON: Joan?

DR. REEDE: I think whether it's anticipating a global overhaul of the system or whatever, I think being very proactive about this, so taking a stance on these types of issues early on, as opposed to waiting until there are more tests available, et cetera, and then saying we need to do something about it would be important for the committee, sort of laying a foundation or groundwork in terms of what are the principles that we think should be operating in terms of compensation and reimbursement, what are the target areas that really need to be addressed or attended to.

MS. HARRISON: I just want to pause here. One thing that I'm curious about is that amongst the ex officios, this is not ranked quite as highly as it was amongst the SACGHS members. I was just wondering if anyone had any opinion as to why that was, or if you ranked it lower, why that was.

(No response.)

MS. HARRISON: No one wants to own up?

DR. COLLINS: Well, that wasn't true for all the ex officios. NIH ranked this, I'm not sure, either first or second.

DR. McCABE: And why was that, Francis?

DR. COLLINS: Of the topics in front of the committee for consideration, going through the guiding questions, trying to identify ones where this committee has strength, jurisdiction, access to decisionmakers, and where there's a pressing issue that no other body is taking on, coverage and reimbursement seems to NIH to be very near the top of the list, maybe

at the top of the list.

MS. HARRISON: Okay.

DR. McCABE: But pursuing Barbara's question to the ex officios, because I think that is important, and it's okay to disagree with the members. But it's important for us to understand why there might be that disagreement.

DR. FELIX-AARON: Again, it was not because it wasn't important, but what drove me was the unique federal role, or not even the federal role but the unique HHS role in that. I saw it as a complex phenomenon where points of leverage were clearly within the HHS -- that is, Medicaid and Medicare -- but 60 percent of the points of leverage are outside of the private sector. I mean, private insurance companies are regulated by state government, and many of those policies are local policies. So even when you look at Medicare, a lot of the policy coverage decisions are made locally and not at the national level.

So the question for me was where are the opportunities for this committee to provide guidance? Where are the immediate opportunities and where are the specific leverage points? I didn't see those opportunities or immediate leverage points.

MS. HARRISON: Paul?

MR. MILLER: I guess with all due respect, it's for exactly those reasons that I think coverage and reimbursement should be ranked at the top of the list, because I think the government does have an influence in those issues, not that HHS sort of governs the entire marketplace, but because what HHS does in terms of its government programs is tremendously influential and can be very groundbreaking in setting standards and pathbreaking in terms of what it does. So in terms of policymaking, I think for those reasons this is an important issue. At least it was in terms of our ranking of where there is a gap and where the voice of the HHS Secretary ultimately can be influential.

MS. HARRISON: Linda?

DR. BRADLEY: I would just add that I agree with the concept of applying leverage, but also the issue of does sufficient data about the issue exist. One of the issues for reimbursement is whether the clinical utility has really been established and whether the case can be made that this is something that should be integrated into health care. So I think that's something that needs to be thought about.

MS. HARRISON: Cindy?

MS. BERRY: So what we might be saying, then, is not that all genetic technologies should be covered and reimbursed, but maybe if our committee addresses this issue it would be to look at and to build on some things that Joan and others have said, maybe establishing some principles or guidelines for, whether it's companies or whether it's federal programs, how they look at genetic technologies and tests and determine whether it's appropriate to cover or reimburse. When does a technology cross that magic threshold that warrants coverage and reimbursement, and adequate reimbursement?

DR. FELIX-AARON: I totally agree with you, and from my agency's perspective we'd be particularly interested in decision support for making policy and coverage decisions. I mean, we do support technology assessment. So as part of that mandate, adding to the evidence base that helps policymakers and other decisionmakers determine what should be covered, how much, doing cost-benefit types of analyses. We'd be very pleased to support that type of building of the evidence base.

MS. HARRISON: Brad?

MR. MARGUS: So at the last meeting, I can remember Debra making some comments with real practical experience about doing tests for people and how this was a major problem and roadblock that had to be solved. Whereas access was something that transcends all these things, I saw coverage and reimbursement as something that's going to be the ultimate roadblock for a lot of these other things. If you succeed with education and training and we have genetic counselors everywhere giving pre-test and counseling, and if we're doing great large population studies and coming up with all kinds of new discoveries about diseases and pharmacogenomics with predictive markers and everyone is aware of it publicly, but in the end the test can't be given because no one will reimburse, that seems like a real problem to me.

So it's really clear to me that we've got to deal with this. I guess my skepticism is just that, again, we may deliberate over it at length and get a lot of information. I'm really excited about the presentations this afternoon. I think because of what happened at the last meeting is why we're doing it. But in the end, are we going to just send a letter to the Secretary that says, oh yes, coverage and reimbursement is important to us? If that's all we're going to do, then it doesn't seem worth all that deliberation. If we're going to really get insights about ways to differentiate between what gets reimbursed or something that's really helpful, then I'm in favor of it.

I'm curious as to what others' views are on what we can actually accomplish in this committee on coverage and reimbursement.

MS. HARRISON: Ed?

DR. McCABE: I was going to make very similar comments about how important this is, because I think the marketplace does drive who goes into the field, who stays in the field, as well as the access of the patients to the technology. If no one is paying for it, it's going to be very difficult to have the technology.

In terms of what we could do, I think that's what we could explore, where the tipping points are and how we could actually have an impact. Just saying that we need better reimbursement probably isn't going to accomplish it. What is the evidence base that we need? Certainly, it's important to have evidence-based medicine. However, as a pediatrician, I would point out if we practice evidence-based pediatrics, we'd have almost no medicine since that evidence base is just beginning to be accumulated. So we also have to be realistic in terms of what we can demand of the technology as well.

MS. HARRISON: Agnes?

MS. MASNY: I was going to make a similar point, and also just to say that one of our mandates was also to identify some of the gaps in the research, and as Linda and Kaytura had brought up, it's not only the clinical evidence but also the gaps in the research, especially in the area of the cost-effectiveness and the cost-benefit ratio, and this may be an area that if further research could be done and the private insurers could see the benefit of such testing, then I think they're more likely to pick up the reimbursement. But we would first need to identify the gaps that would need to be addressed, and this would be something we could make a statement about.

MS. HARRISON: Joan?

DR. REEDE: Just following up on the thoughts that have already been expressed, for me, we're not at this point in time determining what it is we would do or what it is we would say but rather saying is this important enough for us to have it as a priority area for

further study. So just sort of a point of clarification on that.

MS. HARRISON: Debra?

DR. LEONARD: Following up on what Brad said, as well as addressing the urgency issue, if the coverage for genetic tests is not dealt with so that the reimbursement is higher, there won't be laboratories to do this, because right now most genetic testing is done at academic health centers that basically subsidize this testing with better-reimbursed laboratory testing that's available, and almost all molecular pathology, molecular genetics laboratories lose money because of the billing codes that exist and the reimbursement levels that are set for those billing codes.

So as genetic testing grows to consume larger and larger portions of the laboratory testing that is done, these laboratories will not be able to be subsidized like they are now. So while the issue is not so urgent today, if we don't anticipate and correct the problem, it will be a horrendous problem in the future.

MS. HARRISON: Robinsue?

DR. FROHBOESE: It does seem that given the fact that our predecessor committee had already laid the groundwork and actually had a draft report, that this would be a really important project for this committee to pick up on. As an ex officio member representing the Office of the Secretary, I really do think that this report and a letter to the Secretary is good timing. It fits in with the Secretary's overall initiative on looking at uninsured, underinsured, Medicare reform, as well as prevention. So I think it really ties in nicely with a lot of things that are going on in the Department right now.

MS. HARRISON: Emily?

DR. WINN-DEEN: Just listening around the table, I'd say that what I've heard is that not only do we think this is an issue that has some value and urgency to it, but there's also two areas where it meets the meatiness criteria. One is just simply reforming the current system to have codes for things with which there is already an established clinical utility but we're not able to properly capture the activities that are required to generate a test result. The other is to think about whether this committee could provide a framework guidance document for what is sort of the criteria that all insurers, public and private, should use to determine the clinical utility bar and cost-effectiveness bar.

I think if such a guidance document was available, even if all it is is a guidance recommendation, it certainly would help the people who are trying to get tests to that level to have sort of a common set of goals. If I come in with a package that has A, B, C, D, and E, that meets the reimbursement criteria, and I think it would greatly facilitate the design of the right sets of studies and experiments, whether they're large population studies that the NIH funds or individually funded by diagnostic manufacturers or laboratory validation studies for the home brew environment. To try and create some common framework I think would be enormously valuable to the community.

I think SACGT tried to do that sort of with setting different levels of lab tests, but they didn't really address what was necessary to make the clinical utility and the cost-effectiveness arguments.

MS. HARRISON: Debra?

DR. LEONARD: Well, in dealing with one private insurance company on reimbursement issues for all of infectious disease molecular-based testing recently, their criterion is is there a published paper out there, or papers, that basically demonstrate clinical

utility, and that's their criterion. So walking in with your own information about clinical utility has no impact on insurers to pay for something. It's the published literature currently.

DR. WINN-DEEN: But that's still a clear goal, then. The goal is to get a publication so that you have a publication. But I think if we could create a set of guidelines that -- I mean, this is maybe getting into more of a detailed discussion but just trying to go to the meatiness argument, I think there are some very specific things that this committee could work on developing and trying to set standards that would be helpful to the community as a whole, and to Health and Human Services.

MS. HARRISON: Chris, and then Ed.

DR. HOOK: I just want to strongly support Emily's comments. I think that that's a very practical and important thing, working with investigators and clinicians trying to determine when tests should come out, and that influences when they should be reimbursed for clinical services.

Just a comment to put a little asterisk by this, this will of course be a bit of an overlap when we talk about the regulation and oversight as we consider that later on, are we really covering now in this discussion most of what we were concerned about in that topic.

MS. HARRISON: Ed?

DR. McCABE: With those comments, and I think there will be points of contact between these different issues, and we can discuss how much contact there is if they're subsumed by versus just touching upon, but that will be for further discussion. So I'm hearing that the consensus of the group -- I'm not hearing anyone saying that this is not something that should stay on the list.

I'm going to just ask us to vote not only -- we aren't really prioritizing now, but I think it does help us to categorize these given these categories. So what I'm hearing is, with the discussion of meatiness, that that is a criterion for Category 4. So is that an agreement that this is Category 4? Anybody who wishes to speak to it being in another category, being in two categories?

Cindy, did you want to comment?

MS. BERRY: It just sounds like we're categorizing hurricanes -- you know, Category 3, Category 4.

(Laughter.)

MS. BERRY: I put it in Category 4. That's how I vote.

DR. McCABE: Okay. So hearing no dissent to that, all in favor of this being in Category 4, say aye.

(Chorus of ayes.)

DR. McCABE: Any opposed?

(No response.)

DR. McCABE: Any abstain?

(No response.)

DR. McCABE: Okay. So that one we'll move to Category 4.

Thank you very much, Barbara, for discussing both of those.

Number 3, then, is education.

Hunt?

DR. WILLARD: This is an issue that was ranked, again, higher by members than the ex officios. I think I can briefly summarize the questions before us in the

sense that I think everyone acknowledges there's a gap in genetic knowledge of health professionals. To me, as I read through both the issue brief and thought about it and discussed it with people, there are really two questions to be addressed. One, to what extent is this a federal or an HHS issue, as opposed to that of academic and professional societies and other groups? And the second issue is -- and I always hate to come back to genetic exceptionalism, but this is no exception to that.

(Laughter.)

DR. WILLARD: The question is how any of us would approach a gap in knowledge in genetics any different than continuing medical education and gaps in knowledge of any other late-breaking, fast-moving field in the field of medicine, and how health professionals would deal with the introduction of any new technology where there probably are gaps, and if there were equivalent groups to this, people might be sitting around saying, gee, how can we possibly get people to understand new radiologic tests or new imaging tests or other kinds of laboratory tests. So to me, those are the two particular issues that frame this question to get us to an issue of whether this is a class 1 or class 4 hurricane.

But I think first, probably the point to discuss the most is to what extent is this a federal or HHS issue, because if the answer there is no, then that may drive us very quickly. So if there are any who want to address that particular issue. From my standpoint, other than the obvious training issues that the NIH, for example, is involved in, I'm not convinced this is a federal issue. But I'm just speaking as an individual.

Joan?

DR. REEDE: I think there's another aspect of this when we talk about the education and training. The part that relates to educating those who are in the sort of professional pipeline versus the continuing education of those who are already out in practice. But the other part that I think is important is the diversity within that workforce and the training and who is being trained, and I do think that there are some roles for the government when we start to look at diversity in training, and I've not heard that as part of the discussion.

DR. WILLARD: Again, just for a point of information, do you see that as being specific to genetic and genomic testing in this context, or that's a general issue about diversity and workforce training?

DR. REEDE: I think it is a general issue, but I also think it is a specific issue to genetics and genomics. It's something that needs to be at least mentioned or addressed. I'm not saying that this is an overarching issue, but there are a lot of implications if you don't look at diversity within that workforce. So it could be anything from NIH and its training to HRSA and the Bureau of Health Professions. There are different ways in which governmental agencies, DHHS agencies are involved in creating a diverse workforce, and one of the questions within that is is there something that those agencies can also do that addresses issues that relate to genetics and genomics.

DR. WILLARD: Other issues? Suzanne?

DR. FEETHAM: Speaking from the federal perspective, we have identified for the last several years a commitment to the education of all health professionals in genetics. Part of the reason for that is the rapid expansion of the knowledge base, the concern over the traditional time lag which we find with this rapid expansion of knowledge, with direct application to practice that that time lag is not acceptable in any capacity.

Another factor in this, as you've identified, is that it is our responsibility and

part of the focus of HRSA for the diversity of the workforce and having the right health professionals across the country in the underserved areas. So that's another piece of this.

Another aspect of this is that this is reaching all health professionals, all conditions. And that is when you mentioned about other new knowledge, that's another what we see as unique about this, that there's not one condition or a series of conditions or any age group that this is particularly based with. It's everyone, and that's another perspective of why we see this as an important federal role. Also, as you know and already cited, we have strong partnerships with NIH, with CDC. We have done partnerships with AHRQ and some of our funding, because again we see this as a really very important issue.

DR. WILLARD: Other comments? Debra?

DR. LEONARD: Well, getting at your exceptionalism, it's reinforcing what Suzanne just said, that the anticipated pervasiveness of genetics to all of medicine does make it somewhat exceptional. I was struck by a comment you made at one of our meetings, that it's like we've discovered a new organ, and it's called the human genome. Much of the health care community does not know about that new organ system, and yet it affects every aspect of medicine.

So I don't know that the government directly has jurisdiction to educate on a ground level, but I agree with what others have said, that there are many things that the government can do to influence support, push people to create educational programs that will enhance the health care that's delivered when it moves in a more genetic/genomic direction.

DR. WILLARD: Chris?

DR. HOOK: I think the jurisdiction is split in that residency training programs have to be approved in order to receive Medicare reimbursement and so on. There would be ways in which the government could require training programs to improve or to document genetics or genomic education in their programs, or at least showing how it's integrated in that.

We also could put this on the list of things to write letters to the head of the ACGME and the AAMC and others indicating the priority that we believe they should place on including genetics education strongly in the curricula. So even though that may not be under government jurisdiction, there is some way in which I think the committee may be able to have a broader public impact.

DR. WILLARD: Francis?

DR. COLLINS: I appreciate the discussion, and I think this is an area of great importance. I take the point that there are lots of other areas of medicine that are also moving rapidly where practitioners need information that's up to date about a field that they may not have had much exposure to, but I think this notion that Debra mentions here, the sort of newly-discovered organ, does seem to be kind of the reaction of many providers when faced with the need to become knowledgeable about a field that they've had really almost no exposure to and have imagined as sort of something abstract that they'll never have to deal with.

That being said, exactly what the role for the federal government ought to be is something that we've been struggling with now I think for a decade, and I think there are some answers to that, and I think what Suzanne said about HRSA's role is an important one in terms of what the Bureau of Health Professions is doing.

The organization that hasn't been mentioned yet that I think takes this challenge on as its major enterprise, if we're talking about other bodies addressing the issue, is

the National Coalition for Health Professional Education in Genetics, NCHPEG. NCHPEG has now been around for almost five years. It has, at last count, over 125 professional societies that have joined up to be part of this, representing virtually all of the major specialties and subspecialties of medicine, of nursing, of social work, of dentistry, nurse practitioners, physicians assistants. A long list of those who find themselves in a provider role have become part of this organization.

It has obviously a very huge challenge in front of it, to try to achieve some sort of genetic literacy amongst providers in a short period of time, and it only exists now because of initial support from the Robert Wood Johnson Foundation, which has now segued into support from HRSA and NIH as a major effort. It was greatly facilitated in terms of its effectiveness by being co-founded by AMA, the American Nurses Association, and the Genome Institute. So you had the credibility of the AMA and the ANA from the beginning saying this is really important, because I think one of the things we learned is that the government telling practitioners what they're supposed to know and how they're supposed to do what they're doing isn't always all that effective unless their own leadership is also part of that exhortation.

I think NCHPEG has achieved that kind of status. They put forward core competencies for all providers, which have been I think very well received and which are being integrated into the educational plans of many of these professional specialties. There's a lot of CME and other types of activities that are being organized, put out on the web, and integrated into ongoing educational efforts for practitioners.

So certainly before starting down this pathway, I think it would be very appropriate to look closely at where the gaps that still exist in this very important agenda, and Joan, your point is very well taken in terms of diversity. I think NCHPEG sees that right now as a very high priority. They have a whole working group aiming to address that. They have succeeded in getting many of the major professional organizations that represent minorities to join up and to bring that expertise to the table about how to do something about that issue.

So in no way do I mean to say this is taken care of, but I thought it would be good to have this particular set of efforts in front of the group as you try to decide where to place your bets.

DR. WILLARD: Well, if you're not arguing that this is taken care of, then the question obviously is what can this committee do either in terms of collecting information and making that available and/or taking some action that would be perceived as being valuable by someone else.

DR. COLLINS: One of the things that NCHPEG initially attempted to try to have an influence over but has not had all that much luck is licensure and certification, to try to get more of a focus on genetics expertise in things like the national board exams and things like state licensure for health care providers. That's a very difficult system to try to influence, and I think NCHPEG, while making some efforts in that regard, has primarily decided to focus on generating materials that professional societies would voluntarily integrate into their own educational efforts and not putting so much time and effort into licensure.

But that would be an area, I suppose, where this committee, with its reach as a government-connected enterprise, might be able to make some inroads. I don't know how difficult that would be. It might be fairly difficult, but it's a suggestion.

DR. McCABE: So what I'm hearing is that while there are other groups that

are involved with this, that there still could be an impact of this advisory committee taking on this topic.

DR. COLLINS: And again, SACGT had a whole working group that was focused on education. Joann Boughman, who is here in the room, led that enterprise. It would be worth looking back at that activity and what was suggested to try to pick out of that the things which now, a couple of years hence, have not been attended to that were considered by that group as an important part of the next agenda for the future, but again being very careful not to duplicate things that are already very well underway in other quarters.

DR. WILLARD: Ed?

DR. McCABE: I was just checking with Sarah. So that paper does exist in the SACGT archives. The working group had not come to the point of formulating, or at least having approved recommendations. But again, there would be some background that could give us -- a couple of years old, but could give us a jumping-off place.

DR. WILLARD: Suzanne?

DR. FEETHAM: To reinforce what Francis was saying about NCHPEG, and also where we see the federal role coming in, is the encouragement and nudge to the interdisciplinary education and training and practice, and that is something that we can have a perspective on -- and I say we as a government -- in ways that individual organizations without some encouragement would not do.

DR. WILLARD: Members of the committee reacting to what we've just heard? Since we need to assign at some point priority to this.

Joan?

DR. REEDE: Just a general statement as we're listening and we're hearing about coverage and reimbursement and education. If there were other areas where a great deal of work has been done by SACGT prior to this, it would be very useful to know that so that we could have that as some sort of basis and foundation for any of the topics that we're looking at. So to the extent that Sarah or others could inform us about prior work or prior documents, I think it would be helpful.

DR. WILLARD: Each one of the issue briefs has a section that does, at least briefly, mention what SACGT did or what it might have available.

Other comments?

DR. REEDE: But it would be nice to see the whole thing, because the comments are very brief in these statements.

DR. WILLARD: Yes, correct.

Linda?

DR. BRADLEY: Yes, I was just going to comment that obviously CDC also considers education a really top priority, both in the sense of workforce development in general and public health, but also specific training in genomics for the health workforce in general, and has a number of projects, I think one of which you may be aware of, the Family History Project, trying to get the concept of a tool to make the taking of a family history something that's really accessible to physicians in practice and assessing that tool and its effectiveness in identifying individuals at risk.

I think also the Center for Genomics in Public Health and their activities in training and technical assistance, both in the states and to anyone in the health professions, are pretty active.

DR. WILLARD: Thank you.
Other comments on this point? Brad?
MR. MARGUS: The meeting isn't interesting unless someone disagrees. I ranked this one high. It's important, but I guess I don't feel that convinced that there isn't a lot of redundancy with the previous committee, with all these other organizations. There are so many organizations that know so much about this and lobby or push in so many different ways. I just don't feel convinced that our committee is going to add that much new value or new insight into the issue.
Absolutely, education is critical and we want everyone in all of health care to be informed about the latest things in genetics, but I'm not convinced.
DR. WILLARD: Barbara?
MS. HARRISON: I'm kind of feeling the same as Brad, and I was wondering if it's a possible option to have this be one of the topics that we want to be updated on at each meeting to give people who are in these types of organizations an opportunity to let us know if there is anything that we can do to help, on a regular basis, as opposed to prioritizing it for us as an issue to actively pursue. I just think that that may be a viable option, because I definitely want to be able to offer people help, these groups help if they feel that we can help them, but again, just in the interest of wanting to focus on issues that we can really make a difference on today, I just wonder if this is maybe something we can put on the side but that we definitely want to be updated about.
DR. WILLARD: Ed?
DR. McCABE: I just want to comment on process, perhaps. While we've been categorizing things, I think it may be premature to utilize Category 1 at this time. I think that is a category that will be utilized at the end of the process rather than this early in the process. Basically, the issue is does it fit into Category 2, which means high priority, can be dealt with fairly quickly. I don't think it transcends all issues. We could probably force it into that, but I haven't heard anybody speaking to that. So we're really talking about a Category 2 or a Category 4 at this time, and I don't see a way of dealing with it quickly given all of the other organizations that have worked on this and tried to come to grips with it and have not fully.
So I would think that it still is viable, and I would suggest that we let the prioritization at the end of the day determine the Category 1 versus Category 4. It's really if we're going to have any sidestep into 2 or 3 during this process.
DR. WILLARD: I guess, then, my question would be for this group, prior to taking the vote at the end of all of this discussion, can anyone articulate the kinds of specific value added that this group would bring that other groups are not currently or previously dealing with that might raise it in the individual priority list when it comes time to voting?
DR. FEETHAM: Sarah just modified number 2 to say "or through monitoring," and that gives just another perspective on that. It's been identified by Barbara in some of the other discussion. It's important to keep it on the screen. I think your comment about are we going to learn more through more in-depth study through this group, but to keep it visible, to keep an eye on it, to track it, to keep it on high visibility, again with the role of the federal agencies, plus with this group, with the adaption of 2, if people go with that. I think that's another way of dealing with this.
DR. WILLARD: Yes.
Ed?

DR. McCABE: And if we do, I just would point out a significant portion of the discussion has to do with diversity of those being educated and trained, and that should be also an area that we should attempt to monitor should we go to 2, because I think that's one of the most important aspects of this.

DR. WILLARD: Emily?

DR. WINN-DEEN: So I guess I'm going to disagree a little bit with Ed's comment that we couldn't deal with it quickly, because I think in some ways we could deal with it by putting it in Category 2 and saying we endorse the efforts that HRSA and NCHPEG have undertaken, we support them, we think they're doing valuable and important work towards the goal of integrating genetic training into basically all of the health care workforce, and we would be happy to assist if there's something specific we can do, but put it more on their shoulders to come to us with a specific gap which they would like us to address rather than trying to figure out those gaps ourselves.

DR. WILLARD: Okay, thank you.

Sorry. I apologize. I can't see down the line here.

DR. FELIX-AARON: That's okay.

I'd just like to draw a connection for the group, that I see provider education being intimately connected and related to direct-to-consumer advertising, and I think it's a connection that in those discussions we've been having we haven't sort of drawn out that particular connection. I'll tell you why I see it. Much of our conversation has focused on really being concerned about direct-to-consumer advertising, and providers represent an important way that we can deal with that in terms of provider education, patients and consumers going to their providers, wanting more information, wanting to support their decisions.

I think that provider education is important in that respect, and I just wanted to throw that point out for the committee to reflect on that connection.

DR. WILLARD: Thank you for that.

Ed, did you have -- Joan first.

DR. REEDE: I see sort of three possible paths. There's a part that's a very quick response that Emily has suggested, a statement of endorsement for some of the ongoing efforts. Also, in light of what Barbara has said, monitoring to see what has changed and maybe reissuing statements or taking other directions with time, as changes are made.

And then the third part, going to this issue of because we are dealing with it quickly or we're monitoring it does not mean that we can't address issues of education and training as we look at other priority areas.

So for me, if I were trying to do a population study and I had a group of providers that were not educated, I can easily see where I would have major issues around discrimination, access, and a lot of other things in terms of my population study. So I think that it can be revisited. I don't think that the categories have to be so isolated that we can't approach these in multiple ways.

DR. WILLARD: Other comments?

Ed?

DR. McCABE: Just to clarify, I think the point was that I hadn't heard anyone speaking to putting it into Category 2, but I would agree that I think that makes a lot of sense. Likewise, I think we heard on the discrimination that things may fall into more than one category depending on how we look at a topic. So I think that that seems like an excellent way

to approach it, that certainly it could fit into -- what I'm hearing you say, then, is Category 2, to some extent 3, perhaps not as pervasive as some of the others, but wherever there's an opportunity to include it in other discussions, we should, and then 4, that there may be more to do on this topic. Is that correct?

DR. REEDE: Correct.

DR. WILLARD: I think we've had a good discussion and framed the issues, and probably this is one where at the end of the day the chips will fall where they may and we can react to that depending on how highly it's ranked by individuals, or by the group rather.

DR. McCABE: So at this point, having heard the discussion of the group, do we want to keep it in multiple categories, or do we want to narrow it down any further than 2, 3, and 4?

(Laughter.)

DR. WILLARD: I think we have some obligation to do a little better than that.

DR. LEONARD: Well, especially since you said we can't use 1, so we're not categorizing at all, basically. I would see it fitting into Category 2.

DR. WILLARD: Do you want to call for a straw vote before a straw vote?

DR. McCABE: Any further discussion of Category 2?

DR. LEONARD: Well, when we go to our next straw vote, are we going to vote by category? Are we going to rank by category? Because that would seem to be most appropriate. So we need to put all of these in one of the categories or another so that when we do the final straw vote, they're considered by class.

DR. McCABE: Certainly, but we're developing the process as we move forward today, so that's certainly an appropriate way to go.

Paul?

MR. MILLER: Thank you for inviting me to your sausage factory.

(Laughter.)

MR. MILLER: What might be helpful to me, and maybe to the group, I think the people sort of regard education and training as important, but what would be helpful would maybe be to imagine or maybe spend a moment or two and think out and say, okay, if this was a really high priority, and if we were going to spend the next four months thinking about -- let's say we've dealt with all the other things -- what would this committee do to sort of move the ball forward on it? Would we hold seminars? Would we sort of wag our finger at medical schools? What would we do for this committee to get our hands around education and training?

That may sort of help people in thinking about whether it is a number 2 issue or a number 4 issue, because I don't know the answer to that other than the government wagging their finger. That's what we do at the EEOC.

(Laughter.)

DR. WILLARD: Would anyone like to propose what steps we would take if it turned out to be high priority? The default being if no one can come up with something, it isn't a high priority.

Francis?

DR. COLLINS: Well, I think first you'd want to collect the information about what's really specifically already being done. You'd want to have a NCHPEG executive

director come and tell you all the programs that they're currently pursuing, what their timetables are, what their success rates have been so far in achieving their goals. You'd want to look at the SACGT's document to see what their recommendations had been, and then you'd try to figure out, as you were asking a few minutes ago, are there gaps identifiable here where this group has the jurisdiction and where something that could be done that's not already under somebody else's purview.

DR. WILLARD: Ed, and then Joan.

DR. McCABE: Joan?

DR. REEDE: I guess going back to something I said before in terms of point of clarification, I'm not taking an approach now of trying to figure out what is the solution I'm going to offer, the statement I'm going to make at the end, because I think that's too hard without the information. I see this as a process of trying to figure out what are the priority areas that we need more information on, that we want to study in depth, that we may want to act on more quickly.

So without that information, it would be very difficult for me to postulate sitting here something that would be evidence-based and reasonable, that this is a step I think should be taken. I see this as more preliminary, saying do we need to do more in this area. So I think using as a criteria can anybody come up with an action item or an action step is premature.

DR. WILLARD: While I accept that, if we don't do that, we still end up with 12 high-priority items that we're chewing through.

Emily?

DR. WINN-DEEN: I think it's pretty clear that we've identified that CDC, HRSA and NCHPEG are making substantial efforts in this area. Although we could hear in-depth what those efforts are, we at least know that we're not alone, that we've put it as an issue that needs to be dealt with, but there are groups that are actively dealing with it. So my question is just sort of to try and get between items 2 and 4 whether we at this instant in time, with our very limited knowledge about exactly what's going on in all those other programs, would say we think other people are substantially handling it and we just want to endorse that and monitor what they're doing, or do we feel like we at least have an obligation to look in-depth at what they're doing and assure ourselves that they're doing all the reasonable things, or if there are gaps, that then we could address the gaps.

So to my mind, that's the issue, whether we want to just spend some time at maybe the next committee meeting or maybe one of the subsequent committee meetings, and we already spent some time at a previous meeting, looking at what education and training was going on. Do we feel like we have enough knowledge to say it's a Category 2, or do we need to gain more information, as Francis suggests, so we can decide if it's a Category 4 or a Category 2?

DR. WILLARD: Agnes?

MS. MASNY: I just wanted to sort of have us take a look at the number 2 one again and make a suggestion, that as everybody has been talking, since there are government agencies that are already looking at this issue, that maybe we could say, with somebody else making the connection, that the issues of the workforce training could be a subgroup under some of the other issues, like access. Kim mentioned earlier if the health professionals don't know about a test, then the patient won't have access to it.

So I think the workforce issues will be handled under something like access, so that if we could look at Category 2 and say is it a high priority but could be dealt with, and we don't have to say quickly but either through endorsements or recommendations, monitoring, or that it would be handled as a subgroup in one of the other topics, then I think it would maybe help us to look at where -- we still see this as high priority, but it is going to be handled as we are addressing some of the other issues or by virtue of an endorsement or recommendation.

DR. WILLARD: Other comments?

Martha?

DR. TURNER: Just a couple of ways of looking at this, and one is a temporal way, and that is that we all agree that it's happening, and that it's happening in the usual way that technologies are introduced into health care. But if we're not satisfied that that is going quickly enough, then the committee perhaps ought to take action.

The other thing is, as a user of the policies or information that comes from a group like this, if I see that this is a priority on your list, then when I'm allocating resources for education or trying to squeeze in one more hour of education to a block of the curriculum, then I'm likely to add this. If it's not there, then I won't. So if this committee comes out loud and strong that education is a priority, I think that has a lot of actions that follow as a result of seeing that. So I would continue to identify it as a priority just because its visibility makes a lot of people pay attention and will get us perhaps to our goal more quickly than if we just let it happen on its own.

Medicine is not known for its speed in integrating things into practice, or into our education system. So we could use a little help.

DR. WILLARD: Thank you for that.

Over to you, Mr. Chairman.

I'm sorry, Barbara.

MS. HARRISON: I just wanted to hopefully make a clarification with myself, that Category 2 is a no-man's land. So putting something in Category 2 means that we think that it is high priority. It's just that there's no real action that we can take as a committee, although we endorse it and think that's very positive. So maybe a letter of endorsement, as well as monitoring, would be the action, as opposed to just monitoring.

DR. McCABE: So you would make it and/or rather than or. Okay.

I think what we're hearing is a concern that this is an extremely important issue, but nobody is sure quite how one might grapple with it and fear that after a year's deliberations we might end up where we are today, saying yes, we endorse NCHPEG and HRSA and some of the other activities. I think it's important to recognize, however, what was stated before, and that is that we can have influence on other organizations, like the AAMC, ACGME and these sorts of organizations. That can be done either by extensive deliberation or perhaps by monitoring and including that in a more rapid -- I would doubt that there are very many people sitting around this table that would say that education in genetics is not a good thing.

So I think one could include it in Category 2 but not relegate it to a place where it just is hanging there with no action taken. One could take immediate action and then monitor to be sure that things are moving forward, and then if further action is warranted in the future could deliberate on that.

Suzanne?

DR. FEETHAM: Well, as part of your monitoring, at a future date you can bring some of the parties to the table that you've been talking about, key organizations beyond NCHPEG, but the individual professional organizations, and by just bringing them here having them give you some information in addition to further information from the federal partners I think could go a long way to doing what you're talking about.

DR. McCABE: Okay. So some of the organizations that we've heard mentioned in the discussion could be organizations to bring to the table at some point in the future.

So it's narrowed down to 2 and 4. Does anybody wish to make a proposal as to which we vote on?

Chris?

DR. HOOK: I would move that we put it in Category 2 for the reasons that have just been discussed. It is a high priority, but I think if we send a statement that we consider this important, that we at every meeting have a presentation from someone on education, we're communicating, we're continuing to act. But on some of these other issues, I think we're going to find there's a far fewer number of individuals or groups that are working on those topics than this one, and I think that's why I wouldn't suggest we put it in 4.

DR. McCABE: Do I hear a second on that motion?

Yes, Joan?

DR. REEDE: A second on that with the provision that we all understand that as we're talking about education, that diversity is a component of that.

DR. McCABE: Discussion of this? And we can talk about specific action later under Category 2. Anyone wish to speak to Category 4?

(No response.)

DR. McCABE: Okay. So not hearing that, all in favor of education and training, with the additional caveats that we've heard, being assigned to Category 2 for later vote, all in favor say aye.

(Chorus of ayes.)

DR. McCABE: Any opposed?

(No response.)

DR. McCABE: Any abstain?

(No response.)

DR. McCABE: Okay. So Category 2 is where it will go, then.

Number four is large population studies.

Hunt?

DR. WILLARD: This is another one in a very similar state, perhaps, in that the premise here is that we know there are a significant number of large population studies going on in other countries with either particular advantages in the design of their health care system and/or the genetic makeup of their population, and there are discussions in this country already underway, led principally at the NIH, to debate both the need for and design of large population studies here.

I think, at least in order for me to frame the issues and think about it, it would be useful to hear from you, Francis, sort of an update on this point. To what extent is the NIH digging into this? So we can evaluate whether it's in good hands and we just need to pay attention, or whether in fact there is something we can actually do.

DR. COLLINS: Framed in those terms, I'm not quite sure.

DR. WILLARD: I have no doubt that it's in good hand.

(Laughter.)

DR. COLLINS: Well, thanks for asking. I think this is very much a discussion in evolution. As you stated, we are in a circumstance where there are such large-scale longitudinal population cross-section studies either underway or contemplated in quite a few other countries, but not in the United States. There are some 2 million individuals who are currently enrolled in longitudinal cohort studies on various diseases and who are being followed prospectively and on whom DNA has actually already been obtained. So there's a potential there if one could figure out how to put those together into an enterprise that really did cover the range of possible diseases that you'd like to study, and if the consent was acceptable, and if the study design was acceptable -- there's a lot of ifs here -- to perhaps put something together without having to start from scratch, and that's one of the big questions.

Is it possible to cobble together things like the Harvard Health Professional Studies, the Women's Health Initiative, NHANES and a whole bunch of other such studies in a fashion that would accomplish this goal? People that I've talked to both see the advantages and are very concerned about the potential there for that just not being workable because of all of these ifs.

We did hold a meeting December 1st, 2nd and 3rd to ask a group of very highly qualified geneticists, epidemiologists and environmental experts because, let me be very clear about this, the point is not just to look at the G part, it's also to look at the E part, and particularly to look at the gene/environment interactions that play a role in common disease. So you'd want to design a study that carefully collected environmental exposure data as well as looked at biological materials, like DNA, cells and plasma.

So the consensus of the group -- and this was a pretty distinguished group, and they came in I think with some skepticism -- was that such a large-scale cohort study would be extremely valuable. They had no real dissension from that conclusion. They felt also that it would be useful, if possible, to have this across the age range, from childhood to late adulthood, and if you were going to do so, some of the geneticists argued you may as well do this in a family-based approach so that you were covering three or four generations and you had the ability, using the tools that geneticists are familiar with, to be able to test associations and make sure that they're not false positives.

There was some discussion about how this might be connected with the National Children's Study, which is an enterprise which has been under discussion now for some three or four years and which is actually congressionally mandated but not congressionally funded, and that is supposed to involve some 100,000 newborns, actually ascertaining at or before the time of conception, and then following those kids up through adolescence, and would there be a way to put that together with a study that also included ascertainment of diseases that occur throughout the lifespan. There were pros and cons expressed about putting these kinds of things together.

So the big issues, of course, that arose out of this were numerous. What exactly would be the study design? What kind of power would you have being able to look at gene/environment interactions for diseases? Of which particular incidence? What could you afford to do? Because the costs would be very substantial and would obviously scale as you went into larger and larger populations. What kind of environmental data could you afford to

collect? What kind of genetic data and phenotypic data? How would you deal with collecting clinical information, which in this country tends to be rather fragmentary and non-electronic?

Could you take advantage of some of the health care systems that have a somewhat better means of collecting that information and not try to do something in a fashion that depended upon individual paper records in order to collect the data that you need? All those were issues that were put forward and not entirely solved.

The huge question I think that hangs over all of this is do we as a country have the national will and the resources to mount a study of this magnitude? If this is going to be useful for looking at the common disorders that people I think would most like to collect data on -- diabetes, heart disease, cancer, asthma, hypertension, and so on -- it doesn't look as if you could achieve the kind of power you'd like for much under half a million people, and that would end up being a very expensive undertaking and one which would have a life that would go on for perhaps two or three or more decades. So you really have to count the cost before you plunge in.

The cost would be probably substantial enough that without sort of a major effort at a national level to identify this as a program of considerable importance for the future of our nation's health, it would be difficult to do it. I can tell you, frankly, NIH in its current circumstances, particularly in the budget situation that is affecting us this year, next year, and maybe well after that, there would be no way that NIH could mount this on their own, nor do I think we could with our partners at CDC, who were very much a part of this discussion in December. So it would take quite a substantial enterprise in raising consciousness about the importance of this, akin perhaps to the Human Genome Project some 20 years ago, in order to make this a viable option.

So where this all stands is there have been a number of small follow-up discussions, but the plan really is now to try to formalize that a bit more by assembling a working group of experts to try to flesh out some of the questions that didn't get answered in this rather brief two-day workshop. But this is still very up in the air. It was mentioned this morning, the possibility of asking the Institute of Medicine to get involved in this, and that has not been ruled out. But I think the concerns there were partly cost, which again is a real issue right now, and partly sort of timing given that IOM studies generally don't happen overnight, and this is a circumstance where if there's going to be some momentum behind this, we probably don't want to have that go on indefinitely or more than it has to.

It might be possible with the expertise that exists at the NIH, together with drawing in a lot of outside experts, and there are a lot of people that you'd want to ask opinions about this, to flesh out the basics of a study design over the course of, say, the next six months. But again, all of this is just completely hypothetical without some very major sense that this is a high priority for public health in this country.

The arguments to do this in the U.S. and not simply depend upon the studies that are going on in other places are, I think, fairly convincing. If you're really interested in health disparities, and I think that's one of the major arguments for doing this study in the first place, the studies going on in England or Iceland or Estonia or Germany or Japan are not going to address either the very important minority populations in this country or the environmental exposures that are probably quite different here than in other places. So that's a very compelling argument.

I also would think that if we're going to set up a study of this sort, and this

was endorsed by the people in December, that it ought to be done in a fashion where there is fairly open access to the data by both public and private sources, so that you really had a public data set that the maximum advantage could be taken of. By the way, I think there's a real chance there for this to be funded as a public/private partnership as well, but we haven't explored that very much so far.

So I'm a little at a loss to know exactly what to say with regard to the question that I think you're posing in terms of SACGHS at this moment, on March 1st, 2004, what would be an appropriate role to play. I think if this is going to happen, it will take all of the enthusiasm and scientific support and energy of all of the groups that have a stake in such an outcome, and that would certainly include this group. So it would certainly not belong in Category 1 on your list. But whether this is something for this committee to get deeply engaged in right now when things are very much in flux, or whether this is one to pay very close attention to and see how it evolves in the next few months, you might make a case for the latter at the present time.

But I would be very interested in the feedback from this group about the course we're currently on. As you can tell, it's very much a work in progress.

DR. WILLARD: Thank you, Francis.

Comments? Debra?

DR. LEONARD: I think it would be absolutely horrendous, having completed the human genome sequence, which also at the time, as you mentioned, was considered to be an impossible task, to have the human genome sequence and not be able to move it into the realization of all the medical benefits that we anticipated coming from this because we don't have the large patient cohorts. Without this, you're not going to move to the next step.

So I don't see how this cannot be a priority and not be something that this committee fully endorses and tries to influence whatever you need to be able to move ahead with this.

DR. WILLARD: Would anyone like to agree or disagree with that?

Chris?

DR. HOOK: I certainly agree with that. I look at some of our other topics, such as pharmacogenomics, and really for pharmacogenomics to become practical on a large scale, we're going to have to do large population studies and see if there is a cost-benefit analysis to prevent the 100,000 deaths a year that are attributed to adverse effects of medication. So I think it's very integral to the other things we've said are priorities.

DR. WILLARD: Emily?

DR. WINN-DEEN: I think there are two questions. One is, is the study designed disease by disease, or is it global with all diseases coming out of it? That's a question for exactly how it would be handled. I think there's absolutely no doubt in my mind that we have to do this as a country that's committed to making all this stuff affect health care.

What I wanted to ask Francis is, having run one of the biggest budget, big science programs in the nation, do you have a sense for if this is bigger or smaller or about the same in scale and scope as the Human Genome Project?

DR. COLLINS: It's not been fully costed out because so much would depend on exactly what study design is chosen, but it's certainly on that scale in terms of the investment over the course of a 15-year time period. Much of the cost of a longitudinal cohort

study, though, hits you up front, because you need to do the accrual phase. You need to get individuals enrolled and collect the clinical information and the biological specimens, and then the monitoring, the follow-up actually tends to be somewhat less expensive on a year-by-year basis.

So again, I think it would take a major national priority being set for something of this sort to go forward, something that could not be done, I think, with the existing resources that are available to any of the research agencies represented around the table.

As far as your question about the study design, this would definitely be a cross-sectional study that is not focused on any particular disease. It aims to collect information in a population-based sampling strategy and to follow people and see what diseases occur as you go along. Let me say that's a very valuable part, to have this kind of longitudinal study. It enables you to have less biased case ascertainment, so you're not just collecting the most severe cases, as one sometimes does in a case-control study. It does provide you, though, with nested case-control studies for people that really want to drill down into the specifics of a particular disease and find that the phenotypic information that was collected as far as the big study was not sufficient. You can spring out of this lots of case-control studies focused on specific diseases if they're common enough to have enough incident cases during the period of follow-up.

The other aspect of this that bears mentioning, of course, is a huge challenge in terms of how you do the informed consent, especially if we're talking about access by lots of researchers to the material. The participants in this study would have to be not really subjects. They would be full partners in this enterprise and would be engaged in an ongoing way. There's no way this would be anonymized. This would be a circumstance where people's clinical information was part of the record. You could try to protect the identity of the individuals, and we could do that I think fairly effectively with various computational means, but this would be a very different kind of study than what some people have contemplated in the past where there's an irretrievable break in the link between the specimens and the person. You want to be able to go back to them quite regularly.

The size of this would be something like 30 times the size of Framingham. But if you look at what we've learned from Framingham about cardiovascular disease, I think we'll be kicking ourselves in six or seven years if we haven't started this study, and if we haven't started it very soon.

DR. WILLARD: Ellen?

DR. FOX: On the question of whether there's another body that's addressing this issue or better equipped to address this issue, I'd mention the Veterans Health Administration, which in many ways is uniquely situated to address this issue. We have roughly 7 million enrolled patients. We have a highly developed and very sophisticated centralized electronic medical records system and, compared to other health care systems, a really stable patient population that's highly diverse, both geographically and ethnically.

The Veterans Health Administration has been actively pursuing a proposal for the type of study that we're discussing here, and that has received conceptual approval from the National Board of our organization, and we're sort of in the final stages of working out some of the specifics in terms of the informed consent issues and the privacy issues. But this would involve collection of environmental data linking to the clinical records system and

enrolling on the order of more than a million patients. So that is underway.

DR. WILLARD: Thank you.

DR. COLLINS: Can I just say a word about that in particular? Yes, I'm very pleased to see the VA is taking that kind of leadership, and obviously the availability of that kind of clinical records system is a wonderful asset. We have also heard of other organizations that are very interested in a similar way, in participation in a project of this sort. Kaiser has expressed that, the Mayo Clinic has. The Marshfield Clinic in Wisconsin has already initiated an effort of this sort.

All of these have sort of pluses and minuses in terms of exactly what you could accomplish as far as a broad cross-section of age groups, genders, which obviously is a bit of an issue for VA. But I think some combination of taking advantage of those organizations that have this kind of already strong clinical database and a tradition of carrying out excellent research would certainly be on the table of how you would put this study together.

DR. WILLARD: Brad?

MR. MARGUS: So back to Debra's comment about this being absolutely essential. I think I totally agree that you want to apply the Human Genome Project's product and studies to find associations and to come up with markers or new and novel targets for drug development. Those are critical and they should be accelerated.

I don't think -- my sense is that there isn't as much consensus, absolute consensus that the best study design is to have one huge population that you study, first of all because of the sheer cost, whether it will happen, billions and billions of dollars. But there are learned people out there who also think that sometimes it's better to have different studies where you have experts on whatever phenotype you want to study designing at each time, and to design one group upfront could have a lot of risk. So the consensus isn't absolutely there.

The other issue, just getting back to the whole thing, is that right now it sounds like it's all a big debate about infrastructure and resources, of course, logistics. I'd like to have much more consensus that the scientific merit is there in having one big group. I mean, today clinical trials are done everyday for drugs, and they don't use one big population. They go pick their populations.

The most important thing is I don't think this committee is really the committee that stands in any way prepared to render a decision about the scientific merit or what the best design is. So while it sounds really exciting, I think we have to wait, and I kind of go with the idea of waiting and seeing what happens as far as the follow-up diligence and figuring out from the scientists who are going to spend more than two days looking at this, and that's why I asked about the IOM this morning. If they then said this looks like a thing that has to happen, I understand completely that Francis would love to have us endorse it. I think we've got to worry a little bit about a conflict of interest. I mean, Francis' company is the Human Genome Research Institute would be the one that carries it out.

But if, in fact, the logistics and the scientific merit were demonstrated, then at that point I'd like this committee to absolutely start thinking about the ELSI issues, the ethical issues, the access issues, discrimination issues. There are a lot of things that come up, oversight being one of them. But as of today, I kind of urge the committee to maybe, even though we're very interested in this and we feel it's really important, it doesn't seem ready for us to get involved with. Again, I'd put it in Category 2 where we absolutely want to monitor it. Please, please, please keep us posted on what comes out of it. But it doesn't sound like it's

ready yet.

DR. WILLARD: I've got Ed, and then Joan.

DR. McCABE: I wanted to take some of the same information but come to a different conclusion. I think that there probably will be a need for different types of projects, because certainly we need a very large project that's balanced with respect to gender, that includes children so that we can begin to look at some of the environmental influences that affect our health throughout our life course that begin in childhood, and perhaps even before. So it's important to have that kind of study.

It's important to look at other, more targeted studies that may get at other aspects more quickly. The chance that a single study will be the final study I think is highly unlikely. At some point I would hope that, probably not in my lifetime certainly, but we would get to the point where everyone is enrolled in these kinds of studies. If we don't really collect data wherever it's opportune to collect those data, we're going to be missing abilities to develop an evidence base.

But looking at the models, that's why I would say some of the same things Brad was saying, but come to a different conclusion, and I think that we could serve as a forum to at least discuss what's going on here in the U.S., what's going on around the world, and looking at what are the opportunities given different models. I think to merely monitor is a little bit too passive for me. I'd like us to take a little more active involvement in this.

DR. WILLARD: Joan?

DR. REEDE: I'm going to go right in-between the two of you.

(Laughter.)

DR. REEDE: I don't actually think it's the job of our committee to determine the scientific merit or the study design. I think there are much more learned people who will deliberate on that. But I do think that there are things that our committee could look at in terms of equity, in terms of issues such as if we're starting to use convenience data sets, which I would classify things such as Veterans Administration or some of the other data sets that might be Kaiser or other types of things, what happens to the 43 million Americans who are uninsured and don't fall into those categories who may have very different types of environmental factors or other things going on?

So starting to be able to raise those kinds of issues to bring them back to the deliberations; being able to say, as we've already mentioned, issues such as access and education and training, oversight, public awareness. If there's not public awareness, will there be a differential impact? I think those are things that our committee can bring to the front in terms of topics for discussion and saying that as a design is implemented or created or thought about, are these areas discussed, are these areas addressed, and ensuring that they're addressed for our committee, but also for the public.

DR. WILLARD: Thank you.

Emily, and then Ed.

DR. WINN-DEEN: I guess I would like to make sure the committee doesn't lose sight of the fact that there might be some value in what I'll still call large population studies but not quite as broad as the ones Francis described, where the endpoints are more immediate in terms of a shorter time frame, where we could really start to get some translational answers and, as such, develop evidence that would allow genetics to move into the practice of medicine in a time frame earlier than whatever, 15 or 20 years from now when we

might have a different kind of answer from this kind of huge longitudinal study.

So I think we need to have large population studies in that some of the effects that we're looking for are more subtle than the classic monogenic, highly penetrant diseases, but I'm a little concerned about a long time frame before we have anything and a lack of funding for sort of intermediate endpoints and that kind of stuff.

DR. WILLARD: Ed?

DR. McCABE: And I think that's the point. I was going to comment that I think Joan wasn't that different from what I was trying to say. She just said it much more articulately than I was able to say it. I think there is a role, probably not in terms of scientific merit, but I think in terms of all of the variables that Joan iterated, as well as some additional ones. But I think there is a role for this committee. Remember, it's the Secretary's Advisory Committee on Genetics, Health, and Society, and I think it's looking at those issues that we are chartered to examine, and looking at the different models and how they might approach the issues of equity that are exactly why this committee ought to take on this topic and why I think it's fairly important.

DR. WILLARD: Chris, and then Francis.

DR. HOOK: Well, I think listening to the different studies, there's Francis' global study, Emily is talking about a variety of other large population-based studies, and we can envision a number of different ones. But I would think that some of the ELSI issues would be common to them all, and what this committee could certainly do would be to focus on those aspects of it and then provide guidance to whatever large population-based study, be it the NIH or be it some other, that would be performed. Those guidelines need to be out there.

DR. WILLARD: I've got three backed up here.

Francis?

DR. COLLINS: I appreciate the input and the comments. I think those are all very on target. Just a point of clarification, because I was a little concerned that from Brad's comment you might have assumed that I was arguing that this longitudinal study would take care of everything. It absolutely will not.

So if, for instance, you're looking at a relatively uncommon disorder, or if you're looking at drug responsiveness, unless that drug is taken by an awful lot of people, you're not going to learn much about it from this longitudinal study. What you are going to learn about are disorders that affect something like a half or 1 percent or more of the population. So the point of that comment is to say case-control studies are going to continue to be absolutely bedrock critical for our study of genes and their role in disease, and this in no way should diminish our enthusiasm for mounting those and running them in the most effective possible way, focused on particular diseases where we really need that information, which is most of them.

What a longitudinal study does for you, though, is it allows you to look at interactions between diseases because you're looking at everything. It allows you actually to get unbiased information about environmental exposure, which is a huge problem in case-control studies because there is a recall bias that epidemiologists have written many books about, that if you've been affected already with the disease, your recall of environmental exposures is different than somebody who is currently healthy, and a longitudinal study enables you to get past that.

A longitudinal study also provides you, because you're collecting biological

specimens, with an opportunity to look for biomarkers that were sentinels of disease before the disease actually occurred, and a case-control study where you're only ascertaining people after they've been diagnosed doesn't give you that chance. So there are these various scientific arguments to say that while case-control studies are critical and we should be doing lots of them, they're not going to give you some of the most important answers about gene/environment contributions to disease, and what we really need is both.

DR. WILLARD: Debra, and then Brad.

DR. LEONARD: Thank you. I was going to make that point. But my other point is that I think this committee, other than monitoring and looking at ELSI considerations as this moves forward, I think that this committee could also make a recommendation that some decision about doing this and how to do it and how to fund it should be made promptly, because it will be over time, and it takes time to get enough people enrolled and to collect enough data and to follow enough longitudinally that you can start using this as a resource, as an effective resource. There will be things that can be done earlier in the development of this type of population, and then there will be things that fall out later. But it needs to be started as soon as possible so that we aren't 10 years in making this happen.

So I would say the scientific issues can be addressed, and this committee could say please do whatever needs to be done to support making a decision about doing this and how to do it, and then consider the funding considerations. But basically, if you don't do this, why did we do the Human Genome Project?

DR. WILLARD: Brad?

MR. MARGUS: So I would be in favor of having this be one of our subjects to cover if the likely result is that we're going to deliberate over whether we're going to make the recommendation that Debra just said. So if we're going to decide whether we're going to endorse doing it or not. That makes sense. But if it's really for us to go ahead and start discussing all the ELSI issues and access and discrimination, all those issues, it seems a little bit like a waste of time to do it now if we don't even know if this project is going to happen. I mean, are they going to find $5 billion to do it? Maybe by the time you get around to starting it we'll be much more insightful committee members, five years from now or so.

So it just seems a little premature to start down that course of discussing all the ELSI things if it's never going to even happen, and Francis can't tell us today that it's going to happen.

On the other hand, if we're going to discuss, keeping in mind at the same time all the ELSI things, but we're going to really discuss should we endorse this, should we say there's a need for this, and HHS and the whole government should start finding the money, as Debra suggested, then I think it's worth having as a discussion.

DR. LEONARD: The conclusion to my previous statement that this should be a 2 with a letter, with immediate action and not a 4 -- the 4 may come if the study actually happens and gets implemented. That may become a play for SACGHS to look at the ELSI issues associated with this. But I'm putting it in 2.

DR. WILLARD: I'm going to call on myself.

(Laughter.)

DR. WILLARD: Because I thought I was hearing a reasonable consensus that this was a number 4 issue, and people could then vote among the number 4 issues how highly it would rank, because I would argue that, notwithstanding Francis' discussion of his

group and where it's going, there's no guarantee. This isn't a situation that it's either the NIH or it doesn't get done. You could imagine a private consortium getting together to decide to do it. You could imagine one wealthy billionaire deciding that he or she wanted to do this. So I think from our standpoint there are a number of issues that we might address, from the standpoint of genetics health and society, which might add value to Francis' deliberations. It might add value to someone else's thought process on exactly how to go about doing this, whether it's public, private, or somewhere in between.

Chris, and then Cynthia.

DR. HOOK: Well, to comment to Brad and to support Hunt's statement, I agree. I think it is going to happen, and it will be either a collaboration between medical institutions or private industry or something, but to wait and discuss the ELSI issues until the study is up and going is after the fact. It's too late.

MR. MARGUS: Not up and going, just so we know something is going to actually happen. It would be really hypothetical to do it today. We don't know that this is going to happen. I mean, where's the $5 billion going to come from? Are you sure it's going to happen?

DR. WILLARD: But there were three or four years of discussions about the Human Genome Project before we were absolutely sure it was going to happen, at least in the way it finally rolled out.

MR. MARGUS: That's my vote.

DR. WILLARD: I've got Chris and then Cindy.

MS. BERRY: Just a question to the scientists really of the group. What I'm hearing, and especially when I listen to Debra, when you speak it almost sounds like this is the equivalent of going to Mars or some sort of massive vision.

DR. WILLARD: It's cheaper.

(Laughter.)

MS. BERRY: But along the lines that this would be a dramatic development to move science forward -- I mean, if you believe in the human genome and the promise of the human genome, it sounds like what you're saying is that in order to realize the benefit of that, we have to have some sort of national commitment to translating what we learn there into actual practice, research and then clinical practice, and it requires some sort of dramatic commitment on the part of the federal government, HHS, as well as the private sector.

Correct me if I'm wrong. This is just what I'm gleaning as I'm listening to people. If that is accurate, then it seems to me that this does rise to a level 4 category, where perhaps we can weigh in with a very strong statement and an opinion after in-depth analysis. I mean, I don't know that we can just jump right out and do a letter to the Secretary saying this would be a really good thing to do, and then we check it off because it was in Category 2. I think we have to really learn some more about the justification for it, what it means for medicine, for society, and after taking all the information in, then weighing in with a strong endorsement one way or the other.

I could be all wrong, so I ask really my colleagues, who are much better versed in this area than I am.

DR. WILLARD: From my perspective, if it's a number 4, then one of the points would be to address exactly that point rather than presuming that we know the answer to a question that we probably don't know the answer to.

Ed, you had a --

DR. McCABE: I was going to agree with that. I think that to recommend a study of this magnitude, while we agree, I certainly agree that this is required to really fulfill the promise of the Human Genome Project, I think we'd need to look at what is being done around the world and some of the -- I know the British Biobank has been hung up for several years because of the ELSIs there, because of the open nature of the database and that sort of thing. To discuss that I think would be appropriate.

I know there are some others who want to comment, but I think we need to either make a decision that this is going to go on somewhat longer, take a break, get our lunch, come back, because it's going to be a working lunch, or we could try and wrap it up and move it to one of the categories fairly quickly, and then move on to the next.

DR. WILLARD: I guess I would drive it to that point. If people are comfortable saying this is level 4 and let's then move on to the next one, we could do that. Or just take a straw vote and see how many 2's versus 4's we have, and then you can decide whether we need to discuss this more fully.

DR. McCABE: Debra, you wanted to --

DR. LEONARD: My only concern with making this a 4 is that this committee meets relatively infrequently, and I would hope that Francis or others for whom this is more of an urgent issue could do the review of is this scientifically warranted, what are the other models that are out there in a more timely fashion. But I may be wrong.

DR. McCABE: My guess is that that's already been done as part of the deliberations we've had.

DR. COLLINS: It's certainly not done. We've started it. Again, this two and a half day workshop in December was a good start. We have this working group that's getting formed to look at that in more depth, which will have lots of deliberations in the coming months. I would welcome any kind of connection of that enterprise to this committee that you would find would be valuable, and then we could plan a full presentation at the next meeting of SACGHS to see how far have we gotten with this and what are the areas that this committee feels need further attention and would like to get more deeply involved in, however you'd like.

DR. McCABE: I would suggest if we did that we also looked at other models as well.

DR. COLLINS: And we are as well in this working group. That's part of the intention. So can we depend on the other models that are going on in other parts of the world? Could we build this study off of existing large-scale cohorts that are already underway where DNA samples have already been collected? What would be the possibility of this being done as a private/public partnership? Which looks pretty encouraging.

DR. McCABE: I'll take Hunt's comment as a motion for a 4. Do I hear a second to that motion?

MR. MARGUS: Second.

DR. McCABE: Okay, Brad has seconded to the motion.

Any further discussion?

(No response.)

DR. McCABE: Not that we're holding your lunch hostage or anything to that discussion.

(Laughter.)

DR. McCABE: Any further discussion? Because we could table this until after the break.

(No response.)

DR. McCABE: Okay. Seeing the body language around the table, we'll take it to a vote, then.

All in favor of this as a Category 4, say aye.

(Chorus of ayes.)

DR. McCABE: Any opposed?

(No response.)

DR. McCABE: Any abstain?

(No response.)

DR. McCABE: Okay. With that, let's take a 10-minute break to gather the lunches. The lunches for the members and the ex officios are outside the door. They have your names on them. Please pick them up and come back, take a break for 10 minutes, and then we're going to have a working lunch today.

Thank you.

(Recess.)

AFTERNOON SESSION (1:00 p.m.)

DR. McCABE: Why don't we go ahead and get started? We still have eight of the 12 to do. We technically have a half hour to do that in, but we want to be sure that everything has adequate discussion. We have an hour tomorrow that we were going to discuss process, but in fact we've been doing that as we go along today, so we can slide over into tomorrow. There was some sentiment that as we got down to the bottom of the list we could spend less time, but that may be because they haven't had adequate discussion here. So I'm not sure that we want to do that.

So we may hold our second straw vote until tomorrow after we've discussed all 12. Does that seem reasonable to everyone? And it's doable, Sarah, with respect to staff

needs, to hold the straw vote until tomorrow? Okay.

So, Cindy, this is to discuss public awareness.

MS. BERRY: And I'll start with just a real general introduction, then my own assessment of how we might consider this issue, and then open it up for discussion to everyone.

Public awareness, as you know, is a very broad topic, and what struck me, and it actually was specifically articulated in the issue brief, was public awareness of what? Is it about the need for genetic testing in certain circumstances? Is it the availability of genetic testing? Is it awareness or understanding of results of genetic testing once you get those results? Also other questions that struck me, how much of this is really the responsibility of health care providers versus someone else's responsibility or the federal government's responsibility or HHS' responsibility?

Public awareness seems to be more important in the context of direct access to genetic technologies. To the extent that someone is not going through a health care provider or gatekeeper or someone who can really guide the individual, the public awareness and understanding is more critical. Also, if there's insufficient regulation or oversight such that there may be a potential for harm, public awareness becomes much more critical. It's less critical, I think, in the context of an ideal situation where you have educated health care providers who are regularly counseling their patients about the availability of genetic technologies and interpreting those results properly for them.

That sort of gets to the question of what is the appropriate role. Is it a health care provider issue? Is there a role for the federal government? Using our four guiding questions, the first is does the government have jurisdiction or authority? I would argue that I don't know that jurisdiction or authority is necessarily the right term here in this context, but certainly the federal government can play a role in educating the public. There are all types of public awareness campaigns that HHS and other agencies engage in. So I think the answer to the first question is probably yes.

The answer to the second question, can only the government address this, I don't think that's right, although the government may have a role, and there are government agencies and organizations that are working on this problem. To some extent there may be duplicative efforts in play here.

The third question, is there another body addressing the issue, and actually in our issue brief on this topic you can see that there are an awful lot of groups and agencies that are working on certain aspects of public awareness: the Department of Energy, National Human Genome Research Institute, Health Resources Services Administration and the March of Dimes are teaming up, the American Association for the Advancement of Science, and undoubtedly other groups as well. So the answer to number 3 is yes.

Four, has there been a policy solution or are there policy solutions that have already been worked out, I would argue no given what we know so far about the level of knowledge of the general public with respect to genetic technologies. So I think we have the possibility of an appropriate government role. There are agencies and private groups working on this issue. We do need some, I think, more solutions because I think there is a problem there.

The question is for the committee, how much of a priority do we want to place on this? Is this something that we can and should influence? Do we have concrete

recommendations that we would like to consider putting together for the Secretary for additional work, work that's in addition to that which is already being done, or is this something that really is in the Category 1 or 2 where it's somewhat important but there are other issues that are more important, or the second category is it's important but we don't need to spend an enormous amount of time working on in-depth analyses and recommendations. I'm not going to put forward an opinion on that one. I just wanted to kick-start the discussion and then open it up for others, and then we can talk about how we can categorize it.

Yes, Agnes?

MS. MASNY: Just for clarification, again this is one of the issues where the ex officios had ranked this as the number one issue, and I think your first question about the public awareness of what, that maybe if the ex officios would like to respond to that as to what they saw as the need for public awareness.

MS. BERRY: Yes?

DR. FEIGAL: I could start. I think that one of the reasons that I thought this was something the committee could do is the committee is in a better position to take advocacy and to take a stand on issues that some of the government positions might have to remain relatively neutral on. Often there's a perception that it's not a good use of public funds for many agencies to have public information campaigns. I'll just give you a small FDA example.

It's been debated a lot, although it's finally swung in favor of FDA being an advocate, but for the longest time it was argued that FDA shouldn't have any position on generic drugs, either for them or against them. They should just assure that they were high quality. As the concerns about the economics of health care came up, then FDA got active in pointing out the role that they play in keeping down the costs of prescription drugs.

But it's just an example that there are things that can be done in terms of public advocacy, public awareness for these issues that you as the committee can do and can ask the government to do that the government can't ask itself to do.

MS. BERRY: David, as sort of a follow-up, do you have any ideas of what you think might be most effective? I know that in the past people have talked about information brochures. I know that there's been some discussion of website activities. Is it just holding forums? Do you have any sense of what the need is, and then what the most appropriate response might be?

DR. FEIGAL: Well, particularly because Francis brings examples of some of the nonsense that's out there around genetics from time to time, one of the things that a committee like this can consider is staking its position out as a responsible voice in advocacy for issues around this, whether it's some of the consumer protection or whether it's some of the access issues or reimbursement issues, because you don't have a vested interest or you have some complicated vested interests that no one can figure them out. I'm not sure which of the two it is.

But as a body, you can make comments on things. Some of it is even deciding which of these meetings is sort of deliberative and it's fine if they don't have a lot of coverage, as opposed to the meetings where you really have a message that you want to get across and making sure that that message makes it into the press and gets some availability and out there. But there are things like websites and other types of things that certainly would be used.

I think the thing that's unfortunate about a lot of commissions and committees like this is that it can be a fairly anonymous task that produces a thoughtful report, and then it just sort of fades from view. I think that if you really wanted to have the ability to make a recommendation that people would point back to, perhaps they wouldn't form the next committee after this one.

MS. BERRY: Matthew?

MR. DAYNARD: Just a brief comment. I agree with you, David, wholeheartedly. At the Federal Trade Commission, public awareness goes hand in hand with our law enforcement. To the extent you're concerned about consumers being misinformed about genetic testing, what it is, what it can do, what it can't do, whether it's efficacious, whether there should be a doctor involved, you need to get that message out, and we do that in literally every area that we're involved in -- for example, dietary supplements or laser refractive surgery. We've co-authored brochures with the private sector folks, with the FDA. It's imperative that it be done.

To the extent that the committee thinks it can do something like that, like David suggested or other things, I think it would be very important for you to do. In terms of websites, we even have something in the dietary supplement area called "teaser" sites. Consumers, as you know, are going on the web as soon as they have a health condition and finding out some good things and some bad things, some accurate things and a whole lot of inaccurate things. We have a site -- it might be a cancer site, I think it's weight loss or arthritis -- and it's a bold claim made on the site, "Order Here," and the consumer keeps clicking, and at the end it says "Gotcha! You would have just lost your income for the last four months if you had bought this product because it's worthless."

So if you see claims like this, if you see a genetic test that says we can tell you whether you're going to have a retarded child or something, wrong, you're going to lose. There's a lot that can be done.

MS. BERRY: Linda?

DR. BRADLEY: I think one of the things that concerns us is the lack of balanced information. I mean, the public is getting their information about genomics largely from the media, and that varies from out-and-out hype to maybe overly optimistic, to sometimes dire predictions. What might be more helpful is for them to have a source of balanced information about what makes sense and what doesn't right now, currently, based on what we know, what are the gaps in information. I've heard Francis speak many times about the loss of credibility that we could suffer if we don't start differentiating between what are tests and other genomic applications that we have some basis for substantiating it should be in practice and others that are being offered -- and we've all seen some of the websites -- where there really aren't data available.

So I think that trying to look for that source of a credible, unbiased source of information that we're concerned about.

MS. BERRY: Emily?

DR. WINN-DEEN: I thought SACGT was working on some kind of a patient or something brochure, and I think it might be helpful if we could also, as you mentioned before, get a copy of that to see what is happening. I guess I interpret patient awareness as much broader, just really making sure that all the education is there through the school years, but I'm particularly concerned about people who have completed school, and

there's a lot of them out there, and how are we going to make sure that they're getting correct information and not just reading about it in whatever news source. What's on the Discovery Channel or PBS are probably good programs. There's probably just as many bad sources of information out there, and how do we help people know where to go, what to do.

So I'm not sure exactly what this committee can do, but I am really concerned about it as an issue, and I think it does need to stay on the radar screen and be addressed.

MS. BERRY: Ed first, then Martin.

DR. McCABE: Yes, I was going to comment. There was quite a bit of work that was put into patient information brochure by the SACGT that was never completed. So certainly that is something that could be brought to this committee.

MS. BERRY: Martin?

MR. DANNENFELSER: It would seem like it would be difficult for the committee to do this on an ongoing basis. Just I think the basic charge of the committee is to be advisory to the Secretary. So most of the ongoing work I think would have to be done by the Department. But you've got a lot of resources within the Department, and then through other agencies. But I think certainly this kind of objective information, because there are a lot of claims being made out there, and they're conflicting, and the public is confused. Hopefully this would be an accurate, neutral source of information, Department websites and brochures that can be disseminated through doctors' offices and other venues I think would be helpful to the public.

MS. BERRY: Hunt?

DR. WILLARD: I'm having a lot of difficulty seeing what this committee can do, although in general I agree it's a problem and a priority. I mean, again, there are academic organizations that have taken this on, there are government websites, both NIH and DOD, et cetera, which are providing information for the public at large, and I come back to my usual argument about genetic exceptionalism. I'm not sure that getting the public to weed out the information that may be a little misleading or overstated in the area of genetics is not any different, from my perspective, from what I see in cancer, weight loss, hair loss or hair gain depending on your point of view, all the things we get on a daily basis in our email if we don't have good filters.

So I'm having a hard time seeing why this is an issue for this committee as opposed to simply acknowledging that it's an important issue and hoping that more people will go to the good websites than they will to other websites.

MS. BERRY: Well, I was going to ask your exceptionalism question. What is it about genetics that makes the public awareness issue that much more critical, or does it? I mean, is there some unique aspect to genetics and genetic technologies that warrants some sort of special federal or HHS role in public awareness that doesn't exist in other areas of medicine?

DR. WILLARD: As you would predict, I don't see the issue that's specific or unique here, but others I'm sure may.

MS. BERRY: David, then Ed.

DR. FEIGAL: There are two layers to think about, about public access to your opinions. One is as experts on genetics, and that is very broad. But the other is the work of the committee itself. This is a public committee, and although there is a small audience in

attendance at many public committee meetings, the ability to actually have an open and transparent discussion of controversial issues and get them in front of the public is something that's very unique in the United States. We're very aware of that at FDA because our advisory committees are more heavily covered sometimes than our own decisions on the same products.

But it brings the debate to the public in a way that doesn't happen in Europe, for example. In Europe, the decisions are just made, and even the basis for the decision can't be reached by anything like FOI.

So part of my advice to you would be to use your bully pulpit. If there are important messages about this area that need to get across, take advantage of the fact of the stature of this committee, the stature of you as a group. Even though you're advisory to the Secretary, it's in a public fashion. He didn't bring you in in a closed fashion. In fact, that was done initially by using only government advisors. You have an opportunity to really leverage what you want to do just through this kind of process.

MS. BERRY: Ed, and then Emily.

DR. McCABE: I was going to make three points. One is that in terms of genetic exceptionalism, there are some things that we will take up in this committee that are within the purview of our role dealing with genetics that aren't genetic exceptionalism, but we are not advising the Secretary on all issues of health. So to the extent that they may be particular to genetics and genomics, then that falls within our purview, and to single them out is important. It doesn't make them exceptional for genetics.

Secondly, again to make the point, there's a lot of work that has been done by SACGT that has not seen the light of day in terms of brochures and information that could be useful to the Secretary, and completing that work, if we chose to do so, and bringing that forth would be worthwhile.

Then the third point is that a lot of this discussion I really think is very similar to the discussion about professional education and training, and that has to do with being particularly sensitive to the diversity within our culture and making sure that not only 20 percent of the public is aware but as much of the public as we can possibly deal with can be aware so that we deal with the issues of language diversity, cultural diversity, and try and be sensitive to those needs as we educate the public.

MS. BERRY: I've got Emily, and then Francis.

DR. WINN-DEEN: I guess I wanted to address Hunt's comment. I think the one place where genetics is different because of its nature is in its predictive nature. So if you can say your genetic makeup means, even though you're symptom-free today, you're going to have this disease tomorrow, and we do have some specific examples, like Huntington's, where that is the case, I think then you're in a situation where people have to understand that that's the situation and you don't want to be in a situation where people are testing for -- let's just assume for the moment that this is not true, that you carry this gene, so therefore you're obese and you'll always be that way and you can't do anything about your weight, so just resign yourself to diabetes and heart disease and everything else.

Now, maybe there is a genetic component, but until that's proven and well documented, we don't want people getting either the wrong health care or not getting the right health care because they don't really understand what's going on and what's true and what's not true. Now, a large part of that should be happening with a health care provider. But as you mentioned, your email box is filled with misinformation, particularly around weight loss and

that area. I think if we're not careful about educating the public so they really at least know where to go -- I mean, a public awareness campaign can be NIH has this website. It doesn't have to mean that you do all the in-depth education in your primary format.

But I'm just concerned that if we don't do something, we don't make it a priority that the end user ends up being uninformed.

MS. BERRY: Francis, and then Joan.

DR. COLLINS: I don't think anybody would disagree with the premise that it is an important area, that public awareness of what genetics can do for you and what it can't would be a good goal to try to achieve. I think the problem is it's very hard to figure out how to do that in a fashion that gives people information when they didn't really think at the moment they were looking for it anyway. So this notion of trying to identify the teachable moment, and then be sure you have validated information available to the people who are at that moment and looking for it seems like a fairly attractive strategy.

That, in fact, is one of the reasons that we have pushed, I think over the last 10 years, more in the direction of trying to educate the health care professionals, because many people at the teachable moment go to the health care professional and say what should I do about the fact that I just heard that my brother has been diagnosed with colon cancer? Does that mean I should be getting screened? That kind of question.

We have, through NHGRI, and even more from the Department of Energy, funded a fair number of public education projects through the ELSI program over the last 10 years, and they've been a diverse array of projects, some of which were simply public forums, some of which generated materials, some of which supported PBS television shows that some of you have probably seen.

The problem is it's really hard to evaluate what the impact of that educational investment has been, and it may be that the investment has not yielded a big, huge difference. Most people get their information about genetics either from the media in sort of a fashion where they're filtering a lot of other things and may or may not be tracking this one or, as I said, they seek it out at a time when they're specifically faced with a question about themselves or their family and they're most likely then to ask their health care professional.

People who are looking for information on the web, you should certainly be aware there's a lot of pretty good information about genetics and genomics that you can find on a lot of websites. Probably the NIH website more than any other is loaded with information, including some that is specifically designed for people from different cultures, or even from different languages. It's not perfect. There are holes in it. It's not as broad and diverse as it should be. But I think it is possible to get some information if you're looking for it.

I guess here, as some of the rest of you have said, while this is a very hard problem, it's also a hard one to come up with an obvious mechanism to solve the problem, particularly if we're not quite sure right now what the message is. I've always thought it was useful to ask the question if somebody donated money to you, to have a 60-second spot in the middle of the Oscars, just to be topical, about genetics, and you were the one to design that particular 60-second public interest spot, what would you try to say to all of those people gathered around their televisions? What would be the message you'd try to convey?

Genetic testing could help you? Well, that doesn't sound so good. Know your family history. That would be a good thing for people to know about. Maybe that would be a decent message, but it would be a little hard to get a lot of people to jump up off their

couch about that one. What is it that we want people to be aware of, and what actions do we want them to take? I don't think we're even quite in consensus about the answer to that question, which makes it hard to design a public awareness campaign.

It's much better, of course, if you had a circumstance where you really have a message about AIDS prevention and you know what it is you're asking somebody to do.

MS. BERRY: Joan?

DR. REEDE: Well, the pediatrician in me is coming forward. There's a part of educating the public at large, but there is for me a real part of how do we educate those that are in our educational system, our K-12. I know that the briefing mentions it briefly and says that there's a lot being done, but if you look at the standards, if you look at AAAS, if you look at NSF, if you look at the state standards, the various standards, although it mentions genetics, there is really no focus on human genetics. If you look at most of the classrooms, you will spend an entire year studying all sorts of things and one day understanding anything that relates to human genetics.

So I think there is a point to step in and say that understanding what goes on in terms of human genetics is important. I think this dividing it up into standards being set by NSF over here, NIH has developed some curricular pieces, but they are truly not integrated across the board. There are a lot of school systems that don't know that they exist. The agencies actually have to start working together. If a set of standards is being put in place over in one area that completely ignores or minimizes the importance of human genetics, it is hard to move this forward in terms of educating future generations about these issues.

MS. BERRY: Yes, Kimberly?

MS. ZELLMER: I just wanted to reiterate what Francis was saying. I think that when we're talking about public awareness, I think there's a lot of information out there, and I think that part of it is what the public is interested in. I think that personally, I'm an educated person but I knew very little about genetics until my daughter was diagnosed, and that obviously generated an interest, and I found plenty of information once I wanted the information. I think it depends on what specifically you're trying to raise awareness with the public, because I think if you're just talking sort of general genetic principles, those that are interested have plenty of resources to go to and look for.

Those who don't really have an interest, I don't know how you're going to get their attention. I don't know if you put a brochure in the doctor's office and they don't really have any issues, I'm not really sure that that's going to generate any more public awareness. If you provide forums for people who aren't aware of any genetic issues, I don't know how effective that's going to be.

It seems like what we've talked about is sort of warning people about these emails and false advertising and things like that, and I think that's kind of a different issue, more than general public awareness. I mean, to me that seems more like how do we regulate these advertisers and protect people from that than just sort of general public awareness, because I think there's a lot of good resources if people want to know about genetics and different types of genetic disorders.

But I think really what we're talking about is protecting people from the bad information, and I don't know exactly how we would do that. But that seems more like the advertising issue rather than necessarily public awareness.

MS. BERRY: Does anyone else have any comments? Yes, David, and then

Matthew.

DR. FEIGAL: Let me just give a quick counterexample. I think if you felt strongly, for example, in the discussion we were having before lunch, that a large population study was something that was unusual, it's going to take a lot of consensus building to get the kind of trust for something like that to enroll rapidly. So to have an endorsement, to talk about why that's a good idea, how that's going to make the investment in the Human Genome Project pay off and so forth. There may be other people who say it, but don't underestimate the impact that you can have, too.

MR. DAYNARD: I just wanted to add my suggestion that the committee look upon public awareness and its input to that as an access issue. That's the way the Federal Trade Commission looks at consumer awareness about any issue, particularly issues that affect their health. If it's nothing more than telling consumers what the good websites are, or examples of bad websites, it's going to affect their access, particularly when you get into communities that may not otherwise have normal access. So that's the way I'd suggest looking at it. Thanks.

MS. BERRY: Martha?

DR. TURNER: A quick process issue relative to what we're talking about when we're talking about this, and that is that it's not so much that we know today what we want the public to be aware of but that we agree that as we learn about things, the public needs to become aware of them, if appropriate. So if we find something out that we should build into whatever marketing plans and dissemination plans we have, some sort of piece for public education that is not perhaps on the web, because there are a whole lot of people who don't use computers today -- and so when we identify a population we want to know something, then we need to develop ways to make sure that's a part built in, as opposed to something that may or may not happen depending on the economics or the marketing.

MS. BERRY: Brad, did you have something?

MR. MARGUS: I'm not really sure how we can improve awareness. I like the idea of using our pulpit as a committee, anything we decide to support like a large population study, to use our opportunity to shout it from the mountaintops.

I just wanted to bring up one subject, though, and that is are there some more things out there that we could endorse or that we could impress on the Secretary to talk to other agencies about or to help support, such as at the last meeting when the FTC taught us about how much can be enforced. Given the very, very restricted resources and budget, I learned that people pretty much have to be dying from a claim, and even then it can't be on a regional level, it has to be on a national level, all these things that made it really tough to enforce anything.

That was pretty outrageous to me. So while I'm not exactly sure how we can change awareness overnight in any big, broad stroke way, if there are certain things that we could still emphasize so that when the Secretary is sitting in the Cabinet meetings this somehow can be underscored, I think we need to speak up if it affects our area. In the case of the FTC example, that really affected our area. I mean, here we are thinking about how can we educate people better, but it turns out that even if people were out there making wild claims, from what I understood from last time, it's pretty hard to enforce. Maybe we should just go on record as saying that we're not happy with that.

DR. McCABE: We're going to need to wrap this up very quickly so that we

can move on to the public comment.

MS. BERRY: I was just going to wrap up by saying I think, based on the issue briefs and our conversations, it seems like there is a pretty significant gap in public awareness. There are public awareness efforts underway by different government agencies and by private organizations. Are they sufficient or are there gaps? We don't really know, so the question is while we think this is a very important issue, obviously because of the ranking that it achieved -- it's fairly high up there -- what is our role? Without getting into specific recommendations, are we going to talk about starting our own website? Are we going to have forums? Whatever those may be, that's something for another day.

Do we want to have a more monitoring, passive role in keeping an eye on it, declaring the priority that it is but sort of sitting back and watching these other activities? Or do we want to have more of a leadership role and be more aggressive in using our bully pulpit and coming up with concrete recommendations and partnering with different agencies and groups? That sort of leads us to the discussion of the categorization. Where would we put this in the 1 to 4 categories? I'd entertain anybody's motion for a category.

Kimberly?

MS. ZELLMER: I think this is one of the Category 3 is what I would say, in that it transcends all issues and that on a case-by-case basis we should see it as to the issues that we're discussing, whether it's something that maybe we want to make the public aware of, or if there are aspects of whatever we're discussing, whether it's coverage and reimbursement or large population studies or whatever, whether there is some public awareness aspect that we want to make sure that the word gets out.

MS. BERRY: Yes, Barbara?

MS. HARRISON: I think I'd just add a thought that's been going through my mind, which is really how pervasive and how important public awareness is. I mean, the reason why we don't have underrepresented populations participating in studies is because they're not aware of genetics. They don't know how important it is for them to be involved in that clinical trial or for them to be involved in this research protocol, because it significantly contributes to the development of drugs and that kind of thing.

So I think because we're here to serve the public and we want the public to be aware of what we're doing, I think public awareness really has to be up there. I do struggle with how is the best way to do it, but I definitely think that it's a priority issue and I can definitely see it being put in 3, I guess myself.

MS. BERRY: Yes, Joan?

DR. REEDE: Along those same lines, I think one of the things that we might consider as a committee, if we put something into a Category 2, which means we think it's important enough that we need to act quickly or it needs to be monitored for a period of time, or a Category 4, something that we need more information on, that we as a committee also think about how do we make the public more aware of this issue. So as we send a letter to the Secretary or use some other vehicle, at the same time think about the public. It may be that we need to do more than have an open public forum meeting like this. Are there other things that we need to do to inform people about the opinions that we have or the issues? To date, I don't see us having really engaged in that part of the discussion as much.

DR. McCABE: Okay. Well, having heard the discussion -- thank you very much, Cindy. Having heard the discussion, do I have a formal motion? It sounds to me like

this is moving toward a Category 3, transcends all issues, needs to be included in any discussion of any issue about how to make the public aware of that. Can I have a formal motion to that effect?

I'll take Kim, since you brought it up first, and Chris as a second to that.

Any further discussion of this?

(No response.)

DR. McCABE: All in favor, say aye.

(Chorus of ayes.)

DR. McCABE: Opposed, nay?

(No response.)

DR. McCABE: Abstain?

(No response.)

DR. McCABE: Okay. So that, then, is a Category 3, and with that, we'll continue the discussion on these tomorrow.

But now it's time for us to hear from the public. This is something that's extremely important for us. We've just been discussing that this is a public forum for deliberations, and we value the input we receive from the public. We set aside a time during each meeting for public commentary. There will be time today and tomorrow. There are also written comments which appear under Tab 1 of your briefing book, and some additional have been passed out today or are in your table folders.

I'll ask each of our public speakers to please limit your comments to five minutes, and today we'll be hearing first from Dr. Margaret Gulley, Chair, Molecular Pathology Committee, College of American Pathologists.

You can sit or stand, whichever you prefer.

DR. GULLEY: This is what the written comments look like, and there's extra copies out in the hall.

Dr. McCabe and members of the committee, good afternoon. My name is Margaret Gulley and I'm Director of Molecular Pathology in the McLendon Clinical Laboratories at University of North Carolina Hospitals. I'm also a faculty member in the Department of Pathology and Laboratory Medicine of the University of North Carolina at Chapel Hill Medical School. Today I'm here as a representative of the College of American Pathologists, or CAP, where I currently serve as Chair of the Molecular Pathology Resource Committee.

The comments expressed by the CAP reflect a set of fundamental principles regarding genetic testing and quality laboratory medicine. The purpose of these comments is to provide the committee information with regard to genetic testing issues as they relate to the priorities under consideration. Specifically, my comments will describe the College's involvement in the area of CPT coding towards reimbursement for genetic technologies, the CAP's position on patent policy impacting genetic tests and our progress on the College's approach to address genetic test oversight utilizing existing regulatory mechanisms that include laboratory accreditation and proficiency testing programs.

So first, on CPT coding on reimbursement, the College has formed a Genetic Testing Work Group focused on creating appropriate code assignments for molecular genetic testing for recommendation to the AMA CPT Editorial Panel. In an effort to better utilize molecular genetic tests, the work group proposed to the AMA the implementation of a

coding system that will offer diagnostic granularity without changing test descriptions and thus be less prone to payment denials.

The work group includes representatives from the American Society for Clinical Pathology, the Association for Molecular Pathology, the American College of Medical Genetics, the American Association for Clinical Chemistry, and the American Clinical Laboratory Association. A consensus was reached that use of code modifiers in the current CPT system would result in widespread acceptance from payers and enable providers to submit specific information to adjudicate claims.

The College led a breakout session during the AMA's November CPT advisory committee meeting to discuss this approach. The session included representatives from the AMA CPT Editorial Panel, the Centers for Medicare and Medicaid Services, the AAHP/HIAA, and Blue Cross/Blue Shield Association. After careful review of prior options, the breakout session facilitators all agreed that the numeric alpha code modifier system is the most viable solution. Further, the work group concluded that implementation of the modifier option would provide an accurate method of reporting and identifying molecular genetic testing, the ability to track utilization of genetic tests to capture diagnostic granularity, and permit data tracking to determine the genes that are most often targeted for testing, the frequency of the tests, as well as the types of genetic tests that are most utilized.

The work group confirmed that CPT modifiers would result in widespread acceptance from payers. The work group's recommendations were presented to the CPT Editorial Panel and subsequently to the CPT advisory committee members for comment, and placed on the CPT Panel's February 2004 meeting agenda. The College cannot report on the outcome of this proposal because the proposed CPT coding changes are confidential and proprietary until they're finalized. Because code assignments and descriptions can change until just before publication, the American Medical Association, which owns the CPT, asks that participating organizations not publicly release detailed coding information until publication of the CPT volume.

What can be stated is that after two years of intensive work to create a numeric alpha modifier system for molecular genetic test coding, a major milestone was reached this past month when the CPT Editorial Panel favorably considered the proposed system. We're hopeful that the proposed changes will be published this October for the 2005 CPT coding book edition.

I will now turn to patent policy impacting genetic technologies. As medical specialists in diagnosis of disease, the College recognizes that genetic testing is an area of growth and change for pathology and for all of medical practice in the decades to come. Pathologists therefore have a keen interest in ensuring that gene patents do not restrict the ability of physicians to provide quality diagnostic services to the patients that they serve. The CAP believes that gene patents pose a serious threat to medical advancement, medical education and patient care.

When patents are granted, subsequent exclusive license agreements and excessive licensing fees prevent researchers, physicians, and laboratories from providing genetic-based diagnostic services. As a consequence, patient access to care is limited, quality is jeopardized, and training of health care providers is restricted.

The field of molecular pathology uses genes and their mutations to predict or diagnose disease. The list of diseases that can now be diagnosed or predicted from gene-

based tests is growing rapidly. Physicians and scientists can often easily translate the fundamental information derived from studying the human genome into diagnostic genetic tests and use these tests for patient care. Because information about gene sequences is so fundamental to the understanding of specific diseases, patent holders can gain essential ownership of diseases through patents. Exclusive or restrictive license agreements on gene-based tests have been used to prevent physicians and clinical laboratories from performing these tests as diagnostic medical procedures.

Patients suffer because diagnostic test services are less readily available and affordable. Medical education and clinical research are also threatened. In fact, CAP members have received cease and desist notification letters from patent holders indicating that continued patient testing would be a patent infringement. Examples of diseases where testing has been halted due to physicians receiving such a letter include breast cancer, Canavan's disease, Charcot-Marie-Tooth disease, and Alzheimer's disease.

The recent trend of using patents to monopolize gene-based testing services is a radical departure from historical precedent in clinical laboratories, and it works against the goal of making these procedures widely accessible and affordable to the public.

DR. McCABE: Could you wrap it up fairly soon, please?

DR. GULLEY: Sure.

Especially troubling is the fact that under patent protection, the understanding of the utility of the test, as well as the underlying disease processes, also become proprietary, thereby imposing a profound change in how the profession and the public acquire knowledge about these tests.

In 1996, Congress recognized that medical procedure patents might impede the advancement of medicine, curtail academic access, and place unreasonable limits on the research community, and interfere with medical education and the quality of care provided to patients. As a result, in October of '96 legislation was signed into law, the Frist-Ganske amendment, that permanently precludes the filing of infringement suits against physicians and other medical practitioners for the performance of medical activities that would otherwise violate patents on medical or surgical procedures. A medical activity is broadly defined to include the performance of a medical or surgical procedure on a human body, organ, or cadaver, or on an animal used for research.

However, the act does not explicitly affect enforcement of biotechnology patents or extend to clinical laboratory services. With the advent of new and innovative approaches to gene-based diagnostic testing and the promise of enhanced and expanded diagnostic testing, laboratory services and clinicians should have the same protection from patent infringement as other medical providers and other procedures.

We're facing the unprecedented situation in which a single patent --

DR. McCABE: I'm sorry, but we have your testimony in written form. If you could just move to the conclusion quickly, please.

DR. GULLEY: Okay. We believe that patents set an extraordinary and dangerous precedent, and they affect the availability of diagnostic testing.

The final thing I wanted to touch on was genetic testing oversight. We have presented an approach to the oversight of genetic testing that builds on the existing clinical laboratory improvement amendment, or CLIA, laboratory inspection and accreditation process to provide oversight and approval of genetic testing in lieu of federal regulations.

So we would like to suggest that instead of increasing federal regulations or developing reduplicative federal programs, that we work through the existing programs to improve oversight and federal oversight of genetic testing.

So you have the rest of my comments in the handout, and I would like to conclude with saying that the College of American Pathologists appreciates the opportunity, and we're here to answer questions or work with you as you continue to work on policy issues.

Thank you.

DR. McCABE: Thank you very much.

I think in the interest of time we need to move on to the next presenter. That is Dr. Judith Lewis, who is president of the International Society for Nurses in Genetics, or ISONG, and also a professor in the School of Nursing at Virginia Commonwealth University, and a member of the Secretary's Advisory Committee on Genetic Testing.

Welcome back, Judy.

DR. LEWIS: Thank you, Dr. McCabe. I must say it's really nice to see that some of the work that we did that didn't get finished is also being considered by the current committee, so I thank you for that.

But I'm here this afternoon as the current president of ISONG, the International Society of Nurses in Genetics. Our membership spans six continents and includes nurse clinicians, nurse educators, and nurse researchers. ISONG is a specialty nursing organization dedicated to caring for people's genetic health through excellence in the provision of genetic health care services by fostering the professional and personal growth of nurses in human genetics.

There are over 2.7 million nurses in the United States. Of those, approximately 2.2 million currently are practicing as registered nurses. Approximately 7.3 percent of those, or slightly fewer than 200,000, are advanced practice nurses. Half of these, or about 100,000, are nurse practitioners who are delivering primary health care services. Compared to other primary health care providers, nurse practitioners are more likely to be practicing in sites serving patients who are economically or socially disadvantaged or in medically underserved areas. The average salary for a nurse practitioner in the United States is slightly over $60,000.

Of the 2.2 million practicing nurses, over two-thirds of us work at inpatient hospital settings, with the vast majority of those involved in direct patient care. In the inpatient setting, the nurse is the health care professional who spends the largest amount of time in direct contact with the patient. The nurse is often the health care professional who first notes the dysmorphic features of the newborn, who provides the patient with education about the nature of a newly-diagnosed chronic condition, who answers the patient's questions about the meaning of this illness for themselves and their family members, and who deals with the entire spectrum of the human response to health and illness.

The nursing workforce holds great potential in caring for people's genetic health. ISONG has, in conjunction with the American Nurses Association, developed and promulgated the Scope and Standards of genetics clinical nursing practice. This document, which is currently being revised and expanded, delineates the genetic competencies for nurses practicing at the basic level, as well as enhanced competencies for advanced practice nurses. In addition, the Genetic Credentialing Commission, an affiliate of ISONG, offers the advanced practice nurse in genetics credential to Master's prepared nurses in specialty genetic services,

and the genetics clinical nurse credential to the baccalaureate prepared nurse who managed genetic information in a variety of health care settings. These credentials are awarded on the basis of a professional portfolio.

ISONG is committed to working towards ensuring that the nursing workforce is well prepared to serve the patient's and the public's need for genetic information. There are several programs designed to prepare nursing faculty, who may have been educated themselves in the pre-genomic era, with the knowledge and skills that they need to include genetics content in undergraduate and specialty nursing curricula. The National Institute for Nursing Research offers a highly competitive, intensive fellowship designed for doctorally prepared nurses, doctoral students, and advanced practice nurses. The goal of this summer institute is to prepare nurses to become clinicians and researchers in the area of genetics.

Current programs, while providing a valuable service, do not have the capacity to meet the demand. If we are to continue to prepare an educated workforce, the profession needs resources to enhance its education and outreach efforts.

ISONG is committed to ensuring that all individuals have appropriate access to genetics and genomic health care and has approved a position statement defining the role of the nurse in ensuring access. I have provided you all with copies of this statement that just was published this week. In addition, I have with me a single copy of the Scope and Standards document for your use.

ISONG is eager to work with the Secretary's Committee on Genetics, Health, and Society as you define your priorities and begin your work. We look forward to providing you with information on the genetics nursing workforce, the way genetics nurses practice in the United States and throughout the world, and with knowledge of the resources that will be required to ensure that our over 2 million nurse colleagues have the knowledge and skills they will need to practice effectively.

Thank you.

DR. McCABE: Thank you.

We have time for one or two brief questions, if there are any questions or comments.

(No response.)

DR. McCABE: If not, thank you very much.

Our next speaker is Sharon Terry, president of the Genetic Alliance.

MS. TERRY: My name is Sharon Terry, and I'm president and CEO of the Genetic Alliance. I want to thank you for this opportunity to offer comment and for your work on these issues.

You've identified 12 important issues. Some, as you have noted, are subsets of others. Prioritizing them can only be done in the context of a framework. By what metric should these issues be measured and weighted? I propose articulating the metric, and it is improved human health.

There are some premises by which we in the genetics community operate. First, genetics is significant for more than just the "gee whiz" factor. It has something to do with human health. Second, success for the science of genetics means translating this body of basic knowledge into technologies and treatments that improve human health. Third, the government should be involved in facilitating success. Fourth, genetics has engendered these discussions, which set it apart from other basic science to health translations. So whether

genetic exceptionalism is right or wrong, it exists. Against this background, I'd like to comment on these issues.

But first, a disclosure. I have a huge conflict of interest and an overarching agenda. I speak mindful of the millions of individuals affected by genetic conditions. I know what I know because I, as one among them, have worked alongside them for over 10 years. I know what I know because my colleagues, other lay advocacy group leaders, face the loss of their child, face the enormous impact of disabilities, face the inadequacies of the health care system. I know what I know because my two children face blindness and a host of other difficulties as a result of causal mutations in a gene.

I live with the issues you have laid out. I have discussed them in numerous federal advisory committees, analyzed them over drinks, written papers about them. I think that after the collective work of this community and all of your work, I think that the issues you define are only symptoms, symptoms of a disease that needs to be described, and we, like so much of medicine, are much more comfortable dealing with the phenotype rather than the etiology of the disease. I believe that it is the challenge of this committee, if you want to make a difference, to uncover the basic roadblocks and not continue to just describe the symptoms.

In fact, as several people have noted both here and in written comments, many of the issues are a subset of access. Coverage and reimbursement, genetic discrimination, genetics education and training, oversight, direct-to-consumer advertising, patents, and public awareness are all subsets of access. Many of these issues are examined in a kind of isolation that does not reveal the underlying cause, and many of them are examined in a political agenda-driven light. I don't think this committee or any federal advisory committee has the resources to recommend solutions to these problems.

Two of the other issues are a step closer to considering the major priority. If the reason we care about genetics is because it will lead to improved human health -- I've already disclosed that I have an agenda -- then we must put the symptoms together for a diagnosis. The questions that pharmacogenomics and large population studies raise are related and are closer to the root of the problem. Neither can be done well in the current regulatory climate. Both are impeded by important protections that are misguided in implementation, thus thwarting the very research we need to move an enormous body of basic science towards translational research.

The steps along the way, meaningful epidemiology, natural history studies, longitudinal studies, environmental studies, gene/environment studies, are all thwarted, cumbersome, and deincentivized. This committee has a bully pulpit that can have an impact on policy recommendations that could facilitate the climate necessary for these studies.

The ultimate questions are ones of integration. How will genetics be integrated into medicine? How will scientific evidence be integrated into policymaking, payer decisionmaking, agenda-setting for research priorities? Right now, the system in place has no incentive for physicians to be early adopters of proven genomics technologies, for payers to pay for new technologies and treatments, for researchers to strive for health outcomes as the endpoint, for industry to take risks that will benefit marginalized communities, be they racial, ethnic, or rare disease communities.

So the answer to genetic exceptionalism is an easy one. Genetics should be integrated, and the path to integration probably involves both segregation and affirmative action. The question before this committee is whether you are ready to be bold, to look at these

issues without the lens through which you normally look. Are you willing to go beyond the symptoms to understand the etiology of the disease? Are you committed to discovering the real roadblocks in the system that creates all these other issues and grapple with the system, not just the symptoms?

This leaves you with the issue of a vision statement, an issue which could be considered without substance. I contend that if you cast aside your usual imaging tools and look at the whole patient in the context of a community, you have the brain power on this committee to formulate a vision of genetics integrated, of a pathway to translation, of a future where genetics and genomics improve human health. You have the ability to recommend systems whereby politics no longer set the scientific agenda and basic science no longer holds policy hostage.

I strongly suspect the answer might include universal health care, and while you may feel this is beyond the scope of the committee, I suggest that not to name the disease increases morbidity. We, the people who live with genetic conditions every day, who watch our children die, who care for our sick siblings and parents, and who are limited by disease ourselves, know well what the rest of the world will come to know, that science will never step up to the plate and set a health outcomes agenda on its own, and that politics will never understand the complexity of the system without the evidence that science offers.

It is time for the two to be integrated, to formulate, based on hard evidence from all the sciences, a vision for the future. You must identify the roadblocks and recommend the treatments. It is time for us to engage in the future for which we hope. We are ready. We hope you are, too.

Thank you for your service, your thoughtfulness, and your dedication to genetics, health and society.

DR. McCABE: Thank you.

I think, unfortunately, it's necessary for us to move on.

Our last speaker is Dr. Andrea Ferreira-Gonzalez, who is director of the Molecular Diagnostics Lab and Associate Professor of Pathology, Virginia Commonwealth University.

DR. FERREIRA-GONZALEZ: Dr. McCabe, members of the committee, good afternoon. My name is Andrea Ferreira-Gonzalez. I'm a director of the Molecular Diagnostics Laboratory and Associate Professor of Pathology at Virginia Commonwealth University. I'm currently past chair of the professional relations committee for the Association for Molecular Pathology, and I speak to you today as a representative of AMP.

The purpose of these comments is to provide information to the committee on issues that are affecting the ability of laboratories to provide genetic testing services. There are three major issues that I will address today. First is the inadequacy of the CPT coding and reimbursement for genetic tests. Second is the negative effect of gene patents on molecular diagnostic laboratories. And the last issue is an update on advances in the oversight of genetic testing laboratories.

With regards to the first issue, CPT coding and reimbursement for genetic tests, a widely held view which AMP upholds is that molecular genetic tests will influence all aspects of medical practice in the future as we unravel the variations in the human genome that correlate with disease and disease risk. Molecular genetic testing must be financially viable so that physicians and patients may realize all the diagnostic benefits of our understanding of the

human genome.

Currently this is not the case, and several factors prevent the appropriate cost recovery for genetic testing laboratories. These factors are the inadequacy of the CPT coding system available for the billing of molecular genetic tests and the low reimbursement levels set for the CPT codes that are available and currently in use. The Association for Molecular Pathology has been working closely with a Genetic Testing Work Group over the last two years, with the goal of developing and implementing an appropriate billing code system for molecular genetic tests.

The College of American Pathology chairs the work group with members of other associations. The work group has proposed to the AMA implementing a coding system that will provide payers with more specific information about genetic tests performed, and thus be less prone to denials. The genetic working group's recommendations were presented to the CPT Editorial Panel and subsequently given to the CPT Advisory Committee members for comment. The proposal was discussed at the CPT Panel's 2004 meeting, and AMP understands that the recommendations were received favorably.

AMP asks that the SACGHS remains cognizant of the progress in implementing the proposed changes in molecular genetic test coding and the impact on payment for molecular genetic testing in the future.

The second factor affecting the financial viability of molecular genetic laboratories is the current Medicare reimbursement levels set for existing CPT codes. These reimbursement levels, which will be presented later on today, are far less than the cost of performing molecular genetic tests. The reimbursement levels were set more than 10 years ago and were inadequate even then. They do not reflect the current cost of genetic tests, they are technically complex and frequently require highly detailed analysis and interpretation. So AMP asks SACGHS to consider steps that could provide reasonable cost recovery for genetic tests.

The effect of gene patents on genetic testing services. The granting, licensing and enforcement of gene patents is having a broad negative impact on the ability of clinical laboratories to perform genetic tests. While licensing fees may be financially devastating to a molecular genetic laboratory already facing inadequate cost recovery for genetic tests, even more egregious is exclusive licensing or enforcement resulting in a sole provider of a medical service.

AMP strongly holds that a sole provider of a medical service is not in the best interest of the public health. Examples of diseases where testing has been halted due to patent or licensing enforcement includes breast cancer, Alzheimer's disease, Canavan disease, and Charcot-Marie-Tooth disease. The growing trend of using patents to monopolize genetic testing services severely compromises the accessibility and affordability of genetic tests for the public. Particularly troubling is that under patent protection, the growth in understanding of the utility of a genetic test, and even the underlying disease processes, also become proprietary.

Congress already recognized that medical procedure patents impede the advancement of medicine, curtail medical access, places unreasonable limits on the research community, and interferes with medical education and the quality of care provided to patients. As a result, in October 1996, legislation was signed into law that permanently precludes the filing of infringement suits against physicians and other medical practitioners for the performance of medical activities that would otherwise violate patents on medical and surgical

procedures. However, the law does not cover biotechnology patents and does not extend to clinical laboratory services.

In 2003, Representative Lynn Rivers, who was not re-elected, introduced legislation that would protect physicians and other providers of clinical laboratory services against enforcements of gene patents and against liability for infringement of patents on genes. The logic of the bill was that genetic test services are part of medical practice and should be widely available to promote optimal patient care, medical training, and medical research.

We anticipate that a new bill will be introduced in Congress to address this concern. AMP encourages the Secretary's committee to examine the negative impact on medicine of current practices in the patenting and licensing of genetic sequencing and work to eliminate restrictions on the medical use of genetic information.

The last topic I would like to point out is genetic testing oversight. The Association for Molecular Pathology has worked closely with the Food and Drug Administration's in vitro diagnostic division to provide a laboratory perspective on the previous committee's proposal for FDA oversight of laboratory-developed genetic tests. AMP supports the existing clinical laboratory improvement amendment, laboratory inspection and accreditation process to provide oversight and approval of genetic tests in lieu of new federal regulations, and even FDA oversight.

A major concern of the previous committee in the area of oversight was the review of laboratory-developed tests prior to their coming into clinical use. In response to these concerns, the College of American Pathologists has developed and added test validation questions to the molecular pathology checklist that will be used for inspections in the future.

AMP asks the Secretary's committee to review the changes implemented by the College of American Pathology addressing test validation oversight concerns to determine if these changes address the concerns raised by your predecessor.

The laboratory inspection process is only as good as the inspectors performing the reviews of the laboratories. AMP has hosted training sessions for molecular pathology laboratory inspectors at its previous three annual meetings, since AMP members are among the experts in molecular testing. AMP supports the training and use of qualifying inspectors to strengthen the review provided to molecular laboratories during the inspection and accreditation process.

Furthermore, AMP's clinical practice committee is addressing clinical practice issues such as developing a consensus on information to be included in a test report for common genetic disease.

On behalf of AMP, I thank you for the opportunity to speak to you today. AMP remains available to you to assist you with or provide information for your thoughtful deliberations and important work.

Thank you.

DR. McCABE: Thank you.

I think we need to move on because of the pressure of time. We thank all of our members of the public for presenting to us today. We very much appreciate your input.

Now we're going to begin a series of presentations on coverage and reimbursement of genetic technologies and services, and that will be followed by a roundtable discussion. I'd like to invite the presenters for the afternoon session to please join us at the table. Your names are there at your places.

DR. LEONARD: Ed?
DR. McCABE: Yes?
DR. LEONARD: Can I ask a question? Can we get a copy of the comments from the woman from Genetic Alliance, please?
DR. McCABE: Sharon, had you provided us with your comments?
MS. TERRY: I had to do them on the airplane coming here, so I will email them to Sarah. Is that okay?
DR. McCABE: Okay. So the comment, just for the record, is that they will be made available to Sarah as soon as possible. Thank you very much. I think they are important.
Do you have them on a disk?
MS. TERRY: I have them on my laptop. I can bring them to the business session.
DR. McCABE: Perhaps you could work with one of the staff members to get them transferred over so we could have them printed out, because I think they will inform further discussion tomorrow.
I think, as all of you will recall, the committee really decided that this was an important issue, coverage and reimbursement, at our October meeting, and will help add background to our priority-setting deliberations, which will continue tomorrow morning. I want to thank all of the presenters for taking time from your busy lives to be here with us. We look forward to an enlightening series of talks that are going to come at this from a variety of different perspectives.
Because of the time constraints, I'm not going to go through extensive bios. Those are under Tab 1 in your briefing books, and copies of the presenters' PowerPoint slides are in the table folders, this white folder that was at your position this morning.
So our first presentation of the afternoon is by Dr. Michele Schoonmaker, who will brief us about coverage and payment decisions and how they're made for genetic technologies and services by private health plans. Dr. Schoonmaker is on the staff of the Congressional Research Service of the Library of Congress. This group provides objective, bipartisan analyses to Congress on genetics issues.
Dr. Schoonmaker?
DR. SCHOONMAKER: Good afternoon, Mr. Chairman, members of the committee, and the public. Thank you for inviting me to participate in this session on the coverage of genetic tests and services. The views I will present are my own and do not reflect the views of the Congressional Research Service or the Library of Congress.
I'll begin by briefly describing health insurance coverage in the U.S., and I'll focus mainly on how private insurers make decisions to cover new genetic tests. Then we'll provide a general overview for how they pay for them. Throughout, I will give examples of existing coverage policies for genetic technologies.
In 2002, almost 44 million people were uninsured. Seventy-two million were covered by a public program, such as Medicare or Medicaid or the military, while the majority, or 199 million people, had private insurance. Of those with private insurance, 88 percent were covered by group policies, usually through their employers, and 12 percent purchased individual policies. The percents don't add up to 100 percent because there are about 29 million people who were counted in more than one group during the year, for example that

moved between being uninsured and being on Medicaid.

There are two main types of private insurance products. In indemnity insurance, the insurer provides financing only. The insurer pays a provider a fee for service after the patient has received the service. Because indemnity insurance originated to protect people from the high cost of injury or illness, historically benefits excluded preventive services. Most of today's indemnity plans have adopted some element of managed care.

Managed care emerged in the 1980s as an incentive to reduce the cost of health care. Managed care insurers do this by coordinating the financing of care with the delivery of services. Prior authorization and case management are two of the tools used to encourage patients to see certain providers or to control their access to certain types of services. For prior authorization, a patient has to get payer approval before seeking care. In case management, a provider coordinates care through referrals. These practices aim at ensuring that a patient receives only medically necessary services. Unlike indemnity insurance, most managed care products generally include some coverage for preventive services.

Managed care products span a continuum of possible arrangements. Health maintenance organizations are the most managed in that they completely integrate the financing and delivery of services. Physicians are usually salaried employees or paid per member per month regardless of whether or not a patient actually seeks care. HMO patients must see HMO network providers or care generally won't be covered. In a provider organization, the payer contracts with networks of physicians for primary care specialty services. The provider and the payer negotiate discounted fees in exchange for a higher volume of referrals.

A point of service plan is a hybrid between the HMO and the PPO arrangement. The point of service evolved to give patients more freedom in their choice of provider. The patient can choose an in-network provider and have HMO-like benefits with low co-payments, or they can choose to go out of network but with higher co-payments.

I've included the last two slides because it's important to understand the distinction, because the type of organization can impact how coverage decisions are made and how the providers are reimbursed.

I'll now discuss how coverage policies are made and provide examples of existing policies. To prepare for the upcoming slides, I looked at the websites of 125 private health insurers. Though 44 of them posted their coverage policies, only 27 allowed unrestricted access. Of the 27, 24 had posted policies related to genetic tests or services. Sixteen of these were Blue Cross/Blue Shield plans, and eight were other companies.

Insurers make coverage decisions in two main ways. The insurance contract or a policy that an individual or employer can purchase can outline a broad benefit category, such as laboratory tests. Decisions about a specific test are then made on a case-by-case basis when the claims are processed. Alternatively, insurers can develop a coverage policy. The policy is a more precise description of the exact service that will be covered, and the conditions for which it will be covered. Policies are usually developed to respond to new technologies, to new information about a technology, or in response to mandates. Policies define what the insurer considers to be medically necessary, and they state limits on the types of providers that can perform the service or can limit the number of times a patient can receive a service. The coverage policy is written as a guideline. The exact benefits for an individual are usually still determined by what their insurance contract says.

For almost all private insurers, a medical director will decide the benefits,

sometimes in conjunction with a medical policy advisory committee. The committees also often include other plan personnel, as well as local medical experts, consumers, or legal counsel. Employers can decide benefits. Regardless of what an insurance coverage policy says, the employers, usually the CEO or human resources director, can negotiate with the insurer for inclusion or exclusion of specific services. Other large groups, such as unions, churches, academic centers, can negotiate benefits on behalf of individuals; and, of course, federal and state governments can mandate coverage.

What criteria do plans use to determine what services to cover? Almost unanimously, decisions are based on medical necessity. However, like beauty, medical necessity can be in the eye of the beholder. While most plans don't publish specific definitions, others have developed very explicit criteria. The following are the Blue Cross/Blue Shield Association's criteria for deciding coverage.

First, the technology must have final approval from the appropriate regulatory body. Once approved by the body, the TEC, or technology evaluation center, is not bound by the indications in the approval. They can evaluate off-label uses.

Second, the scientific evidence must permit conclusions concerning the effect of the technology on health outcomes. The evidence is evaluated in terms of quality and consistency of results. The evidence should demonstrate that the technology can measure changes related to the disease, and that the measurements actually affect the outcomes. The technology must improve the outcome, and the benefit must be as big or bigger than established alternatives, and be attainable outside of an investigational setting.

So in order for Blue Cross/Blue Shield to recommend coverage for a new genetic test, the test must have FDA approval or conform to the CLIA requirements, evidence must show that the test measures what it's supposed to measure, and that the test will positively impact patient outcomes in the real world.

I want to point out that criteria 3 and 4 go beyond what is necessary for regulatory approval of a new test. Rarely would FDA require that an applicant measure actual clinical outcomes, let alone determine the magnitude of benefit in order to gain approval. CLIA regulates the process of testing but doesn't say much about the evaluation of the test itself. And although Blue Cross/Blue Shield doesn't explicitly use cost-effectiveness, one or two other insurers considered cost-effectiveness but they didn't describe how the criterion is applied.

So where do payers look for scientific evidence? Looking at the reference section of the existing coverage policies, payers primarily rely on the literature, statements from professional organizations, and government agencies. Many turn to the work of technology assessment groups, and some payers adopt all or part of the policies from other payers. Compared to work I did only three years ago, many more payers are turning to the websites as a primary source of information.

Looking at existing policies, private insurers generally find genetic testing medically necessary when personal or family history indicates a high risk for inherited conditions, when the sensitivity of a test is known, when the results will directly impact the treatment or management of the patient, when the diagnosis remains uncertain following conventional workup, and interestingly, where pre- and post-test counseling is provided as appropriate. A few policies even went so far as to specify what the informed consent should be.

In general, genetic testing was not covered for population screening without a personal or family history, regardless of ethnicity. The only notable exception was coverage for CF carrier screening as a preconception service to what one policy called "informed couples," or as a prenatal service to pregnant women. Testing is not covered for informational purposes only or for testing minors for adult-onset diseases. Coverage is usually not provided for a patient's family member who is not also a member of the health plan unless the information from that family member, such as the identification of a specific mutation, is necessary to make an appropriate medical decision for the plan member, and the family's member can prove that they've already tried to get insurance coverage from their insurance company and they were denied.

Nearly all insurers cover tests for chromosomal abnormalities. Most are written for prenatal or neonatal diagnosis, but some insurers have also written policies for preimplantation diagnosis. Covered indications include advanced maternal age, suspected fetal anomaly, history of multiple miscarriage or developmental problems, et cetera. Tests for rare single-gene disorders are usually covered under general policies for genetic testing and counseling. However, some insurers have separate policies for specific conditions, and some of those are for hereditary cancer testing, cystic fibrosis, Tay-Sachs, or hemochromatosis.

Policies for pharmacogenetic or pharmacogenomic tests can be written either in the context of the drug policy, such as for Herceptin, or they can be written separately, one policy for the drug, another policy for the test. Some drug policies simply list the prescribing characteristics, such as HER-2-positive, without saying how the characteristic is to be determined.

I'm going to give you a few examples of policies that have been written. You might be surprised to find out that 12 insurers have written a policy for testing for the genetic markers associated with familial Alzheimer's disease, but none of the policies cover the test. Using primarily the Blue Cross/Blue Shield criteria, these insurers concluded that testing is investigational. There is insufficient information to demonstrate that the genotypes are associated with Alzheimer's disease with a high positive predictive value.

The second example concerns colon cancer testing. There are two kinds of hereditary colon cancer. Hereditary non-polyposis colon cancer is typically diagnosed based on family history and is associated with mutations in two main genes, the MLH1 and MSH2. Familial adenomatosis polyposis, or FAP, is based on personal signs such as the presence of at least 20 polyps in the colon. The patient usually has at least one first-degree relative with the disease. FAP is associated with mutations in the APC gene.

Sixteen insurers have developed policies for genetic testing. Four cover testing without specifying the genes. Five cover mutation analysis in three common genes, four cover microsatellite instability analysis in addition to the common gene tests, one covered APC testing only, and two did not cover genetic testing but would cover other means of diagnosis. Common exclusions in the policies were microsatellite instability analysis in the stool specimen, and specifically testing for the I1307K mutation in the APC gene.

The point with this example is that even though 14 out of the 16 insurers that had policies covered the genetic testing, they varied in the level of detail and also in the specific analyses that they covered.

To give you a pharmacogenomic example, azathioprine is an immunosuppressant treatment for inflammatory bowel disease. It is converted into active

metabolites by an enzyme called TPMT. The activity of TPMT is associated with genotype. Ninety percent of patients are homozygous for wild-type form of the enzyme and have high TPMT activity. Ten percent are heterozygous for a mutation that reduces enzyme activity, and overall they have an intermediate activity. Finally, a small percentage are homozygous for the mutant phenotype, and these patients have extremely low enzyme activity and are at risk for toxicity.

People who are homozygous wild type could receive a standard dose of the drug, and although no studies have measured the outcomes based on knowing the genotype beforehand, the thinking is that a provider would prescribe a different drug or monitor metabolite levels for those with the homozygous mutations, or reduce the dose for heterozygotes. Six insurers have written policies for genotyping the TPMT gene. Three covered both genetic testing and monitoring of the metabolite markers. Two covered only the metabolite markers, and one did not cover either test.

Once an insurer decides to cover a new test or service, they have to determine how much they're going to pay for it. Payment rates are based on many factors, including where the services are provided and the usual and customary charges billed by the providers in that location. Reimbursement rates can be a simple percentage of bill charges that is determined in the insurance contract, insurers can negotiate fees with different providers, or adopt a fee schedule such as those used by Medicare, or they can come up with their own fee schedule. Just because a policy said that a test is covered doesn't mean that it will be paid at a rate the providers find adequate. The reality of the situation is that poor payment can have the same impact as a non-coverage decision.

The payment process involves recognition of a service by the insurer. This is done through the common coding systems. The ICD-9 code tells the payer why a service was done. It codes for the diagnosis, disease condition, signs or symptoms that the patient has. The CPT identifies the procedure or the service that was performed. Basically, if the CPT, or the service, matches the medically appropriate reason, or the ICD-9, then the claim can be paid. Of course, this depends on the provider submitting first the correct information, especially with regard to identifiers and dates of service, and second, where it's required, documentation. The documentation could be a pedigree to show family history, or literature to support the medical necessity of a new service.

The CPT codes used to identify genetic tests are limited. There are codes for molecular diagnostic procedures and for cytogenetics. Usually you have to string together multiple codes to describe a whole test. Providers often complain that these unbundled codes have lower payments associated with them than would a code for a whole test. There have been problems in the past as to what laboratory specialties can use which codes, particularly the molecular codes that are in the cytogenetic section.

Each coding section ends with a code that's three digits plus 99. The 99 codes are for unlisted or new procedures. These are often perceived by insurers to be investigational, indicating that we need timely development of new codes. As many in the audience know, getting a new code can take years. The HCPCS, or Health Care Common Procedure Coding System, is a national temporary coding system that can be established for new tests. Many have recently been developed for gene sequencing and mutation analysis for specific conditions. For example, you'd use an S3820 for a complete BRCA1/BRCA2 gene sequence analysis, and an S3822 for a single mutation analysis for an individual with a known

BRCA1 or BRCA2 mutation in their family. Later, my colleagues will go into more detail about payment issues with laboratory tests and with professional services.

So with that, to sum up, testing for the most traditional inherited genetic conditions is covered by most private insurers, including counseling, but that doesn't mean that there's adequate reimbursement. There still seems to be the perception that insurers are slow in covering new technologies. Insurers may argue that this is because there isn't any data to support the medical benefit of the new test. This situation may in part be due to the fact that the studies designed to meet regulatory requirements rarely evaluate whether the information from the test will impact patient management, and if so, how.

As far as payment is concerned, providers need to go through the cost analysis with insurers so that payers understand how costs are applied and where reimbursement rates are failing. Like many other things, at the heart of the issue is a need for balanced communication and education with respect to the risks, benefits, and responsible use of genetic technologies.

With that, thank you.

DR. McCABE: Thank you, Dr. Schoonmaker.

We're going to hold questions until the roundtable discussion at the end of the presentations this afternoon.

Our next presenter is Dr. Ron Bachman, who is Chief of Genetics Department at Kaiser Permanente, Northern California. Dr. Bachman will describe the financing of genetic services in an HMO setting. Having said that, however, I think it's important to recognize that Kaiser is a different model from the typical HMO.

Please, Ron.

Also, while they're bringing that up, I again will comment that I think it's important to look at the amount of research that comes out of Kaiser in a variety of different areas, because it can be informative in everything from vaccine utilization to genetic services.

Dr. Bachman?

DR. BACHMAN: Thank you. I'm going to discuss the delivery of genetic health care in a large population, and I'm going to lean to both the clinical and financial aspects of it. The care must be organized, consistent, comprehensive, and cost-efficient, and I might add another C, that of being caring. One must consider the introduction of new technologies and the elimination of unneeded programs. Most programs suffer from an infrastructure that is too small.

The problem? Clinical genetics is the health care of a few, where genomic medicine, where we're heading, is the health care of all. Are we prepared? Probably not.

I should probably give credit to where I think I cribbed this from, which was an article by someone sitting at the table today, Dr. Collins. Thank you.

On one hand, we have the problem of clinical genetics keeping up with new genetic technologies. The genetic evaluation is labor intensive. The current barriers are financial, linguistic, cultural, and many more, and there are a limited number of genetic professionals. On the other hand, we have the problem of the primary care provider. The time needed for a genetic evaluation is quite long. There's limited training in clinical genetics for the primary care provider, such things as genetic testing, risk assessment, non-directive counseling, and psychological implications.

I would like to present our program, which we hope will overcome these

problems. As Ed mentioned, I work for Kaiser Permanente in Northern California. In Northern California, we have more than 3 million health plan members, more than 4,000 physicians, and more than 34,000 deliveries each year.

As I mentioned in my introduction, we think our clinical genetic services are comprehensive, consistent, caring, and cost-efficient.

We are fortunate to be well staffed. We have five genetic centers that are strategically located throughout our Northern California region. We have 11 medical geneticists with subspecialty training, four Ph.D. laboratory directors for our molecular and cytogenetics laboratory, 53 genetic counselors, 17 genetic nurses, three metabolic nutritionists, and the support people for the professionals.

I'd like to give you an overview of our program. It includes prenatal services in clinical and screening, neonatal services, ethnic screen, multispecialty clinics for common genetic disorders, the adult genetic services which include cancer genetics, clinical genetics, and screening; genetic laboratories and genetic education both for our providers and our members.

Probably the centerpiece of our program is our prenatal program. All prenatal patients get a genetic and ethnic questionnaire and a video presentation of our genetic services, which assists them in our informed consent and also the selection of the testing that they think is appropriate for them. There are genetic counselors available for discussing that with them. We also have an expanded alpha fetal protein program, with 80 percent acceptance, an advanced maternal age program. All prenatal patients get an anatomical screen, the so-called ultrasound level 1, which converts to a level 2 ultrasound if any abnormalities or questions are found.

We have prenatal cystic fibrosis screening, hemoglobinopathy screening, a fetal pathology program, and genetic counseling when indicated. Our ethnic screening program in the prenatal period includes hemoglobinopathy screening, thalassemia, Tay-Sachs and Canavan, and cystic fibrosis.

Our neonatal programs include clinical evaluation. This is for children born with birth defects or that are recognized as being unusual looking. We also have the standard neonatal screening, and we have a program called our Escape Baby Program. This is a computer tracking system for babies that get tested either too early or get out of the nursery before they're tested. We test for the standard four tests that I listed before, and we are in the process of planning a tandem mass spectrometry program.

Our screening and tracking programs really include a lot of cases. Last year we tracked over 45,000 cases. These are our prenatal testing, our neonatal testing, and our breast cancer and mammography tracking.

In clinical genetics, this is the clinical evaluation by the geneticist, or together with a genetic counselor, or by the genetic counselor alone. Last year we evaluated over 20,000 cases, and this includes case management when indicated, and there's quite a database for outcome studies.

The genetic counselors are sort of the glue that holds our program together. They provide genetic services on their own. In fact, they work autonomously in many different genetic type problems. They assist the clinical geneticist in case preparation. They are involved in case management, psychosocial support of the family, and genetic education. It's actually the genetic counselor which is my hope for the future in terms of the integration of the

genetic counselor at the primary care level so there isn't a need for the primary care physician to learn all the genetics we are placing on him or her.

We also have a fetal pathology program, and we developed this because we were losing important genetic information for diagnosis of conditions and the recurrence risk for those families. Last year we had approximately 2,000 cases.

We also have a group of genetic multispecialty clinics staffed by experienced professionals providing care for these particular more common genetic disorders: spina bifida, craniofacial abnormalities, metabolic genetic abnormalities, pediatric lipid disorders, neurogenetics, a skeletal dysplasia clinic, and neurofibromatosis. When a patient is seen in these multispecialty clinics, the recommendations are given both in writing to the patient and their family, and to their provider. Also, our staff in these multispecialty clinics track the patients to make certain that they get appropriate care and that the recommendations that are made are carried out. This is done by either our genetic nurses, our genetic counselors, or our metabolic nutritionists.

Multispecialty care is expensive but we think cost-efficient, because the patients are getting appropriate treatment, and that includes appropriate surgery. Last year we had over 2,000 patients in our multispecialty clinics. We also have a cancer genetics program where we do genetics risk counseling, and breast and colon make up the majority of it but we certainly do counseling for other genetic cancers. We provide gene testing when indicated, and as I alluded to before, we have a breast cancer tracking system and a mammography tracking system.

The mammography tracking system is for abnormal mammograms. This is not generally in the area that a genetics department works in, but because of our experience with tracking genetic conditions, we were asked to do the breast cancer and mammography tracking, and certainly we thought that the breast cancer tracking system might help us identify some families that had increased genetic risk for breast cancer. Last year in terms of our cancer tracking, we had over 3,000 newly diagnosed breast cancer cases, and over 23,000 abnormal mammograms that we tracked.

One needs dependable genetics laboratories, so we've developed our own in cytogenetics, where we've had over 11,000 cases last year; our molecular laboratory, over 24,000 cases; and we provide the molecular work for the Southern California Kaiser Permanente. Our metabolic studies go to Southern California Kaiser, where they have a metabolic laboratory. We find it very helpful to manage our own laboratories.

I probably, because of time, won't discuss this enough, but we think genetic education and research is very important. We have more experience with the genetic education than research. We provide an online publication for primary care providers which is less than 1,200 words. I'm a member of NCHPEG, and when we tried to introduce a CD-ROM that has six hours of terrific information on it, there were a limited number that had the time to review that. So we send out frequent emails, and they're available online, on issues such as hemoglobinopathy screen, who should be referred for cancer genetic counseling, guidelines for management of specific genetic disorders, and guidelines for who should be referred to genetics.

We have our own website that was developed, and although I must admit it was developed in terms of education of our members, our providers are using it a great deal so they are prepared for the questions of the members.

As I said, we don't have a lot of experience in research. We have the database, we've done a few studies, but not as many as we probably could.

Now I would like to talk a little bit about how we introduce new programs. First of all, it's the decision of the genetics group, and those are the geneticists and the genetic counselors. If we think a new technology should be introduced, we prepare a discussion with our new technologies committee, and if they approve it, we then submit it for the Kaiser Permanente budget process. We do this for large programs. We did it when we established a chorionic villus sampling program and when we introduced prenatal screen for cystic fibrosis. We are currently evaluating preimplantation genetic diagnoses and first-trimester screen for chromosomal problems using nuchal translucency.

After this process, we submit it to our administration, and if they approve it -- and it usually is approved if it's standard of care and cost-efficient, and we make a good case for it -- we establish a cost basis for the new service, we monitor our productivity and actual costs because the actual costs usually aren't less but may be more than we projected, and each year our programs are reviewed and we have to submit a request for an annual budget. So they're reviewed both at the genetics level and also at the administrative level.

This year our budget is going to be over $24 million, although that includes a $3 million pass-through fee to the State of California for cooperation with them in the prenatal and neonatal genetic screening program. When I presented this information at the American College of Medical Genetics in 2002, I used our 2001 financial information and figured out that to provide genetic services for our health plan, it cost 52 cents per member per month. For 2004, that's going to go up to 65 cents per member per month, which is a significant increase, but that includes new programs, higher wages of staff, and more staff.

Last year we had 207 full-time-equivalent employees in our genetics department. We had 13 physician full-time equivalents. Now, you might remember that I mentioned we had 11 physicians who are geneticists, but we have to employ parts of physicians to help staff our multispecialty clinics, like our pediatric orthopedist or pediatric neurologist, and they charge their time to our genetics program. We saw over 103,000 cases last year.

Now, I figured out some cost information that might be of interest to you. Our clinical genetics was $384 per patient. The multispecialty clinics, as I alluded to, is quite expensive care, over $1,200 per patient. Our fetal pathology patients were $270 per case. Our cytogenetics was $362 per study, and our molecular studies were $121 per study. The cost seems high, but when you want to provide a quality program and try to provide everything that's standard of practice and include your overhead costs, it certainly is high. Genetics is expensive.

WE made an assessment of what we're going to need in the future, and this was done in conjunction with a report from the Health Technologies Center, "Impact of Genetic Testing." We think that in the next two to five years the laboratory needs will be more gene testing, more prenatal genetic screening, more neonatal genetic screening, more carrier testing, more ethnic screening, and more predictive testing. In terms of personnel needs, we're going to need more geneticists, more genetic counselors, more genetic services done by the primary care providers, increased genetic education for primary care providers, increased genetic education for all our residents, and use of the Internet to make genetic services efficient.

Now, in terms of the next five to ten years, which I probably should have made five to fifteen years, where we're going seems to be in developing comprehensive genetic

services, genetic practice guidelines, preimplantation genetic testing, chip testing for genetic disorders, SNP mapping, pharmacogenomics, and treatment in terms of stem cells, gene therapy, and proteomics.

Well, on my last slide I want to tell you what we think the solution is. First of all, a more efficient clinical genetics infrastructure. Even though we have a fairly good system, we are constantly honing it to make it better. As I mentioned before, we need more primary care genetic services, and I am of the belief that we can introduce genetic counselors within the primary care department to work alongside the primary care physicians, to evaluate perhaps genetic history and a pedigree that might have obtained by an Internet use prior to the patient coming into the program, and actually doing counseling for some of the more common disorders such as hemochromatosis, thrombophilia, and cancer at the primary genetic care level.

I think we're going to need to incorporate the Internet into genetic services for patient triage, collection of medical history information, pedigree construction and family history, and patient and provider education.

We are making some progress on this solution. I think we have established a cost-efficient program and hopefully a model for delivery of clinical genetic services to other large groups of patients.

Thank you very much.

DR. McCABE: Thank you very much, Dr. Bachman.

At this point we're going to take a 10-minute break. We will resume with the next presentation at 3 o'clock. Again, refreshments for members and ex officios are here in the room, and for others in the lobby of the hotel.

Thank you very much.

(Recess.)

DR. McCABE: So next, the next two presentations will discuss the perspectives of the providers. First we're going to hear from Dr. Andrea Ferreira-Gonzalez, Associate Professor and Director of the Molecular Diagnostic Laboratory at Virginia Commonwealth University, who we heard before during the public commentary. Dr. Ferreira-Gonzalez will give us the laboratorian's perspective.

DR. FERREIRA-GONZALEZ: Thank you, Dr. McCabe.

I would like to thank Dr. McCabe and members of the committee for inviting me here today to share providers' perspective on reimbursement for genetic testing.

As has already been alluded to today, codes are the language of reimbursement. They hold the key for laboratorians to get reimbursed or pay for the services that we provide, either by performing the laboratory testing, interpretation or report on that. The current two levels of codes are mostly used by many providers, insurance companies. These procedure codes are, first, Level I. They're called the Current Procedural Terminology, or what we call CPT codes that were developed by the American Medical Association.

For laboratories, they usually are five-digit numbers that identify specific analytes, either methodology-specific analytes, assay stains, interpretations, even consultation. There is also another set of codes that could be added to the CPT codes. They're usually called code modifiers, two-digit coded, that are added to the five-digit number that further give a little bit more information about what the depth of the procedure or the interpretation.

The second level of coding, the HCPCS codes that were previously

mentioned by Dr. Schoonmaker, is the ones that have been developed by the Center for Medicaid and Medicare that allow to deal with testing or interpretation and reports that don't have currently a CPT code approved, or for those newer technologies as they start gathering information to determine what will be the best level for reimbursement.

So the use of these CPT codes are the means by which the payers match the service with the appropriate limit of the payment. A majority of the payers, Medicare and Medicaid, all of the private payers, actually recognize the CPT codes to identify the services. In addition to the CPT code, we provide billing or filling out claim forms, we also have to add another specific code that identified the diagnosis or the set of symptoms or signs that are required or triggered the physician to order the different testing, and allows us also to determine what is the diagnosis for that particular patient.

For molecular diagnostic testing, there are actually 14 different CPT codes. These 14 CPT codes are used to reimburse for all the genetic testing that is currently used in this country. As you can see here, these 14 codes are procedure specific CPT codes. Here you can see that the numbers are associated with a code from 83890 down to 83912. Each of these different CPT codes has a description associated that allows the third party to identify what part of the procedure, what methodology was used to come up to the diagnosis that we're rendering.

As you can see, for example, CPT code 83890 is for molecular isolation or extraction, and 83891 is also isolation and extraction but for highly purified nucleic acid. So it seems that there might be a little bit of flexibility in some of the CPT code they would currently use, but as I'll show you as we go through the different slides, this is not the case.

So we have 14 codes to allow us to bill for a large amount of different kinds of services. In addition, all these different services, when they require interpretation and report, we have at different levels. This also is represented by the single CPT code.

In here I have provided you the Medicare laboratory fee schedule for 2004. This is the current fee schedule that we use when somebody claims reimbursement for our testing. I'll walk you through this table. In the far corner here, we have the number of the CPT code. Remember the first one I mentioned, 83890 for nucleic acid isolation. As you can see, the first list here is the national limit allowed that Medicare sets for the payment of that particular code. What I don't have here is the lower limit that is allowed, and that is zero. So the national limit goes from $5.60 down to zero.

After the national limit has determined each of the different states, take the code and determine what actually is going to be the level of reimbursement for each of the different states. I have provided you here CPT code and reimbursement with the Medicare fee schedule for different states. In here, this is Georgia, this is Virginia State, and this is Tennessee, North Carolina, and California. What I want to point out here is that even though there is a national limit allowed for all these different tests, there are particular states that reimburse at very low levels for every single CPT code that we use for genetic testing. There are other states that aren't the same.

But the other states -- for example, the State of Virginia, where there is a very similar reimbursement level or the national limit allowed, except for one particular CPT code for reverse transcriptase. That is $17.47.

I want you to look at these levels of reimbursement for a couple of specific CPT codes, for the 83890, nucleic acid isolation, and also for the 83891, isolation for highly purified. What you see is a short description of that CPT code, it's implied that it requires

further manipulation of the nucleic acid to obtain the more purified that is required for the testing. As you can assume, there is more work, label and reagents that are required to perform this highly purified nucleic acid isolation, but the limit is set to the same level. Please keep that dollar amount in mind as I go through.

Before we go through the financial analysis, I think you need to know what kind of services are provided. The Virginia Commonwealth University Medical Center is comprised of three different entities: the Medical College of Virginia Hospitals, MCV Associate of Physicians in private practice, and the VCU Medical School. These are three independent organizations. The Medical College of Virginia Hospital is a 350-bed hospital. It's actually three different hospitals. They are combined under the umbrella of MCV Hospital. We're located downtown Richmond across from the governor's house, so we are downtown in a very large metropolitan city. We serve the central Virginia area of about 850,000 individuals.

We are one of the sole tertiary care centers in that central Virginia area. Our laboratory, the molecular diagnostic laboratory, is what's called a comprehensive laboratory. We provide molecular diagnostic testing for infectious disease, oncology, hematology, and inherited disorders. Just to give you an idea of the volume of testing that we handle in the laboratory, in calendar year 2003, meaning January to December last year, we did 13,200 tests.

Just to give you examples of the levels of reimbursement, I have chosen three example. One example that is highly complex testing and requires highly interpretation is second one, intermediate, and the third one is considered more simple within our standard of high complexity testing. I'm not going to go into detail on Fragile X syndrome because that's not the purpose of this lecture. I'm only going to point out some issues here.

Fragile X syndrome is the most common cause of inherited mental retardation, with a prevalence of 1 in 1,200 for males and about 1 in 2,500 for females. The cause of Fragile X syndrome, it's an expansion of the tri-nucleotide repeat sequence comprised of CGG near the 5 prime M of the FMR1 gene. One of the major issues of the diagnosis or trying to identify individuals with Fragile X syndrome is trying to measure the amount of repeats that are located in this area of the 5 prime M of the gene. The number of repeats with allocate the individual within certain categories or areas. If you have 6 to 50 repeats of that particular trinucleotide, you're considered part of the normal population. Individuals with a mutation will have 50 to 200 repeats. These individuals might not necessarily have any phenotype of the disease but are carriers that can pass it along through different offsprings, and actually that mutation can expand to the full mutation that will produce the full phenotype.

Full mutations contain about 200 repeats or even higher number of repeats. So there is an area that needs to be very accurate in the amount of quantification of the nucleotide repeats to be able to put individuals within normal populations and at risk or having mutation, and it's about 45 to 55 copies. Due to the fact of the complexity of the sequence and the complexity of the measurement of the repeats, we require the use of two techniques in our laboratory, the polymerase chain reaction and southern blotting analysis.

The polymerase reaction allows us to size very good trinucleotide repeats up to 110 repeats. So the normal range plus the mutation. Individuals with larger mutations will not amplify with a PCR reaction. So southern blotting analysis also comes in handy in trying to identify larger permutations and also give us information about the methylation status.

So we perform the test, and then we provide the series of CPT codes to the

provider to get reimbursed for our test. I have provided here the description and the CPT codes that we currently use for the reimbursement of southern blotting analysis and PCR. As you can see here, sometimes, due to the fact of the way we perform the assays, some of the CPT codes are used more than once. The cost of providing it here is actually the direct cost. It is the cost of the reagent plus personnel. I have not added indirect costs because these will vary from institution to institution. So these will allow you to translate more into different institutions.

As you can see here, the total reimbursement for our cost of the testing is $266.34, and what the Virginia Medicare expects is $62.30. Remember from that slide where I pointed out to you that the Virginia Medicare expect was only different from the national limit allowed in a single CPT code that we don't use here. So this is very similar to the national limit allowed for this particular testing.

For the PCR analysis here, we also have different CPT codes. We do not have a code for nucleic acid isolation because it was already extracted when we performed the southern hybridization analysis. There's a clean-up of the PCR product that is required before capillary electrophoresis, so we needed to add nucleic acid isolation. As you can see here, our cost of performing the test is $116.06, versus $17.85. That's what Virginia Medical expect.

What I pointed out to you here is that our cost to perform nucleic acid isolation highly purified is $15.06, and it's about $55.47 for reimbursement. I also want to point out interpretation and report, our cost is $40.00 for this other hybridization analysis, and about $35.00 for that. I want to show you for genetic interpretation, the national limit allowed for all the testing is $5.60.

Now, let's move on to intermediate complexity testing, and I've specifically chosen the immunoglobulin gene rearrangement by PCR because it's also a somatic change. It's not inherited disorder but it's a somatic change, and actually it's intermediate complexity, what we consider complexity in molecular genetic testing.

This actually is extremely important in the diagnosis of lymphoma and leukemia because it allows us to identify the proliferation of lymphoid cells, central to the diagnosis of these two entities, because it allows us to differentiate a diagnosis of reactive lymphoidopathy versus lymphoma or lymphoid malignancy.

Here again we have a description of the codes that we currently use for seeking reimbursement. As you can see here, we have a nucleic acid extraction of 83891, a highly purified nucleic acid extraction. In the previous slide I showed you that the cost was significantly lower than this one. The reason why this one is so high compared to the highly purified for hybridization analysis is because most of the testing is done on tissue that has been paraffin embedded that needs to be further processed to remove the paraffin and then get washed and get ready for the nucleic acid isolation.

What I'm trying to point out to you is that we have two codes for nucleic acid isolation, and I've already described to you at least three different ways to extract the DNA or nucleic acid using different procedures. So there's not much flexibility in the current coding to allow us to account for those differences. In here you will see the particular CPT code we used three times due to the fact that we amplify three areas of the gene or family regions that increase the sensitivity and specificity of our particular assay. Again, interpretation is $40, and we will get reimbursed $18.54 because we submit the interpretational report with the 26 modifier.

But you can see that there's a discrepancy in what it's actually costing us to

do the interpretational report and what we were actually reimbursed, and for that matter for the entire procedure.

The third example I chose is one of the most simple assays we have in the laboratory and that is widely used and performed in many laboratories. Factor V Leiden is the most common hereditary blood coagulation disorder in the United States. We have a prevalence in the general population of 5 percent for Caucasians and 1.2 percent for the African American population. The reason why it's so important to do genotyping for the Factor V Leiden is that we need to identify individuals that are heterozygous, but mostly homozygous individuals, because we have different consequences of treatment for these particular patients.

Being heterozygous for the Factor V Leiden increases your risk of venous thrombosis about five-fold. On the other hand, homozygous it's about 100-fold increase. Individuals homozygous for the Factor V Leiden might be required to place on anticoagulant therapy for the rest of their lives.

I have listed here the number of different coagulopathies where Factor V has been associated with. Here again we have the description of a technology and we have nucleic acid isolation, 83890. That's the lowest level of nucleic acid extraction, and you can see the cost is lower too, at $9.69. This is one of the assays that we perform that has a single amplification technology, currently used in commercially available ASARs have been validated and put together in our laboratory.

Again, here we can see that we have to use the same CPT code several times to reflect the procedure that we're currently using. Here, the more simple genetic testing is a lot closer in reimbursement to what it's actually costing us to perform the test.

Now, this is how the level of reimbursement. What do we actually get reimbursed? I've showed you Medicare will not be able to provide you specific reimbursement percentage for all the third-party payers of private insurance due to contract agreements and non-disclosure issues that we have with them. But I can tell you that we have submitted a number of claims for all the testing that we did, and we get reimbursement from Medicare about 89 percent of the time, 72 percent for Medicaid, and there's a range for the other third-party payers, from 61 percent up to 85 percent.

What it was striking for me to realize that the Medicaid/Medicare reimbursement were getting the national limit allowed. But actually, the third-party payers are paying us almost the identical amount, all of them. So this is something that is across the board for all the different payers.

I think also we need to spend some time in the very crucially important code interpretation and report. As we know, interpretation of genetic testing requires the analysis of the testing plus putting information, clinical history, family history, clear pathological correlation, all together to be able to come up with the right result.

When we looked at our level of reimbursement for the CPT code 83912, with modifier 26, we see that we get reimbursed, and it's the same level that we get reimbursed for the procedure component of the test that we do, again from 93 percent down to 61 percent. But what we get here, the Medicare/Medicaid gives us the national limit allowed for the 83912 with the 26 modifier, but the third-party payers or commercial payers have not recognized the 26 modifier and actually reimburse the national limit allowed for the code without the modifier.

So what are the factors that affecting access of genetic testing? I have shown you a little bit about the level of reimbursement for the testing that we do, and that has

to be crucial to understanding. But also, genetic testing utilization is increasing, and another factor that will dramatically affect access to genetic testing is that the laboratory fee schedule was frozen for five years, from '98 to 2002. After that time, we got a 1.1 increase, and then it was frozen again, and it's going to remain frozen from 2004 to 2008. So we have already lower level of reimbursement, genetic testing will increase, and the fees have been frozen.

Now, our costs will continue to increase. Even if reagents don't increase in cost, we're going to have to adjust the cost of living of our personnel, rent, and other expenses. So our ability to cost shift is extremely limited. I'm showing you some examples of this. I think we need to spend some time in this diagram because it gives a very nice example of what is happening in the field of genetic testing and what is to come.

The molecular diagnostic laboratory of Virginia Commonwealth University started operation in fiscal year '95. We were doing very little genetic testing. This is a diagram of the different molecular genetic testing that is currently performed in our laboratory, and I have done percent increase through the different years. In 1995, we had barely any genetic testing performed in the laboratory, but you can see that there's a little bit of increase in that particular testing or utilization of that testing. In 1999 and 2000, we've seen an explosion in the utilization of that particular testing. We have gone up to over 100-fold increase in about 10 years of service of the laboratory. I haven't put 2004, but I could tell you that it's going to be even higher.

So far we have been able to cope with the genetic testing because we've been cost shifting within the laboratory. With the freezing of the Medicare fees, that will put a hamper on our ability to be able to cost shift. What we see specifically is what happened to the molecular CPT codes. When we look at other molecular testing that is currently done in our laboratory and other laboratories, one can see that our ability to cost shift will be diminished.

I have given an example here of three different tests. All these tests have to extract RNA, nucleic acid, perform a reverse transcriptase reaction, PCR, and then quantification to quantify the chimeric messenger RNA that is a result of the T922 translocation. This is a chronic myelogenous leukemia patient, and this test is crucial for the detection of minimal disease for these particular patients. HIV viral load is crucial for the quantification of HIV in circulation, mostly for patients that are undergoing antiretroviral therapy. More recently, HCV viral load is starting to increase in utilization.

As you can see here, we have a little bit higher cost of performing these laboratory-developed assays, and we have a Medicare reimbursement of $51.65. On the other hand, in the past, the molecular infectious disease CPT code had been reimbursed a little bit better than the other procedure CPT codes. $99.18 is actually the mean value of cost among 25 different laboratories across the country, and you can see the Medicare reimbursement is $114.36. So we recuperating some of the cost and actually making a little bit. But with the increase in use of hepatitis C viral load and other testing that are not fairly reimbursed currently, these are going to put extra strength in the laboratory and our ability to cost shift will be reduced to almost none.

The other factor affecting access to genetic testing that will increase the cost of testing will be royalty payments. Currently we deal with different royalty payments for patented procedures, or even patent genes or sequences. The most common royalty payment for patent procedures is having a percentage fee of the receipts or the reimbursement that we get for the testing that we do, and it can vary depending upon your royalty agreement fee

schedule between 9 percent of what you recover to 15 percent of what you recover.

On the other hand, royalty payment for patented genes and sequences can have different ways to be performed or different fees, an upfront fee plus a flat fee per test, or a one-time payment plus percentage of the charges. I think it's interesting to see what has actually happened with hemochromatosis in this country. There was a requirement of the patent by SmithKlineBeecham Laboratory, which was acquired by Quest Laboratories, to perform exclusive licensing to perform hereditary hemochromatosis, pretty much testing the 12 most common mutations of this particular gene.

Quest entered into an agreement with BioRad by which BioRad Laboratory acquired the rights to the patent and developed commercial kits, and it will further sublicense that to laboratories. So you have two options if you want to perform hemochromatosis. You can either buy a reagent from BioRad at a set level or you can license, develop your test by your laboratory, but we have to provide an upfront fee, which is extremely high, plus $20 per test. You can see what this can do to performing the test for the current cost of performing all the other Factor V Leiden. Also, we can have a one-time payment plus percentage of the charges.

The last issue I would like to point out is access to genetic testing, and also our ability to continue to perform testing. It's from work performed by Cho and collaborators that was published last year in the Journal of Molecular Diagnostics, where they did a survey of 122 laboratories. The main objective of the study was to try to identify current practices by patent holders and the ability of the laboratories to perform genetic testing.

The 122 laboratories were recruited from GeneTests' list and from the directory of the Association for Molecular Pathology. As you can see here, there's a description of the different kinds of laboratories that were enrolled in the survey. It's a little tilted toward university, non-profit private hospital, again because the majority of the genetic tests is currently provided by academic institutions. The companies or commercial laboratories were less represented here.

I think what was striking to see from this study is that there was a number of laboratories that received letters from patent holders requesting to stop, cease and desist performing certain testing. There were nine laboratories that received that notice and decided to stop the testing, performing apolipoprotein genetic testing for Alzheimer's disease, and nine laboratories also for breast cancer.

I think what was also striking from this study was that 25 percent of the laboratories had to stop testing that they were currently offering. But also, 55 percent of the laboratories expressed that they had not developed a test due to the fact of licensing or patent issues.

I hope I've been able to convey to you what is currently happening in the clinical practice of laboratory testing and what some of the major factors are that are going to affect access of this testing to the population.

Thank you.

DR. McCABE: Thank you, Dr. Ferreira-Gonzalez.

Our next speaker will be Dr. Mark Williams for a clinician's perspective. Dr. Williams is a pediatrician and medical geneticist at the Gundersen Lutheran Medical Center in LaCrosse, Wisconsin.

Dr. Williams?

DR. WILLIAMS: I thank you for the opportunity to be able to speak to the committee. I don't know if speaking or whining is perhaps the operative word here. I'm having flashbacks of dealing with my teenage daughters, I'm afraid.

But let me give you a little bit of perspective of a clinician. I'm going to be talking about four different areas, billed services, touch a little bit on multidisciplinary evaluation, access to services, and some issues relating to problems as I see it with the current system.

If we look at actual procedures, they really fall into what we truly think of as procedures, which is amniocentesis, CVS, or infusion, and for the clinician what are called evaluation management services or E&M, and I'm going to talk about each of these separately.

Procedures themselves are pretty straightforward. The indications are straightforward. You do an amniocentesis for advanced maternal age or for a known chromosomal abnormality, and there are specific CPT codes that cover those particular procedures. Now, that being said, there are of course some insurers that may choose not to cover certain indications, as Dr. Schoonmaker said earlier, and it has to do with exclusion of genetic tests or lack of a benefit.

I wanted to spend a little bit of extra time on infusion because there's something new on the horizon here that's going to really impact this not so much for genetics, although that's going to have some impact on us, but particularly hematology, oncology, and some of our colleagues here, and that's the Drug Improvement and Modernization Act of 2004. This defines reimbursement for the infused drugs and biologicals. Essentially, what has been determined is that existing drugs will be reimbursed at 85 percent of the average wholesale price as of April 1st of 2003. New drugs will be reimbursed at 95 percent of their average wholesale price.

Well, this has significant implications for treatment of certain genetic disorders where enzyme therapy is now becoming available, specifically Gaucher disease, Hurler-Schie, and Fabry syndrome. Because these are orphan diseases, the enzyme replacement is very expensive depending on the age and size of the individual, anywhere from $100,000 to $250,000 a year. It's not an uncommon cost. If the reimbursement is not going to be covering the cost of the medication, that could present access issues for the patients that need these novel therapies.

Now, when we talk about evaluation and management, there really are several things that need to be addressed and which I will go through briefly. First is the RV/RVU disparity, and that is that E&M reimbursement is reimbursed at .04 RVUs per minute, whereas procedures are reimbursed at .08 RVUs per minute. So for those of us that don't use scalpels or needles very often, our time is being reimbursed about half of that of our colleagues who do procedures.

This is then combined with the issue of how the E&M is actually scored, and I'm going to tell you the system under which we're currently operating and then give you a brief look into a brave new world. The history, it's possible to have a level 4, which is the highest level of a history intensity and not even do a family history. The system as developed really can be done without a family history, and you don't have any ability to bill more intensively for that.

Physical examination, again, is based on a number of elements. The elements of the dysmorphology examination, which is very specific, are generally not

recognized as elements, although I think it's also fair to say that there are three different element systems out there dating from 1995, 1998, and 2000, all of which are different and all of which can be used to provide documentation to third parties, although depending on the third party, which one they choose to use can vary. And then the third aspect of E&M is the so-called complexity, which is meant to adjust for the seriousness of the condition, risk of mortality, the complexity, but the elements in this part are very poorly defined and are very subject to interpretation.

Now, I want to spend a little additional time on family history because that's sort of the geneticist's bread and butter, as you might expect. The standard that we hold ourselves to is a full three-generation pedigree. We frequently are using statistical analysis, including things like Bayes theorem and some of the cancer risk models that are available. We submitted -- "we" meaning the American College of Medical Genetics -- a CPT code, actually two CPT codes for pedigree analysis to define this as something different from family history and use that as a separately billable code to allow us to be able to capture some reimbursement for the complexity of this pedigree analysis that we do.

We had an interesting thing happen, which was that just before the vote to approve these was going to be taken by the CPT panel, they said, well, we've got this new E&M system; we need to vote on that and then we'll come back to the pedigree analysis. They approved E&M, which I'll go into in just a bit, and then they said, well, now pedigree analysis falls into the new E&M, so it's off the board. So that was an interesting little end-around there.

Well, the new E&M is going to completely get away from the element system that we've grown to know and love. It's going to look at time components, with a maximum time or a level 5 component of approximately 60 minutes. The issue with the new E&M is that the members of the AMA have basically said we don't want the elements, we don't want the documentation, so we're going to develop these clinical scenarios which are really going to define our levels of care. The perspective that I see and that I think Dr. Tunis is probably going to be struggling with in the not-too-distant future is how do you audit that? How do you make sure that people are really doing what they say they're doing? The only way I can really come up with is to audit by time.

Well, genetic encounters, as we've already heard, are not infrequently two to three hours face to face. So if we're limited to a 60-minute time, that's going to be problematic, and there's not direct multiplicity of the level 5 versus the level 1. So if I do eight level 1 codes, which I would do if I was wearing my pediatric hat and looking in ears, I can bill much more per hour than I can bill doing one one-hour evaluation.

The other thing that is not captured here is the pre- and post-encounter time, and this is something that really has never been built into the CPT system, although there are some modifiers that we do have access to that can take into account pre- and post-encounter time. But as we heard from the previous speaker, it is not unusual at all for third parties to reject these modifier codes, and again the reimbursement does not reflect actual time.

Now, there are also codes for coordination of care which we also spend a lot of time doing. Again, these are frequently rejected and do not usually reflect actual time.

The issue of physician profiling. This is an audit technique used by third-party payers. It is used to adjust claims to make sure the practitioners are playing by the rules. It's used to adjust charges, and while we're usually told that they can be adjusted up and down, the reality is that they're usually adjusted down. The geneticists have a real problem because

we frequently are listed in provider networks -- since we're not able to do a genetics residency, if you will, we do a prior training, usually in pediatrics or internal medicine or Ob/Gyn. We then do our fellowship in medical genetics. We get listed in the network as a pediatrician or an internist, and then we're compared or profiled against pediatricians and internists, and as you might suspect, the code profiles are significantly different.

I get information from my pediatric department, and I can tell you that about 95 percent of the codes that I submit are level 5 codes, whereas my colleagues, generally 1 to 2 percent of what they do are level 5 codes. So when a third-party payer sees that, that can lead to problems saying, well, you're really not doing that, you're just trying to get more money out of us, and can lead to fraud and abuse investigations, or just automatic down-coding.

I mentioned the new and improved E&M that will eliminate the elements. These clinical scenarios are going to be developed by specialty societies to define their CPT levels. My current understanding of the process is that there is sort of a beta test of societies that are developing their clinical scenarios to be brought back to the CPT advisory group, and once that analysis is complete, then all societies will be given those as guidelines to go out and do that. Implementation is supposed to be January 1, 2005. Quite honestly, I don't see how that's possible, but that's what they're shooting for. As I already alluded to, the issue of auditing this is going to be, I think, a real nightmare.

Multiple providers. We talked about multidisciplinary clinics. Dr. Bachman indicated that it is expensive to provide care that way, although I would argue that if you have an individual that has something like a cleft palate or spina bifida, you're really not going to save any money by having them see the individual practitioners separately. They're still going to have to see everybody. It's a matter of bringing them all under one roof, and so it's an issue of patient convenience. However, there are prohibitions about multiple providers billing on the same ICD code on the same day. The first one in, only one paid is the rule of thumb, so it does encourage some efficiency in terms of getting your bill turned in.

Now, in the Down's syndrome clinic where I work at, where we have myself and the developmental pediatrician and speech therapist and others, we have a variety of diagnoses I can use. I use the Down's syndrome code, the developmental pediatrician uses the mental retardation code, so we have different ICD codes that we can use. But if you're in the cleft palate clinic, you're basically stuck with that cleft palate code, and that's going to limit the ability to reimburse because of that ICD restriction. This impairs coordination of care, it inconveniences patients, and it decreases, in my opinion, the quality of care.

The last issue relating to multiple providers is the role of genetic counselors and the issue of billable entity status for genetic counselors. The bottom line is that genetic counselors are not recognized as a billable entity, with the exceptions of Washington, Texas, and Ohio, which is pre-HIPAA, which we'll get to in just a bit. Genetic counselors have traditionally not been licensed, although in Utah and California licensure for genetic counseling has been passed. There are restrictions relating to "incident to" billing which are relevant.

"Incident to" basically are services provided by a health care professional under the supervision of a physician, which are billed under the supervising physician's UPIN. While I don't want you to get overly concerned about this slide, the first part of it is relevant. This is directly from CMS rules and regulations. "If an employee of the physician provides genetic counseling and that person is not a nurse practitioner, physician's assistant, certified nurse specialist, or certified nurse midwife," -- all four of these having a specific payment

recognition in Medicare -- "then genetic counseling can only be billed by the physician as an E&M CPT code 99211."

A 99211 is basically office with an established patient, minimal problems, five minutes spent performing. This 99211 was developed for nurses who were providing, for example, immunizations, where they were giving counseling to the parents about the side effects of immunizations. That's what this code is for. But because genetic counselors are not specifically recognized within Medicare with a payment category, they are not able to bill "incident to" at a higher level, as are these folks who can basically have access to all of the E&M CPT codes.

Now, there are a few ways that we can sometimes get around it. Hospital-employed counselors can be billed for as part of a facility fee that's not available to non-hospital-based practitioners. Washington State has mandated coverage of genetic counseling and issues billing ID numbers to certified genetic counselors. They are the only state at present that is doing that. I mentioned before Texas and Ohio. Texas and Ohio had also developed private codes, local codes to allow for reimbursement of genetic counselors. However, one of the side effects of HIPAA was that all local codes disappeared. So all of those systems that were developed have been lost to use in those states, and to my knowledge have not been recovered.

Even though counselors have licensure status in California and Utah, my understanding is that billing rules are still pending, and so whether they'll actually be granted billable entity status in those states is up in the air.

What does this affect? Well, it affects access. Systems don't offer genetic counseling if there's no reimbursement for it. We heard about the labs getting reimbursed at a percentage of cost. Well, the percentage over zero is infinity, so that is a bit of an impediment. Productivity-based reimbursement limits geneticists in the private sector. In other words, if you're in a standard medical group where your reimbursement is specifically related to how much work you do, the amount of work that you're actually able to bill for, given the limitations of the E&M system, really does not make it financially viable in the traditional medical group, although in groups like the group I practice in in Kaiser, where we're on a salary basis, groups can make the decision that this is a value added, and then they'll try and make it up somewhere else.

Geneticists are consequently not seen in health plan networks, in the PPO networks that Michele referred to, and there may be referral requirements to see a geneticist or the traditional gatekeeper model. We're seeing a little bit less of that, but I think there's still the perception that genetic services are expensive and are for only the very few, therefore they're really not necessary.

Now, I think there are a little bit of things to be hopeful about. The first is that in 2006 we'll all be issued new numbers, thank heavens, national provider ID numbers, NPIs. Our understanding from the interpretation of those rules is that anybody that provides medical services will be eligible to have an NPI. That means that genetic counselors will be eligible to have an NPI. The major problem that genetic counselors have right now is that even if a third-party payer wants to pay a genetic counselor -- for instance, Aetna mandates genetic counseling prior to certain of their cancer predisposition tests -- the genetic counselors can't get into the computer because they're not a billable entity. They can't get a UPIN, they can't bill.

If they have an NPI, then certain third-party payers may be able to allow

genetic counselors to use that NPI and be allowed billable entity status. There may be some state initiatives that are going to come along. The HCPAC, which is a representative of non-physician allied professionals that sits at the CPT advisory council is developing CPT E&A codes. This is evaluation and assessment codes for genetic counseling to be brought to the CPT Advisory Group and Editorial Panel, and if these are accepted, once a CPT code is in there, basically anybody can use it. So that may help some.

Then, as we're going to hear about a little bit later, research on the impact of genetic services on cost and quality of care are out there. There's going to be more of them, and I think we're going to be able to make a better case for why there is a need for our services.

Thank you very much.

DR. McCABE: Thank you very much, Dr. Williams.

Our next two speakers will give us an overview of Medicare's coverage and payment policies and decisionmaking processes for genetic technologies and services.

Dr. Sean Tunis, who is Chief Medical Officer, Director of the Office of Clinical Standards and Quality of CMS, will review coverage policies and decisions, and then he will be followed by Dr. Donald Thompson, who is Director of Ambulatory Services at CMS, who will cover payment policies and decisions.

Dr. Tunis?

DR. TUNIS: Well, thanks very much. I notice that we're running about 15 minutes behind, so I'm going to try to focus on just some of the major elements. And I also notice from the last couple of presentations that really all the whining is about payment policy, and that's why I brought a designated whipping boy --

(Laughter.)

DR. TUNIS: -- Don Thompson. The coverage stuff is really non-controversial, and I'll just whip through it, if that's okay.

Just as a broad overview, basically in order to get reimbursed for anything under Medicare, you have to deal with these five bullets, which are regulatory approval, a benefit category determination, coverage, coding, and payment. I'm going to talk about the first three, and then Don will talk about the last two.

By the way, I get to present so often with David Feigal of the FDA that he could probably give the rest of my talk, and you're welcome to it if you'd like it. We seem to find ourselves on the same panel about once a week, and I think maybe we'll switch jobs just for fun at some point.

Regulatory approval. Basically, you all have heard some of this before, but it's required for Medicare coverage if the technology falls under FDA regulatory purview. Regulatory approval is required for at least one indication, but Medicare has complete flexibility to cover off-label indications for uses of tests, devices, drugs, or anything else, and there's a lot of Medicare payment for things for off-label uses.

Obviously, any new guidance adopted by the FDA related to genetic testing, changing the regulatory framework, would affect CMS coverage by virtue of the fact that we would follow that regulatory oversight. On the issue of home-brew tests, since they may not be under the FDA regulatory purview, they do not require FDA approval in order to be reimbursed by Medicare.

So really not much more needs to be said about the regulatory issues.

The next issue in some ways becomes one of the key issues regarding some

of the limitations around Medicare reimbursement for genetic tests, and that's the benefit category issues. Medicare is a defined benefits program, which means we can only pay for things that are specified benefits within the Medicare statute, Title 18 of the Social Security Act. So as examples of defined benefits, there's inpatient services as a benefit category, outpatient services, ambulance services, durable medical equipment. As some of you might have noticed, a new benefit category was added in December of 2003, prescription drugs. So those now become payable by the Medicare program, couldn't be paid for before because there was no statutory basis to do that.

Diagnostic services are a benefit category, whereas screening services and preventive services are not. So obviously, the critical issue is what's a diagnostic service and what's a screening service, which turns out to be a rather subtle distinction and an important distinction.

So, first of all, this is kind of current policy in Medicare. You have to ask around a lot to actually get this laid out for you. But for purposes of diagnosis, the distinction here is based on whether a person has signs or symptoms of disease or a personal history of illness. So obviously, someone with a history of multiple colonic polyps, they have a history of disease. Genetic screening in that case may be considered coverable.

A strong family history would not by itself qualify to make a test a diagnostic test. So genetic testing in high-risk patients with a family history of breast or ovarian cancer would be considered screening, no matter how high the pre-test probability is. It's still considered screening. In some sense, the proof that this is the way the program is set up is that last year we had a discussion about diabetes screening for high-risk patients, and there was a lot of discussion at the Department of Health and Human Services about whether we had the legal authority to do diabetes screening in patients with no signs or symptoms of disease simply based on a profile that would make them very high risk for having diabetes.

Essentially, the outcome of that suggests to you what the answer is, which is diabetes screening was just added in the Medicare Modernization Act as a benefit under Medicare. Now, that having been said, our general counsel has long held the view that there is nothing in the statute that actually explicitly prohibits us from designating testing in high-risk individuals with no signs or symptoms of disease and no personal history, nothing that stops us from deciding that that is diagnostic testing. But in order to do that, we would have to go through rulemaking because it's been longstanding agency policy that that's not how we approach it.

So if you all were interested in tomorrow deciding what kind of interesting windmills you'd like to approach, one of them would be rulemaking around genetic testing, not that I'm suggesting it.

Obviously, any tests that identify a treatment responsive subpopulation, most pharmacogenomic tests, would be diagnostic tests because those are done in patients who have existing signs and symptoms of disease, generally.

So that is, kind of in a nutshell, the benefit category issues. Obviously, because of the current situation regarding screening versus diagnostic tests, many of the genetic tests that you all are concerned about are not an issue from the perspective of Medicare reimbursement. We can't reimburse them under the current scenario.

Under the situation where tests would fit within the benefit structure and would be potentially coverable, then you move on to the coverage issue, which emerges from

Section 1862(a)(1)(A) of the Social Security Act, which says that coverage and payment are limited to items and services found reasonable and necessary for treatment of illness or injury. You've heard a lot of discussion earlier about medical necessity, reasonable and necessary, how that's defined, et cetera.

The Medicare program makes coverage decisions at the local and national level. By local level, we mean the Medicare contractors around the country who process claims for Medicare, the local insurance companies. In the absence of a national policy, the policies of those local insurers who process Medicare claims are the coverage policies. Those are called local coverage decisions.

We haven't talked about it a lot today, but cost, cost-effectiveness, cost-benefit analysis are not considered formally in making reasonable and necessary determinations within the Medicare program, and the asterisk there is just there to say that's a longer discussion. I wouldn't want to stand up here and suggest that economic issues are not a factor, and I'd be happy to answer questions on that if I'm still around during the panel discussion.

So in terms of current situation around coverage policies for genetic testing, we have one national coverage decision, which is on cytogenetic testing, and it specifies it's covered for AML, acute leukemias, congenital abnormalities, and myelodysplasia, I believe. That policy actually dates back to 1979, was updated in 1998, I believe, through the national coverage process.

So most other coverage basically, to the extent that there is a test paid for, is under local coverage decisions. A number of the contractors do pay for HER-2 testing. There are some that pay for BRCA testing, although most don't because they consider it to be screening and they are under the same obligatory purview in terms of screening versus diagnostic tests that applies at the national level.

So we ran some numbers for 2002. Don's folks did this earlier today. There were 270,000 claims paid at a total cost of about $13 million. Well, we almost never do a national coverage decision on anything that is less spending than $50 to $100 million. That's not a firm or fast cutoff. That just tends to be the way it is, that we're not going to deal with issues that have less impact. So it's likely that there's going to be more national coverage decisions with coming advances in genetic testing, pharmacogenomics and personalized medicine. So the national coverage process may not be particularly relevant to you all now, but it probably will become more relevant as this field advances, particularly if you can get that little thing fixed related to family history of disease and high-risk patients.

There is a formal process for developing the coverage decisions by the contractors, the medical directors, carrier advisory committees. There's a development of draft policies, et cetera. So they do have a formal process. There's even a process for reconsidering policies. They basically also apply reasonable and necessary, and I'm going to give you the current definition of reasonable and necessary in a moment. I'd just like to point out that at the local level it's understood that more weight is placed on expert opinion versus empirical evidence. So it tends to be more of a consensus-weighted process as opposed to an evidence-weighted process.

So in the context of an earlier stage of development of the evidence around genetic testing, my guess is that there's going to be a lot more tests added at the local level before we ever get any additional tests actually covered at the national level. Local policies are not binding on administrative law judges, and they can be appealed. When there's variations

amongst different local coverage decisions in different jurisdictions around the country, that will often be a basis for something being referred up to the national program for a national coverage decision.

This is the diagram of the national coverage process. Again, we could spend a long time on this, but basically this is just to emphasize that there is a formal articulated process. This is in the Federal Register written out just this way. It involves the possibility of technology assessments being done, usually through the Agency for Healthcare Research and Quality. We have a Medicare Coverage Advisory Committee, and the time frame for this is now six to nine months. These are new time frames that were imposed as a result of the Medicare Modernization Act. We had target time frames in the past which we applied rather loosely. So anyway, now there's a nine-month time frame during which a decision had to be made.

So here's the definition from Medicare's point of view of what's reasonable and necessary. There needs to be adequate evidence to conclude that the item or service improves net health outcomes, and in terms of health outcomes we emphasize outcomes that are actually experienced by patients. So functional status, quality of life, psychological outcomes, as well as morbidity and mortality, all of those are meaningful outcomes when it comes to evaluating the impact of a diagnostic test.

We usually look for evidence that's generalizable to the Medicare population because there are sometimes significant differences between the performance of the technology, including genetic technologies I imagine between younger and older populations, and we also look for things that are as good or better than currently covered alternatives. We use a standard evidence-based framework, the same sources of evidence as I think Michele Schoonmaker put up, published literature, systematic reviews, expert guidelines, et cetera.

The key factor here is that we weight the evidence based on the source and the methodology. The whole evidence-based medicine approach basically says you put more emphasis and place more weight on evidence from sources that have less potential for bias.

So let me just talk, then, about determining the adequacy of evidence related to diagnostic technologies. We use a framework which is not unfamiliar to anyone here, but it was articulated by our Medicare Coverage Advisory Committee, that basically there are sort of two critical pieces. There is test performance, the sensitivity and specificity or accuracy of the test, and then there is the clinical utility, impact on patient management and outcomes. In some cases, of course, the clinical utility will depend on there being a beneficial intervention available.

So then we come down to an important question, which is under what circumstances does information itself provide benefit? Well, we certainly don't assume that information itself and increased certainty is inherently beneficial. At least, I'm not aware that that's an assumption that we've been using.

So the value and the impact of the information is likely to vary by the test and by the specific clinical circumstances, and what I would say is that ideally, if one is going to argue for the benefit of information, whether it's a Huntington's disease test that presumably affects people's lifestyle choices or other factors, we would look for some evidence to empirically demonstrate that the information in fact has that impact. Simple qualitative arguments that that might be the benefit of a test are not going to be sufficient, at least at the national level, to merit coverage.

So that covering the regulatory issues, the benefit category issues, and a quick intro on reasonable and necessary, and we'll let Don take all the hard stuff.

DR. McCABE: Thank you.

Mr. Thompson?

MR. THOMPSON: I was sitting in the back listening and taking an interest in Dr. Ferreira-Gonzalez' presentation, and it was so good, about halfway through I started thinking what idiot is in charge of the Medicare physician clinical lab fee schedule? And I realized that was me.

(Laughter.)

MR. THOMPSON: So not considering myself an idiot, I'm going to talk a little bit about how we do new determinations for payments, and then a little bit about how we got to where we are, because when I first took this position and I looked at the Medicare clinical lab fee schedule, I came to many of the same conclusions that some of the earlier presenters have came to. You have to dig a little to kind of understand the tortured history and kind of understand a little bit about how we end up in a position where you have some of those slides that were presented earlier that have such payment anomalies surrounding them.

But first, let me talk a little bit about how we handle new lab tests. We have two methodologies primarily for handling payments for new clinical lab tests under the Medicare clinical lab fee schedule, gap filling and cross-walks.

By the way, everything I'm saying here applies to all new technology under the Medicare clinical lab fee schedule. We don't have anything specific to genetic technologies.

So gap filling and cross-walking. Gap filling is a process where we essentially go to all of our carrier medical directors, all the medical staff in our contractors, and we say we have this new test that CPT has created, because the beginning of this process is a new CPT code. That's how this comes about. So we get a new CPT code that gets created, we go to our contractors, and we say we'd like you to kind of go through, examine this test, and look at a variety of factors that I'll touch on in a later slide, and determine a payment amount for your area. That's the gap-filling process.

The cross-walk is done in Central Office. So in cross-walking, what we say is we have a new lab test and a new CPT code, and we think that this is similar in certain respects to an existing test. We just cross-walk the payment amount to an existing test.

So those are the two ways. Gap filling, it's a decentralized process where we send it out to our carrier medical directors. Cross-walking we do in Central Office where we look at what existing tests under the clinical lab fee schedule might be appropriate and we cross-walk the payment to that.

We don't do this in isolation. We have public meetings. We have public input on this. The one for 2005 will be on Monday, July 26th, for those of you that are interested. Any interested parties can give testimony. The test kit manufacturers can come in. ACLA can come in. It usually comes in. AdvaMed gives presentations. Everyone gives us recommendations about how they think we should either gap fill or cross-walk and, in the situation of cross-walk, what code they think we should cross-walk to. We then take these tentative determinations and we post them on the web for additional public comment, and we make the final determinations usually around the early part of November, and that would be for the 2005 tests.

Gap filling. Let me say at the outset I'm not a huge fan of gap filling. It is a great process in concept, not fantastic in execution.

What we say on gap filling is a carrier should examine a variety of factors, and we do not weight these in any way. These are just kind of guidelines for them. Charges for the test, routine discount to charges -- so look what the lab is charging for it -- and look at the resources required to perform the test. Look what other payers are doing in your area, although as an earlier presenter mentioned, that's somewhat circular because to the extent that they're all keying off the clinical lab fee schedule, it's hard to look at what they're doing because they're waiting to see what we're going to do. Then charges, payment amounts, resources required for other tests that may be comparable or otherwise relevant.

Then in addition to kind of those core items that they look at, it's also clinical studies and information provided by clinicians practicing in the area. They obviously have a network of physicians that they can tap into. Manufacturers and other interested parties are allowed to submit comments to each of the carrier medical directors when they're making their gap-fill determination.

So kind of against this backdrop, which is how we've been doing it for some time, which is this gap filling versus cross-walking methodology, you have the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. There were two primary provisions in there that affected the clinical lab fee schedule and more of a secondary one that might have some long-term impacts, but let me talk about these two first.

As an earlier presenter mentioned, no updates to existing lab fees until 2009. That is a blanket freeze. There is no administrative discretion there. So there's not a whole heck of a lot we can do at CMS in terms of adjusting lab fees for existing tests until 2009. So some of those slides that you saw earlier that had some of those payment anomalies in will continue to exist for some time, and there are many stories in the clinical lab fee schedule like that. That is isolated to genetic testing by any means.

Then the other section, though -- there is a small ray of hope here -- in 942(b), Methods for Determining Payment Basis for New Lab Tests, it goes into a little bit about the need for us to publish regulations in this area. We have not had regulations in the past. Most of the payment methodologies under the clinical lab fee schedule have just been a past practice. They've kind of arisen over time and they have kind of self-perpetuated, but we do not have formal regulations, and our general counsel would indicate our past practice has the force of regulations. If we have an established process, we can't just say, you know, we think next year we're going to change the whole thing around. So the fact that we have past process means that if we want to change that, we have to go through a regulation and now what Section 942(b) does is say, okay, we're required to go through a regulatory process.

The odd thing, though is when you look at what Section 942(b) says, it describes to a certain extent what our current process is. So it didn't give a lot of guidance in terms of what Congress might have intended for us to under 942(b), other than one could envision the kind of process that we were currently using, which is get public input, the cross-walking, the gap filling.

So we're struggling with -- my last point there, differences from current process -- we're struggling with this and what we intend on doing is going through a formal notice and comment. So we will this year have a formal regulation, a proposed rule that we're going to put out, and we'll kind of go through what we think our interpretation of 942(b) is and

seek public comment on that. I'm very interested myself in seeing what kind of comments we get, and then we'll go through a final rule process after that.

So the issues for reform, we touched on the relative payment rates are essentially frozen, and this is for two reasons. Not only the explicit freeze in the MMA, but in addition, going into some of the history of the clinical lab fee schedule, it is the oldest fee schedule in the Medicare program. It dates back to the early 1980s. It is very archaic at this point.

However, there's no mechanism for revising it. There was some optimism that perhaps in the recent law we would get authority, that CMS would get authority, to revise the clinical lab fee schedule in its entirety. I mean, not just for genetic testing, but in the whole thing, look at it comprehensively and say what do we have here? We have a system where the clinical lab fee schedule was established in the early 1980s and life is a lot different now, but yet we still have these same relatives locked in place from the early '80s and it's difficult to get at them.

In addition, maybe give us a different methodology for adding new tests. The 942(b) was helpful in that respect, but it would have been nice maybe if Congress had more explicitly provided some guidance, but we will struggle through that from a regulatory standpoint.

To a certain extent, going back to some of the earlier slides, this is where the problem is. You have this 1980s fee schedule that we've attempted to kind of modify over time, even though the basic construct stays the same and we don't have any statutory authority to revise it. We've tried to modify it over time to make it work for new lab tests.

But as you can imagine, one of the immediate issues that comes about, think about cross-walking. Okay, you have a new test. You say this is kind of like this existing test, but the payment rate for the existing test was locked in in the early 1990s. So you're in a situation where the logical choice for the code -- you say okay, this definitely walks right to this code, this is similar, and this is how you should pay it, but the payment amount for that code doesn't necessarily make sense. So you're kind of in a bind.

So at that point, what do you do? You say, okay, we'll throw it out to gap filling and see what happens there, but because of the decentralized nature of that, sometimes the proponents of the CPT code can be nervous sometimes about going out to that gap-fill process.

It's a little bit of a Catch-22. You're cross-walking to what may be a mispriced code or you're sending it out to gap filling, which is a decentralized process where you have to deal with all our individual carrier medical directors.

So where does that kind of leave us? Not in a great spot. One of the things that we'd like to look at is there was an Institute of Medicine report that talked about revising the clinical lab fee schedule and they had a lot of excellent thoughts and suggestions about how we might go about doing that. Now, we have no statutory authority to do it, but at least we might make some more progress thinking about those thoughts.

Along those lines, one of the recommendations in that report was to look at kind of a competitive bidding process. For those of you familiar with other sections of the MMA, there is competitive bidding now for durable medical equipment, there is competitive bidding for Part B injectable drugs that will be coming up in 2006, and there is a demonstration project to do competitive bidding for labs. So that's one concept one might use in thinking

about revising the lab fee schedule in total, is that kind of competitive bidding approach.

Another one might be negotiated rulemaking. That's worked successfully, for example, on the ambulance fee schedule. That's another road we might go down.

There was some optimism about looking at charges for this. For those of you familiar with the kind of Tennant fiasco and some of the problems we had on outlier payments, that's thrown a little cold water on the concept of using charges, but it still might be something worth looking at.

So those are kind of the options out there, but again, no statutory authority to implement them. The only thing we can do, with respect to some of the older technology tests, we do have an authority in the statute, inherent reasonableness authority. What we're allowed to look at there is things that are inherently unreasonable, payments that are inherently unreasonable, and there's a process in the statute.

There was a moratorium on using that authority. That moratorium has been recently lifted, and one of the things we're examining very early in that process, once we issue instructions to our contractors, is in fact the HIV/HCV viral load that was mentioned earlier, where you have the payment rate for the HCV load is roughly half of the HIV for what is almost the identical procedure.

So that's an early candidate for us, is inherent reasonableness. It may be difficult to revise an entire fee schedule brick by brick, but the inherent reasonableness authority is one avenue we could go down and we're interested in using that. Hopefully, this year we'll have those instructions out and be able to at least start with some of the more egregious examples.

I can take questions during the roundtable.

DR. McCABE: Thank you, Mr. Thompson.

Now, Dr. David Veenstra will discuss cost-effectiveness analyses of genetic technologies and informed coverage and reimbursement decisions and the data needed for conducting such analyses. Dr. Veenstra recently joined the University of California-San Francisco School of Pharmacy and is an assistant professor in the Department of Clinical Pharmacy.

Dr. Veenstra?

DR. VEENSTRA: Thanks to the committee for inviting me to come and present today.

The other speakers I think really gave a great background for talking about cost-effectiveness. I just want to give a little bit of an overview of cost-effectiveness, kind of the 20,000-foot level, talk a little bit about economic evaluations of genetic technologies, and then go over some examples to kind of give you an idea of what types of information you can get out of these types of analyses.

I guess the kind of message I want to get across is that cost-effectiveness analysis is not about just looking at cost only. It's really about putting a value on all of the things that we look at in health care, including quality of life and life expectancy, and really I think the advantage of formal cost-effectiveness analyses is that they provide a framework for evaluating the complex and conflicting factors that are involved in making coverage and reimbursements decisions in health care, and I think we all realize that with genetic technologies that's even more of an issue.

Another advantage that you can have here, and we'll see this as we go

through the examples, we can look at multiple different strategies and many times, when we use modeling techniques, we can get information to decisionmakers when they're trying to make that decision, as opposed to years later.

I'm not going to go into all these different details here, but I just want to highlight that within this kind of area of economic evaluation in health care, there are a variety of different methods that folks use. A lot of times these are all referred to as cost-effectiveness analysis in general.

I think really kind of the gold standard in the field is what's called cost-utility analysis, and the reason that basically people like it is that you look at outcomes in quality-adjusted life years. So you look at life expectancy as well as the impact on quality of life in patients, and of course, costs are measured in typical dollar terms.

So one of the questions that was put to me was what information does cost-effectiveness analysis provide to health plans? Well, unfortunately, it's just one little piece of the puzzle, and I think as we've heard from the discussions today, there are a tremendous number of issues that go into decisionmaking. So I don't want anyone to feel like I'm advocating using cost-effectiveness analysis to make decisions about what to cover. It's just one piece of the puzzle, but I also think that it can highlight some strengths and weaknesses in these other areas.

Another tough question is is cost-effectiveness information used in reimbursement decisions in the U.S.? Well, I think we heard one perspective from Sean, and I can bring a little bit of another perspective on this issue, more from the managed care arena. The short answer to that question is sometimes, and it's changing.

I think a nice example that's out there of the use of economic information in decisionmaking are the guidelines that have been put out by the Academy of Managed Care Pharmacy. These were put out and approved by the board of directors in October of 2000, and basically the objective of these guidelines for making decisions about pharmaceuticals were to improve access, improve the transparency of the information of the decisions, and try to achieve a consistency in making decisions, cover and reimbursement decisions about drugs to put on formularies.

Basically, what this format does is the managed care companies go to the manufacturers or the pharmaceutical and biotech industry, and they say give us all the information you have on your drug, including unpublished studies, and also provide us with evidence of cost-effectiveness.

So it kind of provides a framework for looking at this and it enables, when these decisions are made and when folks are making decisions in managed care, instead of just looking at one or two or three studies or the ones that have been published, you're able to have access to all of the information that's out there. There's obviously a lot involved with checks and balances and making sure this information is accurate and exhaustive, et cetera, but basically, it ends up giving the decisionmaker more information with which to make that decision.

So cost-effectiveness is a piece of that. The rest of it is really based around evidence-based decisionmaking.

This I think is about six months old, but the utilization of this format has become fairly popular. A lot of managed care organizations across the U.S. are adopting it, including a few of the states, and it's really become kind of -- hopefully, it's not a trend. It's the

current kind of gold standard I think in managed care. There's a lot of other folks out there that have been doing this type of thing for a long time and doing it very well, such as Kaiser, et cetera, but there are a lot of smaller plans out there that really haven't been adopting a formal evidence-based evaluation as well as cost-effectiveness.

Just in our experience with running training programs, et cetera, when do you actually use cost-effectiveness information? Well, it's generally when you have, for example, more than one drug in a class of drugs and you're basically making your decision based on price, and so you may be wanting to look at things such as the cost of side effects and monitoring things like that.

I think the area where it draws the most attention is when you have an expensive and novel technology. So maybe, for example, when Enteracept came out for the treatment of rheumatoid arthritis. This is probably the situation where some genetic technologies are going to find themselves and this is when payers start to get interested in issues of cost-effectiveness.

This issue of do payers care yet, I think it's not quite on their radar screen yet. I think when you talk to them about genetic testing and pharmacogenomics, a lot of folks start to think, "Oh, biotechnology, biologics. Big budget impact. Now I'm concerned." So if it's something that they feel is high tech and expensive, they'll start to get interested.

I think in some of the data that Sean showed, it's not really having a big enough impact quite yet where at least folks in, for example, managed care have it at the top of their list. I think once we start to get more common genetic testing or tests that really influence the utilization of expensive drugs, you're going to start to see a lot more interest in cost-effectiveness of genetic technologies.

That's basically what I've covered here. Also, obviously, with regulatory intervention there would be greater interest also.

So what are the determinants of cost-effectiveness of genetic technologies and what makes something cost-effective? I just want to flip through a couple of issues here, just some work I've done with colleagues thinking about what could be important.

Really, for pharmacogenomics, there's a lot of information out there about drugs where their metabolism is influenced by genetic makeup in terms of drug-metabolizing enzymes, but you really have to ask yourself how serious are the side effects? Are they going to have significant patient impacts and economic impacts? If you're using pharmacogenomics to select a drug, is that an expensive drug? Is that something that's used over the lifetime of a patient? How much money are you going to save?

The same thing with disease genetics, looking at disease risk. You really have to consider what are the ultimate outcomes you're trying to prevent.

Another issue that I think that I've especially felt that in pharmacogenomics is often ignored is the concept of what's the next best thing? What's the comparator? What's the alternative?

So are you going to use genetics to decide which drug to use for a patient to treat their hypertension or do you just have them come back into the office every few months and over a six-month time period or a year time period, you get it figured out which drug works for them and which dose? That may not be too expensive, so paying a lot of money for an expensive test may or may not be worth it.

Of course, I think this audience here is familiar with the issue of association

studies on the correlations between the genotype and the phenotype. A lot of the folks out there I've seen will focus in on test sensitivity and specificity as opposed to considering actual clinical outcomes in the patient and actual phenotype. Obviously, genes that have a higher penetrance will be more cost-effectiveness in terms of testing.

There are issues around the cost of the test. I think the presentations here today have covered a lot of this. There are things that we need to consider, such as the induced cost and additional clinic visits.

I think there are some benefits and potential benefits in genetic testing that does differentiate it from other types of diagnostics in terms of the ability to use that information throughout the lifetime of the patient. For example, this Roche amplichip, which looks at a series of drug-metabolizing enzymes. Basically, you can look at your entire drug-metabolizing profile on one chip. For instance, if you got that test when you were a young child, you'd have that information available to you for the rest of your life, and the cost is really kind of alleviated that way.

The last point is basically that genetic testing is essentially a screen or preventive medicine, and for those of you that work in that area, you know that cost-effectiveness is highly driven by the prevalence of the underlying disease, and in this case that would really be the prevalence of the genetic variant. If the prevalence of a genotype is only 0.5 percent, we have to go and test 200 people. So obviously, this is going to have a big impact.

We did a hypothetical cost-effectiveness evaluation of testing the TPMT gene, which Michele mentioned earlier, for childhood leukemia treatment with 6-mercaptopurine, and we basically used decision analysis and built a decision model in terms of whether you would test or not and whether the patient was deficient or not and whether they had a serious adverse drug reaction and there is potentially mortality associated with that.

Now, this was just an example, so we kind of tripped this thing out, but basically we put in some parameters for the cost of the test, the mortality due to the adverse drug reaction, and then the prevalence of the deficient genotype. We found that these three parameters represent three of the dimensions in cost-effectiveness. The cost of the test, the economics; the genetics, the prevalence of the genotype; and kind of a clinical outcome.

What I'd like to show you on this graph here is basically what we've done here is plot -- this is the mortality associated with the adverse drug reaction, that's the cost of the test on this axis, and on this axis here we have what's the incremental cost-effectiveness ratio. Basically, just to make this simple, things that cost less than $50,000 per quality-adjusted life year in the field is somewhat considered reasonable and cost-effective. When you're between 50 and 100, not quite so. It's more of a question mark, and then above 100, it's generally not considered cost-effective.

So in this example, when we're using the default prevalence of the genotype of 0.3 percent, you can see that depending on these other parameters, you may or may not be cost-effective. It may not be a reasonable way to spend your money compared to other interventions that you could be allocating your budget to.

But when we change this from just 0.3 percent to 1 percent, you can see the significant impact it has on the cost-effectiveness. So even small changes in the prevalence of the genotype can have a big impact, even in terms of budget impact in terms of the number of people that you identify.

Now, I just wanted to give you guys a few examples from the literature. This is a study published recently, November 2003, looking at newborn screening for MCADD, and this was using a tandem mass spec technique. Just briefly, basically what they did was they created a cost-effectiveness model using decision analytic-type techniques, like I just showed you there, and they did a cost-utility study. So they were looking at cost per quality-adjusted life year.

They assumed the cost of the test was only an additional $4. This was assuming that there was already some type of tandem mass spec testing going on, and they looked at what would happen with screening versus no screening in looking at the 2001 birth cohort.

Well, they found that you'd end up with longer and better lives. So you'd have a gain of 990 quality-adjusted life years. So let's just say 1,000 life years is what you'd save.

You would have, however, a higher overall cost of $5.5 million, but if we convert that into the cost-effectiveness language, we end up with $5,600 per QALY, which is a lot less than the $50,000 per QALY. So this might tell a payer that this is a reasonable technology to reimburse.

If we look at colon cancer, there's been some work in this area. Scott Ramsey has looked at testing for HNPCC, and again, I think Sean outlined this nicely. Basically, what they found is that the incremental cost per QALY is about $40,000 per QALY if you look only at the patients, but when you include family members, the siblings and children of those patients, all of a sudden you get tremendous more gain for the amount of money you've spent. I think that might have interesting implications in terms of who's covered and who's reimbursed for genetic testing and obviously can run into some difficult reimbursement issues.

I think there is also some interesting information that's come out of some of these studies where some folks have advocated universal screening as opposed to folks that fit within the Bethesda guidelines, et cetera, and have found that the cost, the annual cost, in the United States could be pretty dramatic if we were to end up full testing on all patients.

Breast cancer. There's been not as many studies as you might think of the cost-effectiveness of actual screening, but Grann and colleagues have a study looking at Ashkenazi Jewish women, and again, not to go through all the details of the disease, basically what they found was that for a cohort of 10,000 women, you could avert about 80 deaths by having this screening program. They found in their calculations that you were doing this at a rate of about $30,000 per life year saved, so something that seems very reasonable.

However, they conducted that analysis with a default value for the test of about I think $400, and when you plug in something perhaps a little closer to what might be reimbursed, now you're up in the $85,000, pushing $100,000, per QALY. So a payer might utilize an analysis like this to give some pushback on the cost of a test or try to negotiate on the cost of a test based on its value.

Now, does this happen every day with the Academy of Managed Care Pharmacy guidelines? No. It's a much more subtle effect, I think, but it provides a framework for these types of negotiations.

Then lastly, for pharmacogenomics, this is some work that Katherine Phillips, a colleague of mine from UCSF, has led. It's actually working with the FDA, doing some work with them. She did a systematic review looking at cost-effectiveness studies of

pharmacogenomics.

Basically, just to sum up, she found 10 studies out of a total of 253 citations that were identified. Four were in thromboembolic disease, a couple were in chronic hepatitis C, two were looking at the enzyme thiopurine methyltransferase, and a couple in other areas. Eight found that genotyping was relatively cost-effective, while two studies found it to be less cost-effective than other options. So that's kind of the landscape of what's out there for pharmacogenomics.

I'll skip this slide.

So what are some of the unique challenges of looking at cost-effectiveness of genetic technologies? I think a lot of it is fairly obvious. Basically, there's a lot of information, it's complex, and it's interacting, and so there are pretty significant data needs.

I think some of the things that need to be worked out are what are really the induced costs surrounding testing. A lot of these issues of the cost of adverse drug reactions, for example, I don't think have been costed out very well, and the whole issue I think of patient preferences and quality of life needs to be looked at a little bit more closely.

You know, I feel that using a decision modeling framework, you can kind of bring all these complex factors together and with additional data in these areas in the economic outcomes, the patient outcomes, as well as obviously, as the committee discussed earlier, the clinical outcomes and association studies, with this type of information I think it is possible to provide useful cost-effectiveness information to decisionmakers.

So along the lines of what I think everyone's been talking about and thinking about are providing some types of guidelines and policies for the reimbursement, using an evidence-based approach, and incorporating some aspects of cost-effectiveness into the process.

I think some issues that I've seen will be who will be responsible for these decisions. Is it going to be the P&T committees or medical services? I think for pharmacogenomics, it may very well be that it falls under a P&T pharmacy services area.

I think there's particular interest with regard to pharmacogenomics in terms of it's a real pain for them to try and control drug use by requiring prior authorization, but if a drug comes with a genetic test that's required, it kind of makes them easier to control drug utilization and expenditures potentially.

So in summary, I think cost-effectiveness evaluations in health care is challenging to begin with. I think in genetic technologies, it's probably one step further.

I think because, however, the decisions are so complex and there are so many factors involved, that decision analysis and cost-effectiveness analysis at least provide you with a framework and it can highlight where your data uncertainties are and where additional resources need to be invested.

I think that as more tests come to market, that the need for these types of studies are probably going to be increasing as payers are faced with more decisions in this area.

So that's it. Thanks.

DR. McCABE: Thank you very much, Dr. Veenstra, and thank you to all of the presenters for these very informative and helpful presentations. Now we can explore these in a roundtable.

Just while you're sitting down, Dr. Veenstra, you talked about the complexity of these issues, and one point that wasn't raised, but one of our fellows presented

some work at the Western Society for Pediatric Research and has a manuscript in preparation. What he found -- this was in a study of newborn screening for severe combined immunodeficiency, SCID -- was that it was most sensitive, looking at newborn screening, to the sensitivity and specificity of the test to the test parameters because that determined the false positive rate and those sorts of things.

So there are even additional issues, and that analysis was much more sensitive to those issues than to the frequency because of the cost implications in a screening test. So I think these are just incredibly complex issues as we move forward and it will depend on the setting in which the testing is performed as well.

Now it's time for the committee to ask questions and make comments about the presentation. Yes, Joan?

DR. REEDE: One of the things that was very striking to me was bringing home a clear recognition that as we talked about the need for more evidence and the challenges that we're facing or going to be facing for those who are insured is the widening gap for those who are not insured, and the fact that these issues just sort of see us moving toward a potentially two-tiered system, that as we move towards advancing technologies and use of these technologies and trying to figure out how to pay for them, there is a huge portion of our population where these will not be accessible.

I'm wondering, from any of the presenters, if you could give any comment to what might be done in terms of addressing this part of the population that has been left out of this discussion.

DR. McCABE: Members of the panel? Marc?

DR. WILLIAMS: I'll take a crack at it. I mean, I don't see anything different here than what we're facing in medicine in general. I mean, the issue is we have a two-tiered system. We have rationing. We may not want to use those terms, but that's the reality. We have a limited budget and limited resources, and so in some sense it does seem a bit silly to be arguing about who gets what when we know that there's a large population of people that probably don't have access to much of anything. But I don't know that there's anything specific to the genetic piece that separates that out from that issue. Pick any sort of access to service.

I can tell you that in my own clinical practice, that because of the nature of genetic disorders, that a lot of these children and adults do qualify for coverage under some of the special needs pots of money that are somewhat separate from other Medicaid pots, KBAC and other of those sorts of funds.

So at least in Wisconsin, we haven't had a tremendous issue with children and adults affected with certain genetic disorders in terms of getting them qualified, and thus eligible for services. So I think that in some sense having a genetic disorder may actually make available some reimbursement systems that aren't available to those that, by nature of lack of employment or whatever, don't have any coverage at all.

DR. McCABE: Michele, I'm going to put you on the spot. Does that come up at all in your advisory role?

DR. SCHOONMAKER: Well, I've just been with CRS for only a few months, so I'm not really at liberty to discuss what policies Congress may or may not be considering, but it is a fundamental flaw, if you will, with our health care system and the way health care is delivered in this country. Perhaps if that's something that the committee could

contribute to by framing policy issues or making recommendations, I would encourage you to contact your members of Congress or the committees that would have jurisdiction over those issues and presenting an argument.

DR. McCABE: Just to remind everyone, though, don't get so excited and call them tonight because you can't do that while you're a special federal employee.

Sean?

DR. TUNIS: The only thing I would add is it's become a standard part, when I talk about coverage and reimbursement for a new technology, to talk about all of the existing unmet needs for technologies and services that are very high value, very cost-effective or cost saving, that are not part of a benefit package or not particularly highlighted or talked about.

I think it's an excellent point to raise here that, even within the realm specifically of genetic services, there may be those that are extremely high value to populations that we tend to forget about, and to take the opportunity to highlight those, rather than entirely being attracted to sort of what's five or 10 years over the horizon in terms of the fanciest stuff for people who have insurance. I think that's an important element to every discussion about new technology. We've got a limited amount of resources to spend in health care and I don't necessarily think that we're attentive enough to the notions of getting the best value for resources.

DR. McCABE: Anyone else on the panel want to take a shot at that?

(No response.)

DR. McCABE: If not, Hunt, and then Cindy.

DR. WILLARD: I was struck, and Marc, I think you said it most eloquently by saying you were whining, but four or five of you, the obvious take-home lesson from everything you've presented was we want to be paid more for our laboratory tests or we want to be paid more for our clinical services. Yet I've spent enough time in hospital CEO offices to realize that that's not going to happen anytime soon.

So the ray of sunshine here was Dr. Veenstra. So my question to him, and the whiners can chip in as they will --

(Laughter.)

DR. WILLARD: My question to him is how large a group do you represent? I know of only a few groups like yours nationally who are really trying to address this issue of cost-benefit analysis in order to make an argument to someone that in fact this does eventually pay the system back or even save money in the long run, even though in the short run it's probably much more expensive. So how rare a bird are you?

DR. VEENSTRA: An N of 1.

(Laughter.)

DR. VEENSTRA: No, my perspective is definitely coming more from kind of the pharmaceutical reimbursement area, and I think 10 years ago there was a lot of cost-effectiveness analysis. I think really the methods had been fully developed and there's a lot of research in the area. You didn't see them applied too much. There were guidelines in Australia for requiring cost-effectiveness analyses before reimbursement of tests.

Now, we have a situation where in a lot of countries, and in particular in the United Kingdom, there's a National Institute for Clinical Excellence, NICE. A lot of people call it not so nice, but they look at clinical evidence and they also look at cost-effectiveness

before they make coverage decisions, and it's having an impact on the way drugs are brought to market and it's starting to impact the pricing, and what I explained to you about this AMCP format, that's really grown over the last few years, and so you're starting to see somewhat of a change of a perspective there.

So I would say that there's a strong academic community, but in terms of actually influencing decisions and playing a role in decisions in the real world, I think it's really just starting to happen now.

DR. WILLARD: Because I must say, in terms of what the committee might do, that focusing on that issue going forward of how we might take advantage of that body of expertise to examine the future of applying genetic and genomic technology for a larger and larger set of patients is more likely to be well received than simply arguing that a group is underpaid for the services we're already providing, and therefore we'll really be underpaid when we start providing even more. But if we can wrap that around an argument, assuming it works out that way, that this does have a positive cost-benefit ratio, then that would be time well spent.

DR. McCABE: Marc, and then Michele in response to that, and then we'll move on to another question.

DR. WILLIAMS: Yes, I think that's certainly reasonable. I think, though, it's also fair to look at what is happening in the private sector, and I think Ron's example in Kaiser and to some degree even in our relatively small integrated health care delivery system, there is the recognition, even though we don't really have the capability -- at least our group doesn't, and Kaiser probably does -- to actually internally do those types of studies, I think what you recognize is that some of the relatively low-cost interventions that we do, like taking a family history and doing genetic counseling and providing those services, actually in many cases reduces the number of higher-end technologies that are being utilized. Of the patients that are referred to our cancer susceptibility clinic, only about 1 in 10 actually go forward with a test.

So I think there are savings to be accrued to the system by doing things well in the front end, and while I think you're right, particularly when you look at the editorial panel and the fact that there are no family practitioners, internists, or pediatricians that are actually a voting member of that panel, it does tend to understand a little bit about why there's a skew between procedure versus, if you will, cognitive services in this country.

But there are cases to be made and within an integrated health care delivery system, I think those cases are being very effectively made. The problem is that that doesn't necessarily translate into the way the care is generally delivered in this country.

So I think beyond the academic approach to cost-effectiveness or cost-utility, I think there's some practical experience in well-integrated systems that would demonstrate value and quality as well.

DR. McCABE: Michele?

DR. SCHOONMAKER: Thank you, and again, these are my own views.

I think a problem that precedes whether or not we can use cost-effectiveness information is a problem that we need a better way of collecting data to assess effectiveness. As you heard Sean say, CMS and FDA are both bound by the legislation and the regulations that say that they look at safety and effectiveness or medically necessary and appropriate, and perhaps one thing that the committee could explore would be a better way to or a way to

promote the better coordination between those two agencies in the evaluation of new technologies that would enable you to collect the type of data to make effectiveness determinations, and then adding the cost may be relatively straightforward or not. I see it as a way of more efficiently handing the baton from one agency to the other one without stifling the innovation that's going on in the field.

DR. McCABE: That was a windmill that we tilted at under SACGT. It would require legislative change because of the way the laws, the enabling laws, for the two organizations -- and the cultures of the organizations. These fundamentals are firmly embedded. So we had decided not to, while we recognize that it's a fundamental tension between those agencies, because where one determines that it's safe and effective, the other determines that it's not valuable enough for reimbursement, so it does create problems and it is a problem in the system. We could decide if we wanted to take that one on, but it's fairly deeply rooted, as we learned during those previous deliberations.

Cindy?

MS. BERRY: One of the frustrating things in trying to change a policy, particularly in federal programs and Medicare in particular, is the fact that to get a change in the law, the Congressional Budget Office has to look at the proposed law and determine how much it's going to cost. Unfortunately, CBO is dealing with narrower budget windows, where maybe we're dealing with five or 10 years, and maybe some of the research that's out there that demonstrates real cost-benefit and effectiveness is looking farther out than that.

Then on top of that, I think, even though they might not admit it, but you're cheaper if you're dead than if you're alive according to CBO.

So does anyone have any strategies or ideas for how we can combat that? Because to the extent that some of the changes that we might want to see made require legislative change, legislation actually passed by Congress, we're going to have to deal with the Congressional Budget Office and its way of analyzing these things. So it's a perennial challenge, I think.

DR. McCABE: First, I'm going to toss that one to David, and then have you chime in, Marc, but my understanding at a very superficial level is that's one value of the cost-utility models because it does put a premium on survival.

DR. VEENSTRA: Yes, I think that sums it up pretty well. If you're doing a cost-utility analysis, you're looking at quality of life and life expectancy as your output. That's what you're producing. That's what we're all here in the business of, is improving people's lives and helping them to live longer.

So when you're doing that type of analysis, it works well, and it's not best to let everyone die, but if you are just looking purely at cost and if you don't have any way of assigning even a monetary, economic value to someone's life, then you're correct. You're always going to end up that it's cheapest for everyone to pass away.

That can be a serious challenge and I think the use of cost-utility analysis is pretty well entrenched in the academic community, and if there's a need to encourage the use of it, I think there are a lot of folks that would be willing to help out.

DR. McCABE: Marc?

DR. WILLIAMS: I think that a lot of the things we're talking about don't have that long a window. There is evidence emerging in the BRCA group that cost savings accrue to health plans who cover testing, predispositional testing, to women based on the

decisions that they make then to perhaps undergo either hormonally-based therapies, preventive therapies, or surgical preventive therapies, that the cost savings in a large group of insured actually accrues within one to two years. So we're not looking at a 10, 15, 20-year window.

I think also with some of the ability to detect susceptibilities to drug reactions, a couple that were mentioned today, and then the other one I would put on the table would be malignant hyperthermia, where we have the ability to identify about 80 percent of the individuals that are susceptible to malignant hyperthermia reactions to anesthetic agents and those can be easily avoided then.

The cost there would be immediately recognized as soon as that person either was going to be exposed to that drug or underwent that procedure because then we would be avoiding a medical catastrophe that would have attendant costs associated with it.

Again, I think some of the graphs that were presented by Dr. Veenstra clearly showed that at even relatively low prevalence levels, these can be identified and be very cost-effective. So I don't think, even when we're looking at chronic diseases, we're not necessarily looking at a 15 to 20-year payback on some of the investment.

DR. McCABE: Yes, David?

DR. FEIGAL: Is there any estimate in the genetic testing area or from any of the advocacy groups what percentage of that testing ends up being out of pocket for patients? I remember when the SACGT was meeting, there was some testimony presented. I remember one scenario where they had to pay $2,500 per family member per test, and it could only be run if they paid for the test because it wasn't covered.

We've got the figures in round numbers for drugs. Do we have the same thing for diagnostic tests?

DR. McCABE: Andrea?

DR. FERREIRA-GONZALEZ: Yes, I don't currently have those numbers and it may be a little difficult to get to those numbers because a portion of the way we track the reimbursement, like at a large academic center, you bill as a global billing, where the patient comes in, sees the physician, and there's radiology, pharmacy, and laboratory practices. So a bill is sent to the third-party payers, but also the division might choose to pay out of pocket the genetic test. So they will be assigned a different account and so forth. So it would be very difficult to track that information.

We can try to get that information for the committee for the future. I think it would be very interesting to see that.

DR. FEIGAL: Part of what makes this challenging is sort of the increasing practice that you don't have to go to the laboratory to get your test done because the samples can travel to central laboratories, and so there may not be a physician interaction and there may not be an institutional interaction. Some of the examples are actually from academic medical centers, where they might be providing a scarce test for people all over the country, and when you've got that kind of arrangement, I imagine it's more challenging to figure out the billing, but it would be interesting to sort of look at that dynamic.

DR. McCABE: Debra, you want to follow up on that? And then Marc.

DR. LEONARD: Well, as a laboratory director, that's hard to determine. My laboratory does get testing from across the country and even internationally, and we ask everyone outside of the University of Pennsylvania Health System to pay upfront for the test. So there's this trickle-down effect that we aren't going to eat the cost because the

reimbursement is so poor. So therefore, we ask for full payment of our charge, but then downstream, the patient has to work with their third-party payer or the health system has to bill or the health care provider or the genetic counselor, and then they get the poor reimbursement. So we actually prefer to do testing outside of the University of Pennsylvania than for our own patients because the reimbursement is close to 100 percent.

DR. McCABE: Marc, is your comment on this point?

DR. WILLIAMS: Yes, and I think the point that we don't want to miss here is that looking at it from the laboratory perspective backwards, in addition to the problems noted about that, it's going to miss the other side of the equation, which is those that chose not to undergo testing when they realize that it's going to be out of pocket.

As the person that sits down with the patient and works with the insurance companies and tries to get the payment for the testing upfront, I can say that we probably are successful, depending on the test, anywhere from -- well, anywhere from 0 to 100 percent, but for the common ones, the BRCA and the HNPCC, we probably bat about 400 or 500 in terms of getting third-party reimbursement, and then those other individuals are left either to pay out of pocket or we actually have established a fund for those that are really in dire financial need. We can actually subsidize testing in those individuals, thanks to a generous donation.

But it's going to have to be a two-pronged approach to try and get a handle on that because I think there really are a lot of people that would like to be tested, but choose not to be tested because of the out-of- pocket expense.

DR. McCABE: And certainly, that gets back to the stratification issue that Joan pointed out before.

Emily?

DR. WINN-DEEN: I guess I want to put the CMS guys on the hot seat for a second here because, despite all these presentations, I still don't get it.

If I have a new test and I come out with that, I can put all my stackable codes together and figure out how many PCR reactions and how many probes and what the Medicare default reimbursement might be, but if I had an excellent health economic argument, what I heard is that CMS still wouldn't change the reimbursement. They would only use that to determine if something would be reimbursed.

So it sounds to me like despite whatever value a test could bring to the overall health care system, that at least for the next five years until 2009 when lab fees are unfrozen, that we're stuck.

DR. McCABE: Don?

MR. THOMPSON: Sure. It's multiple parts to the question, but let me try to address it in pieces.

To the extent that this new technology or this new test could be broken down into existing CPT codes, you are correct that it would be frozen until 2009, and the only avenue that CMS has available to it, and we're not quite there yet, is what I spoke about inherent reasonableness, which is our ability to look at a fee and say this is inherently unreasonable and there is a rather long process in the law for changing that payment amount.

The reason that's a long process is they were more terrified about us reducing fees than they were increasing them, but it's the same process. The sword cuts both ways.

So to the extent we have a new technology covered by existing CPT codes,

we're a little bit handcuffed in our ability to change those payment amounts, though I did mention IR, inherent reasonableness, is in the future and one of our first candidates is the HIV/HCV viral loads. That's one avenue, but that is again kind of a brick-by-brick approach.

Now, to the extent that you have a new CPT code for this test or there's no way to add the component pieces in the existing codes or we require a new CPT code and that comes into play, now it goes through the CPT process and the code is approved, in that scenario, that's where kind of the 942(b) comes in, the ability that Congress said, well, publish some regulations on how you want to go about doing new lab tests.

Again, one might argue that the directions they gave in the statute would mean just take your current process and put it in regulations, but that's why we're going through notice and comment.

So it's kind of a little bit of a, like I said, window, a small ray of hope, if you will. To the extent that you get a new CPT code, there is some flexibility in there on how we might set the price.

So is that helpful? Probably not.

DR. WINN-DEEN: Yes. I guess I'm still concerned that you could have a test that has got a huge amount of economic value and CMS still would not recognize that economic value, no matter what your health economic argument would bring to bear.

DR. McCABE: Sean?

DR. TUNIS: Yes. You know, the fact that for the most part Medicare doesn't use cost-effectiveness or economic evaluations as part of either coverage or reimburse has been 20 years of intense lobbying by the medical device industry against that, and the reason for that obviously is they'd like to be able to charge high prices for things that don't create a lot of value, but the downside of it is that you can have very high-value things that you don't get fair prices for.

I think, and maybe this committee wants to take it on, that there is no sensible way to get good value out of health care resources, whether it's Medicare or elsewhere, without having the ability to do the kind of work that was discussed here today and make it influential in coverage and payment policy.

But it's not because -- you know, Congress put those prohibitions in place pretty much under pressure from industry lobbying efforts that have undermined several efforts to make cost-effectiveness a factor in reimbursement policy in Medicare.

DR. McCABE: Debra, a comment on this point?

DR. LEONARD: Yes, a question. Wouldn't Section 942(b) apply to the new alphanumeric modifiers? So with this whole alphanumeric modifier system that was proposed by the Genetic Testing Work Group that we could do something for genetic testing reimbursement?

MR. THOMPSON: That's one of the things we intend on seeking comment on in the new regulation on the 942(b), is when is new new? And that's an open issue.

DR. LEONARD: Because this is completely new.

MR. THOMPSON: Right. Understood.

DR. McCABE: Yes, Andrea?

DR. FERREIRA-GONZALEZ: But these new codes are going to modify existing CPT codes.

DR. LEONARD: Don't point that out. They're new.

(Laughter.)

DR. FERREIRA-GONZALEZ: They know that already.

DR. LEONARD: I know that.

DR. FERREIRA-GONZALEZ: But we still bring in new technology or new tests that have clinical necessity and will be effective in treating the patient, but even the modifiers, the only thing it's going to allow is for third-party payers to identify what they're paying for.

Now, the new CPT codes that are going to be coming down the pike, hopefully to address microarray technologies, et cetera, hopefully they will be put in a different pot and seek advice from laboratories, end users, and advice from community associations to see what is the level of reimbursement and so forth.

That's a statement and a question.

MR. THOMPSON: Again, not to be evasive, but I don't like to get in front of my chain of command in terms of the clearance process. We are going to go through notice and comment rulemaking in the issues you just brought up with the modifiers, and without question, the issue of the new CPT code, that does fall into kind of the new technology pot.

That's not to say that if you get new CPT code and we look at it and we see it as cross-walking in a straightforward manner to an existing CPT test, that we might not be in position where, again, we'd be somewhat handcuffed, but granted at least it's in the new code process. The modifier is a little more of an open issue, but at least if you get a new CPT code, it definitely runs through that process where we have a public meeting, we get input, and we decide gap filling versus cross-walk.

DR. McCABE: I just want to make a comment and point out something that was said by Sean, and that is that there might be some benefit to looking at cost-effectiveness for these tests, and also to remind everyone that coverage and reimbursement was in a Category 4, which suggests that it needs more discussion, and that we have both agency public representatives and representatives from private companies here and we've been told that the reason we have this system is because of lobbying by medical device companies, but in fact for testing we have those individuals represented on this committee.

So as we're thinking about our deliberations and how we are positioned to look at recommendations, it seems to me that we have a forum here with the appropriate people sitting around the table for pursuing these discussions.

Chris?

DR. HOOK: Thank you.

I want to just throw a question out to Dr. Veenstra. One of the issues that we're going to be talking about tomorrow is to pursue a bit further the question of pharmacogenomics on a larger scale, and I'm not aware, but I don't know if anyone has informally done the thought experiment along the line of if we look at the JAMA study from '98, 106,000 people per year dying from attributed drug reactions, of which only 5 to 10 percent were probably preventable because of clerical error or physician misprescription and so on.

If the country or if the FDA were to go to the effort of or have the law modified to require now submission for new drug approval require pharmacogenetic information be included, what's sort of the cost-benefit analysis that that might bring?

DR. VEENSTRA: That's a great question. From what I understand in swapping voicemails with Katherine Phillips, I think basically planning for doing a study like

that is underway right now. I think we'll be working with the FDA as well as some other folks in trying to get a general ball park idea of what that might look like.

It is going to be a bit of a thought experiment because we don't have a lot of these association studies, but just laying out the basic parameters, where do we end up? How many lives are saved in general? Is there any chance that it might make sense? So I think it's a great question and it's something we're going to try to look at.

DR. McCABE: Before we go to Joan, Sarah was just showing me on her Blackberry here one of her latest entries is "Gene Testing Families Risk Overheating Updated." Monday, March 1st, at 4:27 p.m., so extremely current, and it's by an AP medical writer, Lauren Neergaard, N-E-E-R-G-A-A-R-D, and basically about Uncle Joe waking up from minor surgery packed in ice, so it was the malignant hyperthermia, which not only has morbidity but also mortality still associated with it. We didn't scroll down to read the whole article. I'll leave that up to you tonight to catch it on CNN, but certainly very timely.

Joan?

DR. REEDE: Just a point because we had the other earlier discussions about population studies, and one of the concerns I have when we start talking about pharmacogenomics and these types of issues are assumptions that end up being made that the answers that you get from these studies are able to describe or explain variation that may also have, and most probably has, environmental or other factors involved, and real risk. I think here about some of the discussions that I have had with people who make assumptions that many of the health disparities and other things we see can be explained just on the basis of genetic variation.

I'm just concerned that as we go down this path of pharmacogenomics and we start looking at cost-benefit and we start getting into these fine numbers, that we leave out the environmental influences and just want to make sure that as a committee we don't fall sway to the idea that genetics by itself is going to answer these types of issues.

DR. McCABE: Emily, you want to comment on that, and then we'll go to the panel?

DR. WINN-DEEN: I just wanted to also encourage you while you're thinking about this thought experiment to think about the fact that the really severe ADRs, the ones that you would most like to prevent, are the ones where we'll never have enough statistical power, probably, to find out what the underlying genetic lesion, if it was there, was because you're never going to leave something on the market long enough for the right statistical number of people to die to do the study.

So it means that that adverse drug reaction benefit to genetics is not in the really severe, severe reactions. It's in the sort of moderate, like the hyperthermia kind of things, but things that induce people to die, I mean, we've seen how many drug withdrawals in the last five years because of unexplained deaths. I mean, it's not ethical to leave those kind of things on the market.

DR. VEENSTRA: That's another potential study where you're thinking about what's been the loss to society of having to pull those drugs off the market? All the money that was spent to develop them. They could benefit patients, but maybe because of genetic variation, we've had to pull them off the market. So I think that's a strong belief of mine is that most of the drugs that cause a lot of problems because of pharmacogenomics aren't on the market.

DR. WINN-DEEN: Yes. The question is just can you ever actually find out? It's not that I don't believe there might be a genetic source to that adverse drug reaction, but can you design a statistically valid multivariate study to actually find whatever the genetic lesion or combination of six or eight genetic lesions that cause those few individuals to have this very severe reaction? You know, it's a statistics problem.

DR. McCABE: It is influencing care. I think I've mentioned before at this committee the fact that we had a threat of a pharmacogenomics lawsuit at UCLA when a child was on an aminoglycoside, gentamicin, and failed the hearing screen when they were leaving the NICU, and the family threatened to sue us, having gone to the Internet and looked up aminoglycoside-induced hearing loss.

It turned out the child did not have the mitochondrial mutation, but I was speaking and actually presented this at a forum at UCLA recently, and the head of neonatology pointed out to me -- this was two years ago -- they had stopped using aminoglycosides as one of their first-line antibiotics and had gone to a much broader spectrum, cephlasporin, and now we're seeing the consequence of that that was predictable with a lot more Gram-negative-resistant organisms. So there are all kinds of consequences to these decisions that could be ameliorated by the appropriate testing.

Marc, did you have a comment?

DR. WILLIAMS: Yes. This is related to something that I maybe read between the lines appropriately or inappropriately about the comments that you were making, and I think it is an important issue because there are certainly a group of individuals that are looking at genetic variation with an agenda to say that, well, a lot of the disparities that we're seeing are really buried in this genomic variation, and of course then that also can sometimes get translated into other issues relating to race, ethnicity, and what have you.

I just wanted to let the committee know, if you're not already aware, that a group of population geneticists, particularly Dr. Len Jordy at the University of Utah, have been doing some really outstanding work looking at some genetic variation within certain disorders that we've recognized as occurring within a higher frequency with certain racial groups and have not really found that this is a race-specific variation, that this is actually much broader.

So I think that what's actually going to come out of the science as we begin to understand the variation more is that it's actually going to have less of an influence on the types of disparity, particularly racially and ethnically-based disparities, that have previously been looked at. But I think if this is work that you're not familiar with, it would certainly be reasonable to have a presentation on that.

DR. McCABE: Thank you.

Yes, Joan?

DR. REEDE: A follow-up to that. I think the important part here is also perception, and if you look at what the public perceives as what you're going to be able to do with genetic testing or pharmacogenomics, there's this sense by some of the public that this testing is going to tell you the difference based on race/ethnicity or deal with all of the health disparities, and there are many other variables that are there.

So I think there's a risk of going down a path that we've been down in the past that is not a healthy one for our country in terms of thinking that the science is going to be able to explain some things that it may not be able to explain.

DR. McCABE: Martin?

MR. DANNENFELSER: Just a clarification on two points for the folks from CMS. You talked about reimbursement and I guess through Medicare, it sounded like in your presentation, for the genetic testing. Is it only through Medicare or is there any kind of reimbursement through Medicaid for genetic testing?

That's one, and there will be a follow-up on that.

MR. THOMPSON: Sure. Yes, but in the Medicaid program, again, that's kind of a decentralized program, so individual states are making individual terminations. Some of them look at our fee schedule amounts when they're setting those rates. As I think some of the earlier slides showed, they look at our kind of national limitation amounts in setting those. That's not something we control at CMS. That's kind of more at the individual state level, although many of them do mirror the clinical lab fee schedule.

MR. DANNENFELSER: But they have the ability or allow the use, if you will, for a broad range of genetic testing at the state level?

MR. THOMPSON: I'm speaking from a payment perspective. I'll leave it to Sean from a coverage perspective.

DR. TUNIS: It's pretty much the same situation regarding the medical necessity issue in that it's a decentralized decisionmaking subject to state laws, state policymaking, sometimes more generous than the Medicare national policy. Sometimes they look to the Medicare national policies or they'll look to some of the local policies within the state, but there are no mandates from the Central CMS on what the state Medicaid programs would cover.

MR. DANNENFELSER: And with respect to Medicare, are there any eligible, is it people, in terms of Medicare who would be seeking reimbursement for prenatal genetic testing or is it other kinds of genetic testing?

DR. TUNIS: It's possible under the -- you know, since it's elderly, disabled, and end-stage renal disease, presumably within the disabled category there are some folks who would be seeking prenatal testing. It's just not particularly common.

MR. DANNENFELSER: Thank you.

DR. McCABE: Debra, and then Brad.

DR. LEONARD: Could I ask for clarification? From the private insurance perspective, it's said that you had to have the test be FDA-approved or cleared in order to be paid, and then you guys said that you would also consider laboratory-developed tests for payment. So can you clarify whether tests are only paid for if they're FDA-cleared?

DR. McCABE: Michele?

DR. SCHOONMAKER: I'm sorry. That was FDA-approved or those that conform to the CLIA requirements. So if they're performed in a CLIA-certified laboratory, then that would be the regulatory approval that would be pertinent.

DR. LEONARD: So FDA approval is not required.

DR. SCHOONMAKER: Not for tests. Right.

DR. LEONARD: As long as they're performed in a CLIA-certified laboratory.

DR. SCHOONMAKER: Right.

DR. McCABE: Marc?

DR. WILLIAMS: It ain't that simple. The problem is that each private insurer can make their own decision and they can decide that they will only pay for FDA-

approved laboratory tests.

So while many insurers will look to CMS regarding coverage and payment, they're certainly not obliged to follow that, and there are no other national things that they need to follow, and so basically they're all on their own, which leads to the frustrating situation that I know you've experienced, because I know we've experienced it, which is you have to go insurer by insurer and basically fight that battle with every single one of them. There's no shortcut to be able to do that.

Again, the FDA approval has to do with a situation where you have to have something that says somebody's looked at this, and that's sort of been the standard, but it just doesn't fit the paradigm of these individually-developed tests.

So we've actually referred insurers to the American College of Medical Genetics testing, voluntary testing, and saying this is really the standard that the industry is using and so this is really what you should be asking the laboratories about because the FDA, at this point at least, does not have the full jurisdiction over these.

DR. LEONARD: Well, with the coding system the way it is, also I don't know how payers know, since all genetic tests use the same codes, what would be FDA-approved and what wouldn't and what would be laboratory-developed and what the testing was even for.

DR. WILLIAMS: You've got that right.

DR. McCABE: Brad?

MR. MARGUS: Just in response to Joan, I wanted to mention that my company is involved in doing massive association studies with large numbers of cases and controls and what we think are sufficiently powered enough to find things that are real, and while a lot of scientists publish those things all the time, I think most geneticists are now arriving at the conclusion that you really need to replicate in other populations and other environments. So there is pretty much an effort in place to not jump to conclusions that you definitely know it's genetic until you actually can prove it in different environments and replicate it. So you should feel better about that.

I really appreciated the tutorial today for all this. I guess I have a question about if you came up with a new association, an anomalous association that has tremendous value, even though I understand CMS may not care, and you go about making a CPT for it, my first question is how long does it typically take to get a new CPT?

Then the second question is this subject of cross-walking and gap filling. So if the new test, the content for that test, the loci that you're interrogating are new but the approach is still a PCR-based assay that just has different primers or something like that, do you then conclude that it's cross-walking and you actually can easily find and you already have an established ancient rate that you apply to it or does the fact that it's a novel test give it a chance for a new rate?

DR. McCABE: Don?

MR. THOMPSON: Sure. The approach that we take, it's on a case-by-case basis. So during that kind of public meeting process, we kind of rely on the industry and clinicians. Any member of the public can come in and give us recommendations, and based on that information we have, we kind of huddle with our clinical staff and our clinical folks and our contractor staff, and we look at that case by case. So there's no blanket rule for when you cross-walk and when you gap fill. It would be dependent on the individual situation and the

public input.

Then your first question, I'm sorry, was?

MR. MARGUS: How long for a CPT typically?

MR. THOMPSON: Rapid is not a word that comes to mind.

(Laughter.)

MR. THOMPSON: It can be a multi-year process. Unfortunately, or fortunately, depending on how you want to look at it, we have kind of relied on the AMA and they have kind of formalized CPT process that they go through. It's a deliberative process, so anybody can request a code, but it is, again, not rapid. It can take a year or two years, and sometimes they can table the code and come back and they may seek additional information. So it can be rather involved.

MR. MARGUS: So what repercussions or impact do you think that has, the time it takes? Does it hurt things or not too much?

MR. THOMPSON: A loaded question, but if you're asking does the fact that you can't get a code or you don't have a code in a rapid fashion for a new technology have an impact on access, going back again to some of the earlier presentations, there are kind of miscellaneous codes that you can go under, but the problem is there's a certain administrative burden associated with going down that road. If you have your own code, it's in the system. It's a much more rapid administrative fashion. You can have a public discourse on the price at a national level, whereas when you go with some of the more miscellaneous codes, you may be able to get access, but there might be an administrative burden associated with that.

I'm sure, given the reaction from both sides, I think, that we have some thoughts on the CPT process.

DR. McCABE: If this is a comment on this, and then Joan and Hunt, and then we're going to wrap up.

Andrea?

DR. FERREIRA-GONZALEZ: I want to bring an additional issue. It seems to me that a way to look at changes in the reimbursement for Medicare is through the inherent reasonableness. My question is when can we expect this process to take effect and maybe if there is anything that this committee can do to provide reinforcement to the Secretary to move this process faster?

MR. THOMPSON: Sure. As I mentioned, we were under a congressional moratorium with respect to inherent reasonableness for many years. Again, I think out of fear that we were going to reduce prices. That moratorium has recently been lifted and in the wake of that, we are now struggling with coming up with instructions for how that process is going to work because we want to ensure that we have a kind of fair and equitable process because it will be used in both directions. You know, prices can come down and prices can go up under it, and it's going to be the same process either way and we make sure, given the additional congressional input that we received on inherent reasonableness, that we follow that. So our hope is that this year that we will be able to issue those final instructions on inherent reasonableness and then begin the process for changing those payment amounts.

Again, both up and down, and this is kind of focused on genetic testing, but in kind of looking philosophically at the clinical lab fee schedule globally, we have a number of tests that one could argue, and some have argued, are in fact overvalued. For example, if one looks at urinalysis CBC, some of which are kind of the bread and butter of some labs, and even

some, I would argue, at VCU, to the extent we're overpaying for those and we decide to go after some of those high-volume tests, which may represent 50 to 60 percent of the clinical lab fee schedule, the hue and cry if we don't get the process right will be loud. So we've got to make sure we get it right for both the increases and the decreases.

DR. McCABE: And a follow-up on that, is there anything this committee could do?

MR. THOMPSON: At this point, I can't tell you the internal pressure to get those turned around, so I can't imagine adding another voice would cause the process to be any more rapid, but again, the committee may feel otherwise.

DR. LEONARD: Can I clarify something on Brad's comment?

DR. McCABE: Yes.

DR. LEONARD: Which is that the understanding is that you do not add new CPT codes for every single genetic locus. Otherwise, we could end up with 25,000 times however many mutations there are per gene.

MR. MARGUS: So it has to be a new technology for even analyzing.

DR. LEONARD: It would be technology-based. Right now, a laboratory implements a new test that classically would have gotten a new CPT code using these -- isolate DNA, do a PCR, run a gel codes, and so we don't go through the new CPT code process.

MR. MARGUS: But if it were just a new set of SNPs tomorrow for looking at something else, they already have a CPT for it, they'll apply that rate, and then it's five bucks whether it's worth $50,000 in savings --

DR. LEONARD: Yes. You've got it. So all the new genetic tests that are going to be coming out are constrained by this CPT coding reimbursement process.

MR. MARGUS: Everybody just closes their eyes and says wait until 2009.

DR. LEONARD: And it's not clear that in 2009 it will be freed up. It could still remain frozen, right?

MR. MARGUS: So one question is, Ms. Lab Lady, aren't there any drugs, aren't there any tests --

PARTICIPANT: She's Dr. Lab Lady.

(Laughter.)

MR. MARGUS: Sorry. Dr. Lab Lady, aren't there any tests over the last five years or whatever since the prices were locked in where a technology has helped to reduce the cost and now you're making buckets?

DR. LEONARD: No. I can emphatically answer that no. There probably are technologies out there that would reduce costs, but because of the health care finance system, we have no capital equipment budget, so we can't buy robots for automated nucleic acid extractions and 96-capillary electrophoresis instruments and those kinds of things. So technologies may be out there, but the hospital systems in academic health centers where this testing is performed generally don't have capital equipment budgets to be able to be proactive and think about reducing costs in these ways.

DR. McCABE: For example, when they got the capillary system in our sequencing lab, then they were able to decommission the old gel-based systems. We gave the one that we had contributed years ago to the sequencing corps, we gave that to our orphan disease testing lab, so they could start doing sequencing. So they're using ancient technology, but it's because it was free, and that's the nature of the capital improvements in our academic

health centers.

Joan, I'll give you the last word for the day.

DR. REEDE: Thank you.

Not withstanding the research and the work that Marc is mentioning is being done or the work that Brad is mentioning with regard to his company, I think that we would be remiss if we did not also take into consideration the fact that not everybody is of the same opinion or sway that we are. So if you look in the literature, you can see articles written by physicians talking about "I am a racially profiling physician," using our genetic information as their justification for racial profiling.

So I think, as we talk about our prioritization and we talk about issues such as education and we talk about issues such as making the public aware and moving forward, that we have to be cognizant of the fact that not everyone is going to use this information in a way that we may think is appropriate.

DR. McCABE: Thank you very much. That's a very good way to end the evening. Thank you everyone for putting in a long day today.

Let me remind you that you do not fill out your second straw vote ballot tonight. We will hold that for tomorrow.

I want to thank our presenters again for your time and your participation. It was extremely helpful.

I want to remind those who are joining us for dinner -- committee members, ex officios, presenters -- please meet in the lobby at 6:40 p.m. and we will then take cabs to the restaurant. Our reservation is at 7:00 p.m.

Just to remind you, because we have two busy days, we are starting earlier than is our custom tomorrow. So we will be starting at 8:00 a.m. tomorrow, and that will be with public comment, so I would ask all of the committee members to be here to be respectful of the public comment session.

Thank you.

(Whereupon, at 5:35 p.m., the meeting was recessed, to reconvene at 8:00 a.m. on Tuesday, March 2, 2004.)