U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

Twelfth Meeting

Monday,
March 26, 2007

Founders Room
Inn and Conference Center
University of Maryland
3501 University Boulevard East
Adelphi, 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 (8:04 a.m.)

DR. TUCKSON: Good morning.

PARTICIPANTS: Good morning.

DR. TUCKSON: We have two very intense days.

Let me thank everybody for being here and all the members who are in the audience. We appreciate your involvement, everyone that's looking in and following this on the Web. It's always good to get these emergency emails on my BlackBerry by somebody out there who says, wait a minute, what about this? So we know that there are people who are extremely attentive.

This is the 12th meeting of the Secretary's Advisory Committee on Genetics, Health, and Society. The public was made aware of the meeting through notices in the Federal Register, as well as announcements on the SACGHS website and through our listserv.

I want to welcome all of you again and for everyone's interest in the work.

By the way, any members of the public that would like to testify, we urge you to sign up at the registration desk.

Our committee is a little larger today thanks to the Secretary's appointment of a new member. We are very pleased to introduce Dr. Marc Williams. How are you doing, Marc?

DR. WILLIAMS: Fine, thank you.

DR. TUCKSON: Great. Marc, you happen to know yourself what the rest of us may not know that you are a board certified clinical geneticist.

(Laughter.)

DR. TUCKSON: And if you didn't know, you're the Director of the Intermountain Healthcare Clinical Genetics Institute in Salt Lake City, Utah. In addition to your clinical work, you are an expert on the role of medical genetics and health care delivery. You chair the Committee on the Economics of Genetic Services for the American College of Medical Genetics, and you serve on the Subcommittee of the Health Care Systems of the Section on Genetics of the American Academy of Pediatrics. So all those things, including your editorship in chief of the Manual on Reimbursement for Medical Genetic Services, really makes you and your background extremely important to this committee, and we really thank you.

DR. WILLIAMS: Thank you.

DR. TUCKSON: Terrific.

I also want to welcome back two of Secretary Leavitt's key staff: Sheila Walcoff, Counselor to the Secretary for Science and Public Health; and our friend, Dr. Greg Downing, Program Director of the Secretary's Personalized Health Care Initiative.

You will recall that Sheila met with us in November to tell us about Secretary Leavitt's commitment to improving the safety, quality, and effectiveness of health care by leveraging advances in genomics and health information technology. She told us that accelerating personalized health care is one of the Secretary's top 10 goals and that he felt an urgency to that.

Well, I want to tell you that as of Friday, I saw that urgency in action. The Secretary allowed me to represent you at two extraordinary events, and I will tell you -- and you will hear more about those from Sheila in a moment -- that clearly this is a Secretary who is inspired, who really gets it, who understands this is a historical moment at being able to merge together the benefits of science and health information technology to advance better health care for each individual.

I also want to say that he gets it as far as this committee. In any of the history that I have participated in in this committee or the prior one, I have never seen this committee treated at the level of respect, not to denigrate any other past -- so this is just an extraordinary added attraction in terms of how this Secretary treats this committee. And I think he's listening to us. So the good news is that

you're really respected. The bad news is you're going to have to work a lot harder. So we appreciate that. We'll be hearing much more.

Let me just say a quick word about Sheila. And where's Greg. Greg Downing and Sheila are just terrific people. Greg has been behind the scenes just doing so much work for and with us. We have long wanted somebody to represent and carry our issues forward, and we always have wanted a good ear and someone at the level of Sheila. So I just want to say to you publicly that we are extremely pleased by what we are seeing, and it really makes the work that we're putting in seem so much more real and relevant.

Following the comments from Sheila in a few moments, if I ever get done, we'll hear from Robert Kolodner, whom I'm really interested in seeing, the Interim National Coordinator for the Office of Health Information Technology, and Ms. Jodi Daniel, their chief of policy and research, about the role of health information technology and how this will move this agenda forward. I will tell you again that Robert is also just terrific, and I've had a lot of time to work with him in the days past.

Welcome to all of you and thank you very much for coming.

Well, our committee has a very broad charter and mandate. Within that broad charter and scope, our agenda has been guided by a strategic plan, and I want to put that out. Everyone in this committee -- and Marc, you'll catch on -- knows that I will go through a laborious effort at the beginning of every meeting to review this strategy and agenda. I think it is very important that at the end of the day, that we are able to say that we have kept our commitments, that we are moving our committees and our work forward in a logical way designed to produce results. It's too much work to bring you all in here and just have lovely conversations that go up in the ether somewhere.

So let me just remind you quickly of where we are, and you'll see it on the slides. We've identified 12 issues that we thought warranted our attention or in-depth analysis. The topics at the top, access, public awareness, and genetic exceptionalism, are cross-cutting issues that affect all of them. So they are always addressed in our work. The priorities on the left side are checked because we have produced reports and our recommendations on those issues. The priorities on the right are ones that we are currently focusing our analytical efforts on.

As I rip through these quickly, I want you to keep in mind for preparing you for tomorrow afternoon. We're going to relook at these priorities and our status. I want the committee to feel comfortable that there's not a sin of omission or commission up here on this agenda. If you feel that something else is emerging that we should be attending to, that something here is less important than something else, we should be revisiting that to make sure that we are maximally relevant to the events of our times. So I want you to really keep this close in mind.

Genetic discrimination we made as our highest priority. Over the last four years, we've written a number of letters to the Secretary championing the enactment of federal legislation. In 2005, we provided a legal analysis of the adequacy of current law, a compendium of public comments the size of a phone book, and we gave a DVD that documented the public's very real concerns and fears and really compelling public testimonies in front of this committee. We've kept a close watch on congressional developments at every one of our meetings, and in a small way, we have, within the limits of our appropriateness of a committee such as this, tried to bring folk together for common conversation to resolve differences of opinion.

We are thrilled to see how much progress is being made in the current Congress, and we will be looking forward this morning to an update from the HHS Deputy Assistant Secretary for Legislation and several key congressional staff on what's going on with the new GINA, as it's called, bill. So we have great promise for GINA, and I'll leave it to them to update.

In 2004, we made recommendations to the Secretary about the importance of genetic

education and training of health professionals and how it should be enhanced. We know that this is largely a public sector responsibility, but government does have a role to play, and we asked the questions: where do genetics education and training stand today; are we in better shape today than three years ago? Well, tomorrow we'll discuss the strategic plan that is being developed and we'll revisit our recommendations in light of this issue.

I want to let you know that there are some developments. The CDC is planning a major initiative called Genetics for Early Disease Detection and Intervention. Like everything, it has an acronym, GEDDI, as in GEDDI knights. I don't know. It sounds pretty cool. It will educate the public and providers about genetically based disorders, whose early detection can lead to interventions that can improve outcomes.

We know too from our last meeting that the CDC/NIH CETT Project, the Collaboration, Education, and Test Translation Project, is working to enhance to communications in genetic testing both between providers and patients and providers and the testing laboratories.

The American Nursing Association to its credit, the International Society of Nurses in Genetics, ISONG, and other nursing groups published an excellent set or core competencies for the nursing community.

The well-respected NCHPEG, the National Coalition for Health Professional Education in Genetics, has continued to advance its hard work. Its latest targets have reached speech language pathologists and audiologists, and new programs for physician assistants and dieticians are on the horizon. They're also developing a database that will deliver concise, clinically relevant genetics information to nongenetics providers at the point of care and are working with the Personalized Medicine Coalition and Feinstein-Keene Healthcare to create a program on pharmacogenomics for health care providers. So that is important.

So we will see whether or not you are comfortable with these things and whether we want to move forward any further on revisiting this important topic.

In 2006, we transmitted a report and recommendation to the Secretary on coverage and reimbursement for genetic tests and services. We highlighted the problems in the system that we thought affected patient access, and we identified nine steps that could be taken to overcome the barriers. These recommendations cover a range of topics, including evidence-based coverage decisionmaking, Medicare coverage of preventive services, adequacy of CPT codes for genetic tests and services, billing by nonphysician genetic counselors, and genetics education for health providers.

Cindy Berry and I had the opportunity in June to brief then-CMS Administrator Mark McClellan and his leadership on the coverage and reimbursement issue. It was a positive meeting, and they expressed a strong interest in the report's recommendations.

We're going to turn to Jim Rollins now -- Jim Rollins isn't here yet. So you're going to hear later from Jim Rollins on an update on where things stand in CMS concerning activity on these recommendations. Let me again say that Mark McClellan was just terrific, and his leaving out does not mean, though, that this just dropped so that there are activities moving forward at CMS and we are well aware of that. So we'll come back at some point and hear from Jim. So whenever that happens, the key emphasis in my comments to you is we have been attentive to making sure that Cindy and I did not just have a nice meeting. So that's the key thing, that we are moving forward.

In '05 and ' 06, we wrote letters to the Secretary on direct-to-consumer marketing of genetic tests. Our efforts in this area led to enhanced collaboration between FDA, CDC, CMS, and NIH, and the Federal Trade Commission. In '06, the FTC issued a consumer alert to warn consumers about using at-home genetic tests that have not been evaluated and to be wary of the claims made by the companies marketing these tests. The alert is a product of interagency collaboration and it is a

tremendous accomplishment in that respect, and we commend HHS for its leadership in moving forward in this regard.

But what has been the benefit of the alert in terms of public health? Has it helped? How many people did it reach? Well, I want to thank Matt Daynard, our ex officio, for providing us with some data on how widely the alert has been disseminated. The Web hits on the alert on the FTC website total 6,461 so far. Almost 12,000 copies of the printed brochures have been distributed, which means the total distribution for both print and Web is around 18,000. In addition, the consumer alert has been widely covered in the media, stories in the Wall Street Journal, the New York Times, NPR, U.S. News and World Report, Contra Costa Times, American Healthline, the FDA News, and Medical Device Week. So it is out there and moving forward. If anyone can think of other ways that that alert ought to be disseminated, please let us know.

I'm extremely pleased to say that we completed our report on the policy issues associated with undertaking a new large U.S. population cohort study of genes, the environment, and disease. It was transmitted to the Secretary earlier this month. Copies of the printed version are now publicly available. You each have a copy in your table folder, and copies are available at the registration desk for the public or you can also download the PDF version on our website. I actually handed a copy to the Secretary in a one-on-one meeting in his office Friday. So I know he absolutely has it and we'll quiz him on it later.

(Laughter.)

DR. TUCKSON: On behalf of the entire committee, I want to extend our thanks to Hunt Willard, who will be attending tomorrow's session, and to the Task Force on Large Pop Studies for guiding this effort through a long and difficult fact-finding and consultative process. We are indebted to the many experts who helped us identify the policy issues and broaden our understanding of the challenges and potential benefits of such a study. Our report was also greatly enhanced by the public comment process we carried out last summer.

Let me acknowledge the important role of staff in bringing this report to fruition, particularly Yvette Seger, Betsy Earp, Katie Kohler, and in the early stages our friend Amanda Sarata.

Our draft report and recommendations on pharmacogenomics has also progressed. It was released for public comment this past Friday to coincide with the Secretary's announcement of his Personalized Health Care Initiative at the National Press Club. I want to thank and appreciate our task force, led by Kevin FitzGerald -- Kevin, thank you -- as well as the Office of the Assistant Secretary for Planning and Evaluation, the Lewin Group, and the staff for working so hard to get the draft report ready for release in time. It was a race to the finish, but you couldn't possibly miss the opportunity that the Secretary is going to announce this whole thing, and to be able to have it at his press conference on Friday was pretty terrific. I also handed him a copy of this report personally. I know he has it. We will quiz him later.

We're also making progress on our study on the impact of gene patents and licensing practices on patient access to genetic technologies. You'll recall that at our meeting in November, we approved the study scope and approach developed by the Task Force on Gene Patents and Licensing Practices. Tomorrow our friend, Jim Evans, chair of our study task force, will provide us with some foundational knowledge and prepare us as they move forward with the study. We'll learn about the basics of the patenting system and how licensing of intellectual property works in federal and private sector agreements, and we'll have an in-depth presentation on patent policy issues and developments. We'll be updated on the progress of our study by both Jim and Dr. Robert Cook-Deegan from Duke, who is working closely with us on the information-gathering component of the study.

This slide illustrates, by the way, the structure of our study and the components being

carried out by the Duke group. We'll revisit this later in the meeting.

Jim will also be holding -- an announcement, by the way -- a task force meeting tonight. There are no basketball games.

(Laughter.)

DR. TUCKSON: -- with Bob and his collaborators. Committee members who wish to attend, those of you who really are looking for a fun thing to do, should let Jim and Sarah know. We'll be making provisions for overflow seating.

(Laughter.)

DR. TUCKSON: SACGHS has had extensive discussion about the oversight of genetic tests at our last meeting. We heard that CMS will not be moving forward with the notice of proposed rulemaking on a genetic testing specialty under CLIA. After several presentations and much discussion, I think it is fair to say that the committee was left with many questions about the adequacy of the federal oversight framework for genetic tests. Therefore, we decided to engage in further fact-finding at this meeting.

We have since learned that HHS formed an internal working group to examine the roles of federal agencies for both analytical and clinical validity and to determine where problems and gaps lie within the federal government's oversight. This group will be keeping SACGHS apprised of their findings. In a few moments, Sheila will speak to us about a specific charge from the Secretary's office to us related to this.

I will just say this once again. And I don't want to embarrass Sheila or Greg, but I have to say it was very encouraging to me that there's no question that each of you and I personally, at the end of the last meeting, were confused and we were concerned. The responsiveness by HHS and the Secretary's office to that anxiety was palpable. They are on top of their game, and I am personally convinced that this issue is a high priority. I've had several meetings with them, and I will tell you that I understand that they're taking this seriously. So I just want to say to you that while there was a lot of anxiety among the committee at the last meeting, I can at least say to you that those anxieties are being attended to in a professional and responsible manner, and we'll hear more about that as we go forward.

Well tomorrow, finally, we'll be considering whether to take on two new topics, one proposed by our colleague, Steve Teutsch, on the economic consequences of genomic innovations, and another proposed by our ex officios from AHRQ, our good friend, Gurvaneet, and this dude Muin on the evaluation of real-world outcomes of gene-based applications. So we look forward to your terrific ideas. There won't be any time for it, but we'll be happy to have them.

(Laughter.)

DR. TUCKSON: Before we adjourn, we will also have time to discuss whether we need to start developing a new long-range plan. Depending on your decision about the two study proposals and also the oversight issue, we may have to outline new stuff. But as we do this, I think it's useful to keep in mind that as long as it took me to rush through and be out of breath to read all of that, it's important that we have done enough to have to read all of that and rush through it, and it would take that much time. You've been a busy committee, and I hope that when you check off your little form around effectiveness in your annual survey, which is in your packets, that you will be able to grade yourselves pretty highly by saying that you guys don't fool around. All in all, I think we can feel fairly good about what we have accomplished.

Before we go on with the meeting, I want to pause for a moment -- and I will slow down for this -- and acknowledge Joseph Hackett, who died last month. Dr. Hackett participated in a number of our meetings and task forces on behalf of Steve Gutman and the FDA. He was an extraordinary civil servant, dedicating 30 years of his life to carrying out the important mission of the

FDA. He was an expert in methods standards and in in vitro diagnostic devices and had many achievements during his long career. He was one of the first scientists at the agency to realize how important genomic and pharmacogenomic testing would become, and he fostered some of the first interactions FDA had with industry on these important topics. These gatherings, I'm told, were affectionately called the Hackett Staff College, undoubtedly a reflection of his appreciation of an openness to new ideas and his dedication to mentoring.

Steve, I know Joe was a valued colleague and friend and that his passing has been a profound professional, as well as personal, loss for you and your colleagues. On behalf of the entire committee, please accept our condolences. Thank you.

Well, since our last meeting, there have been some staff changes. Tara Hurd joined the team in January to help with administrative tasks. Amita Mehrotra took another job, and we want to thank Amita for everything that she's done. A search is underway for subject matter experts to support the committee's analytical work.

And whoever is responsible for the Reedster bunny joke --

(Laughter.)

DR. TUCKSON: -- we'll be speaking to you at performance appraisal review time.

(Laughter.)

DR. TUCKSON: And finally, some housekeeping matters related to lunch and dinner. To save time at lunch, I want to encourage the committee members to order lunch from the hotel menu. So please fill out the form in front of you, I am told, before 9:30, or else Abbe Smith will hit you in the back of the head.

Also, because of the special task force meeting tonight, the full committee will not be gathering for dinner. There will be a heck of party in room 309. Those of you who have already signed up for the task force meeting and prepaid for dinner will have a dinner buffet during the meeting.

Sarah, time for the official ethics, "scare you to death" comments.

MS. CARR: Right. Conflicts of interest. 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. While we waive conflicts of interest for general matters because we believe your ability to be objective will not be affected by these interests, we also rely to a great degree on you to be attentive during our meetings to the possibility that an issue will arise that could affect or appear to affect your interests in a specific way.

In addition, we've 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 you to recuse yourself from the discussion and leave the room.

I also want to remind you about lobbying. You're special government employees and you're prohibited from lobbying and, thus, we may not lobby, not as individuals or as a committee. If you lobby in your professional capacity or as a private citizen, it's important that you keep that activity separate from our activities.

Just keep in mind as well, as Reed has, that SACGHS is advisory to the Secretary of Health and Human Services. We do not advise the Congress.

And I thank you, as I've always thanked you, for being so attentive, as I know you are, to these rules.

DR. TUCKSON: Just remember to go home and tell your families that you are "special."

(Laughter.)

DR. TUCKSON: If you note by your clock, it is actually 8:29. I have gotten through that a minute early, and this is the standard that we want to keep for the rest of the meeting.

(Applause.)

DR. TUCKSON: Although I told Sheila she can have as much time as she wants because she really is special. So let me turn now to Sheila Walcoff, who is here representing the Office of the Secretary. She is the Counselor for Science and Public Health of the Office of the Secretary and an extremely important person.

MS. WALCOFF: Well, thank you, Reed, and I'm beginning to wonder if today is "International Complimentary Day." I think we had that a couple weeks ago in our office, and it was a lot of fun.

But I do appreciate the opportunity to return to the SACGHS to update the committee on the Department's work on accelerating personalized health care.

And I will say I did, right away, notice the Reedster bunny. I admire Reed's energy so much, and while that's not consistent with our prevention initiative --

(Laughter.)

MS. WALCOFF: -- it does make me feel like whoever is not here is probably going to suffer the consequences of the bunny sometime later on today.

I have a few slides that I think I'd like to outline.

To reiterate what Reed said a few moments ago, Secretary Leavitt on Friday outlined to the Personalized Medicine Coalition our Personalized Health Care Initiative, and I would like to provide a brief overview of his remarks and discuss the steps that are already underway to develop this important information, as well as steps he's taking to build the foundation for personalized health care and ensure that gene-based medical data and health information technology are used appropriately.

About a year ago, Secretary Leavitt defined 10 priorities on which he intended to spend a significant portion of his personal time and leadership, and those are listed out there for you. As you can see, personalized health care -- we've always put it at the top of his top 10 list, but it's definitely on his top 10.

The Secretary understands that advances in medicine, biomedical science, and technology present opportunities for enabling health care practices to be increasingly patient-specific by taking into account individual differences in health states, disease processes, and outcomes from interventions. The desired outcome is improving effectiveness and safety of medical practices and, as he noted a number of times on Friday, increased value and transparency for patients.

Up here you'll see the Secretary's visions, and these are really the Secretary's words. Personalized health care describes approaches applied across the health care enterprise that place a high value on individual, consumer-focused health by using modern tools, technologies, and information to improve safety and effectiveness. The Secretary often notes that we have a health care sector in the United States, not a health care system, and I know you'll hear later from Dr. Kolodner, and that's one of the key things that the American Health Information Community has been focused on as well.

Our initiative emphasizes a health care system strategy which incorporates new methods of genetic analyses to better manage a patient's disease or predisposition towards a disease and facilitates the discovery and clinical testing of new products. Ultimately, it's about getting the right treatment or preventative approach to the right patient at the right time every time.

Some of our long-term goals -- and the Secretary looks at this as both a long-term vision, the "project of our generation" we sometimes refer to it, and also has very specific short-term goals because he understands -- and I believe we have 666 days left with the Secretary at the wheel of HHS, and we all have countdown clocks. I mentioned them at the last meeting. And we are very aware

of the limited time we have to make a very significant difference in accelerating personalized health care and building the foundation for moving forward.

So I'll just talk a little bit about some of our long-term objectives over the next 5 or 10 years. They are to promote connectivity through a national system of health care information networks; assess the need for new policies, technologies, and oversight approaches; develop incentives across the health care system to use genetic information; foster new business models for the pharmaceutical and diagnostic industries; encourage consumer participation in medical decisionmaking, health care management, and prevention through new information-based tools; consulting support and incentives; and establish real-time decision support for disease management strategies using health information technology systems.

Some of the short-term goals, which I'm going to go into in a little greater depth this morning, are to present the AHIC with recommendations for what we are calling a version 1.0 of genomic medical test and family medical history data adoption for electronic health records. We're also looking at developing policies and programs to strengthen consumer and health care provider trust in parallel with infrastructure and technical capacity development; encouraging development of validated clinical genomic testing capabilities, as Reed mentioned also in his earlier remark; and to establish networks of interactive data sources.

You'll see on the slide a diagram which we use pretty consistently to describe the overall vision that we have, and I think this pyramid really captures where we are. At the base is health information technology and knowledge development because underpinning this initiative is the confluence of two powerful global forces that will shape consumer health-based care: information technology and knowledge management. So you see that at the foundation. The full potential of these forces cannot be realized unless the electronic systems, clinical databases, and knowledge repositories currently under development are based on a common set of definitions and standards.

Next, moving up the pyramid, is intervention development and review. There's an increasing need for and value placed on integrated data sets and higher quality information about efficacy and safety outcomes. Using integrated databases, the ability to assimilate and relate experiences is enabling incredible predictive power for outcomes in disease management. As technological capabilities develop across the health care system, better information based on individual differences will aid in future medical product evaluation and postmarketing assessments of safety and efficacy. An expanded set of health measurement tools will foster research and development for conditions where there are currently few successful health interventions or preventive approaches.

Finally, translation into clinical practice. The key players in this transformation are health care providers. With new tools, doctors will play new roles. Understanding the unique aspects of each of us as individuals in health care management requires continued advancement in biomedical research. This is particularly evident in the need for better bridges between research and health care delivery. At this time, we lack the infrastructure and analytical strategies for data management and knowledge development across biomedical research and health delivery enterprises. Barriers exist to standardize formats that can enable information exchange among willing partners in our health care, but we are hoping to create a health care system. We envision a continuum of transformation that builds on knowledge management to support the integration of discovery, development, and delivery in the health care enterprise and paves the way for a more modern doctor-patient relationship where value for the patient is the ultimate objective.

Basically we describe the Secretary's role in this initiative as being two parallel tracks moving along, hopefully, very quickly and together: technology development and the appropriate policies to support that technology.

So up here you'll see an outline of the first set of goals we have, and those are our technology goals, which include establishing the foundation for a networking partnership to enable researchers to search research and clinical data in almost a Google-like search fashion.

If any of you have taken a break from reading the extensive materials that your committee puts together, you'll look in that small document, the President's FY '08 budget, and note that it does include $15 million for the Personalized Health Care Initiative at the Department to begin building and seeding this distributive network which will ultimately link both genomic and clinical data to add efficiencies to therapy development, identify clinical best practices, and provide a better method of tracing adverse events. So we're right at the starting line for that and we're excited about having that money, and that is actually going to be coordinated through Dr. Clancy's office over at AHRQ.

Also, as I noted earlier and I know Dr. Kolodner will give you a much greater perspective on, part of this technology track includes establishing standards for including genomic health information and personal family history and electronic health records. Last year, the AHIC established a special working group for personalized health care to advise the AHIC on these issues.

Our second track is to support the appropriate use of genetic information. Because genomic information is immutable and we know that the American public is concerned about issues of privacy -- it's definitely in the news right now, as well, with the Genetic Information Nondiscrimination Act. But people fear discrimination in health insurance, employment, even public attitude based on the disclosure of their genetic information.

The Secretary has announced a number of times that he supports the passage of legislation to prohibit discrimination in employment and insurance. Just before the Secretary stepped to the podium on Friday, we received word that the GINA bill had successfully been marked up in Energy and Commerce and is, hopefully, headed very soon to the House floor.

In addition, the President has indicated a willingness to sign such legislation, which will provide a level of comfort for those that seek to participate in genomic research, as well as patients who are seeking to improve or inform their health care through genetic testing.

And I think we can not ever go past a discussion on this legislation without turning to Dr. Francis Collins to thank him for his leadership on this. I think, instead of calling it GINA, perhaps calling it Francis would be more appropriate, but we couldn't figure out how to get that acronym to work.

(Laughter.)

MS. WALCOFF: But we did get GEDDI.

Another area of policy focus is analytical and clinical validity of genetic testing technologies, which Reed also touched on earlier. The research and development of new genetic tests is ever-increasing, and the clinical validity of genetic tests should be assessed to determine the test's usefulness in making important clinical medical decisions. Yet, there is certainly a lack of clarity in the regulatory oversight system.

Finally, the initiative seeks to standardize access policies. Research using human genomic sequence databases, supported by public funding, will increase and create many new opportunities that will benefit public health. Currently policies for accessing these genomic databases are inconsistent about who has access to specific information and the time frame in which this information will be made public and the level to which it will be made public. So this initiative is working to harmonize and bring consistency to those policies and move forward effectively and efficiently in terms of that kind of research.

As I noted earlier, the AHIC has established a personalized health care working group composed of a broad cross section of stakeholders, and we've just listed those out for you here so that you can get a sense of where we're going on that. We've recently had a meeting. I think it was about two

weeks ago. And I was really encouraged by the comments that I heard while I was there and the extent to which folks are taking this extremely seriously and really putting in a lot of time and effort to work through these issues.

Currently, there's a lack of consensus on policies surrounding incorporation of medical genetic tests and family history information in the electronic health record, and that could impede further systematic and useful adoption of this important technology.

Genetic tests are increasingly being used in mainstream clinical care. However, no standards have been vetted and certified for genetic tests and family history information to ensure incorporation of this important information in electronic health records. So you'll see up there the broad charge and the specific charge and some other issues that this work group is going to be taking a look at over the next two years.

If standards are not widely accepted, a patchwork of many different systems of electronic health records will impede interoperability and the exchange of useful health information. Initial primary care physician acceptance and understanding of this new medical technology is not keeping up with the rapid pace of genetic research, and this represents the broad and specific charge of the work group and it's something that is very much a part of the Secretary's Personalized Health Care Initiative.

Dr. Downing should also have a bunny with him because he, I don't think, ever sleeps. He's working on all of these issues so hard and is really the string of continuity through the various issues happening at the Department that will promote the Secretary's initiative.

So I'd like to wrap up my remarks with the focus on an area where we believe that the SACGHS could assist us in developing knowledge to support some of the work that I've just referenced. Fortunately, since my system was not working very well last night -- we still have some glitches in technology -- Reed doesn't have this in advance. But I'm just going to go ahead and outline the charge that he referenced earlier, and I'm going to leave a copy with him so that the committee has a chance to look over that and consider whether it would like to take that up on behalf of the Office of the Secretary.

As part of the Secretary's Personalized Health Care Initiative, it's certainly come to our attention that appropriate and clearly defined oversight of genetic testing is a matter of concern for many stakeholders. This is a complex issue and involves a number of departmental agencies. SACGHS has heard over the last few meetings a range of testimony on this subject and many, but not all, of the HHS agencies involved in oversight of this important technology have participated in the discussions that you've heard. Through this process, the committee has identified a number of unresolved issues concerning oversight of genetic testing technologies. We understand and recognize the importance of this discussion and also see the complexity as the use of genetic technologies expands and plays a larger role in the personalization of health care.

The Secretary is committed to accelerating advances in quality health care and value by enabling appropriate regulation without stifling innovation. And so, as we look back on the committee's work to date, we've been carefully reviewing your work and the work of your predecessor committee, the Secretary's Advisory Committee on Genetic Testing, which is still relevant in today's conversation. In particular, many important topics and recommendations were covered in the July 2000 report, Enhancing the Oversight of Genetic Tests. We agree with the principle stated in this report that the public is best served by ensuring both adequate oversight of genetic tests and the continued development of such tests.

Subsequent to this report -- you're a very, very busy committee, Reed -- in September of 2001, that committee released conclusions about the development of classification methodology for genetic tests. The committee at that point found that the feasibility of categorizing tests for genetic

purposes, based on a limited set of elements in simple linear fashion, was not possible.

We've been closely following the information gathered by a broad cross section of stakeholders in forums like this to better understand the issues and to discuss internally how the Department should coordinate oversight of this complex area of public health and science.

To that end, we are interested in the work of this committee and ask you to continue to provide valuable information to inform the Secretary's initiatives. Specifically, we would appreciate your input on a number of questions critical to the Secretary's priority. As I noted in my earlier remarks, the Secretary has announced that the Personalized Health Care Initiative is seeking to better understand the intersecting oversight and regulatory policies concerning genetic tests, to identify the scientific information and oversight needed to assure that tests are being developed and properly used, to encourage innovation and patient access to better genetic tests, and to improve transparency of the system of oversight overall.

To help inform the Secretary's policy progress, we suggest that this committee undertake the development of a comprehensive map of steps needed for evidence development and oversight for genetic and genomic tests with improvement of health quality as the primary goal. We suggest that the map consider and address the following questions. Generally, what are the existing pathways that examine the analytical validity, clinical validity, and clinical utility of genomic tests? What organizations are currently responsible for each of these aspects and what are they doing to address the issues? And what are the potential pathways to communicate clear information to guide test and treatment selection by providers?

We would also like input specifically on both the analytical validity and clinical validity of genetic tests, such as, what evidence of human harm exists regarding genetic tests? Is that harm attributable to analytical validity of the tests, clinical validity, and/or clinical utility? If evidence does not exist, what threats exist that are currently not being addressed in the regulatory oversight? What distinguishes genetic tests from other laboratory tests for oversight purposes? And what resources, such as standard reagents or materials, are needed to develop proficiency testing requirements? What is currently available in terms of proficiency testing kits for genetic tests, and what information is provided by proficiency testing? What new approaches or models for private and/or public/private sector engagement in demonstrating clinical validity and utility for developing effectiveness measures for use of genetic tests? And what should be considered and why? And finally, if, where, and how additional revised government oversight would add value for patients.

On behalf of Secretary Leavitt, I appreciate your time and attention to these matters, and I look forward to receiving additional input from this committee on these issues and the other broad range of issues that you went over earlier this morning, Reed. You have your work cut out for you. Thank you.

DR. TUCKSON: Well, thank you very much. First, again -- and I won't belabor it -- we really appreciate your personal leadership, Greg's, and the attention of the Secretary.

So in the spirit of the almost always true dictum, be careful what you ask for, we asked for an assignment. I think we've gotten one. We got a pretty big one, a pretty powerful one.

What we will do is -- and I am well aware of the anxiety that goes with someone trying to present a report on Sunday night and your computer doesn't work and you're running around with the senior people at the White House and HHS trying to get the computers to work at 6 o'clock on Sunday night to get something in. That's always no fun.

We will take a copy of what you have here or what we're able to get here, and I'll have it xeroxed for the committee and we'll return to this issue tomorrow. Then we'll start to think about it.

I think that this charge is important. Now, again, I want to just quickly, while we

have Sheila here because I know she's got to get back downtown, say that I'm comfortable and excited by the charge especially because I think it is important that the committee understands the context of the charge. And I want to have Sheila comment on this specifically because it's not good enough for what I say. You have to hear it from her.

I, through a series of meetings, am convinced that HHS understands the importance of protecting the public and that they are doing their work to coordinate the federal agencies and are looking carefully themselves at what CLIA and CMS and what FDA and what FTC and all that are supposed to do. So I want the committee to be confident that as we look to take on the assignments that we have, that it is within a context of an overarching activity at HHS.

MS. WALCOFF: Well, that's exactly right, and in that overarching activity is the Secretary's initiative. It's one of the policy areas that we identified pretty early on, and there are a number of folks here that are very, very engaged in this from the Department's perspective. But it's something that we think, in the next two years, we'd really like to move forward on and try to establish some clarity and consistency so that the area of personalized health care isn't stalled. We continue to promote innovation, always with an eye out looking at that issue of public trust.

DR. TUCKSON: Actually, you ended exactly where I wanted you to end -- where I was hopeful that you would end.

One of the things that impressed me about the Secretary's comments in this whole area of personalized care and particularly HIT has been his realization of the public's anxiety around privacy and confidentiality. That's the sister, as it were, of this issue of trust of oversight. I think that it's pretty clear to me that this movement is not going to go very far or very fast if the public is not assured that there's confidentiality and trust, there's anti-discrimination, but this idea of trust on the regulation side has to be addressed. So I do see that as being keenly important.

MS. WALCOFF: Well, thank you. Also, too, I know that Dr. Kolodner will talk more about what the AHIC is specifically doing in the area of privacy and security, and it's certainly something that is moving along as part of that track I spoke about earlier, right along with technology and the other policy areas that we're trying to develop.

DR. TUCKSON: One other thing. Then I want to give the committee members -- I'm buying time for your computer brains to figure out the question you want to ask Sheila. But let me also say that this is the second meeting now that Sheila has come before us and mentioned "the clock." Again, one of the things I like about the way that the Secretary does his business is that he's keenly aware that he's only there for a certain period of time. So he's not interested in a lot of yama, yama, yama. He wants to see something happen.

So we're going to have to think carefully about what things we can deliver to him in time for his watch in these areas and as that committee process goes forward. So maybe through Greg Downing, we can have a way of continuing to keep track of -- you know, maybe help us, Greg, to think about, as we try to organize ourselves to respond to some of these challenges, what the timeline is for us on this. So it's something that we have to consider.

MS. WALCOFF: Well, we really look forward to continuing our work with you, and I know that I also have an assignment because I'm going to have to go back and prepare the Secretary for not one, but two quizzes. So I might have to start traveling with him on his overseas travel so that I can have some flight time to do that.

I'm happy to take any questions before I need to head back to Washington, if anyone has any.

DR. TUCKSON: Does anybody? Yes, Joe?

DR. TELFAIR: Good morning and thank you for the presentation.

If you could just speak briefly, if you can, on the initiative. If you can say a little bit about financing and access issues, one, and secondly, consumer and public education and engagement as it relates to the rolling out of this involvement. I know that on the committee you have listed some of that, but in your presentation, you didn't discuss it that much. And I was just seeing if you can say a little more about it.

MS. WALCOFF: Sure. I think you're asking specifically about reimbursement policy and education, if that's right.

DR. TELFAIR: Well, reimbursement policy is one thing, but also literal access to whatever comes out of the work itself by those it directly affects. So it's more than just the reimbursement policies actually because what I'm speaking of is the education as engagement. In other words, it's one thing to be aware. It's another thing to be educated. It's another thing to be involved. So I'm speaking with that part of it, which I know is an outcome of the work, but has there been a discussion for that? Have there been some thoughts around that so far? I mean, I realize it's just getting started.

MS. WALCOFF: Sure, and absolutely, we started actually about a year ago with this initiative. The Secretary came to me and asked me to take a look across not just my portfolio, which is science and public health, but really across the Department to try to figure out what we could do and what he could do as a focus of this initiative. In that, we looked at a pretty big vision, a long vision, a generational vision, and then tried to narrow it down to some specific areas where we thought he could have direct leadership over the next couple of years. Absolutely, in those discussions, we talked about transparency, education of not just providers, but consumers, researchers in terms of the spectrum of stakeholders, reimbursement policies. That list that we have on the AHIC slide is really kind of a brief snapshot, I think, of a broader number of issues that will certainly touch on this and are worthy of discussion as we continue to go through.

We haven't identified some of those as our priority issues mainly because we know we have limited time and, to some extent, limited resources, although I really don't think Greg Downing ever sleeps. But I can let you know that we are engaged in those kinds of discussions and that we continue to seek input and information on those because they do inform our other policy processes, as you noted.

DR. TUCKSON: Terrific.

Any last questions? Oh, yes, Andrea.

DR. FERREIRA-GONZALEZ: Thank you so much for a great presentation.

We really appreciate the Secretary's coming to provide us some charge to specific issues of oversight. Since I haven't seen the charge in detail or have had some time to look it over, there are a couple of things I would like you to go further on or a little bit more explanation. If you cannot do it today, maybe at a later time, as we go more down into the charge, you can provide us with more detail of specifically what you're looking for.

In the area of oversight and the role of the states and the federal government, could you tell us a little bit more about that? Do you want us to actually look at the role of the federal government and the states and the private sector in oversight of genetic testing?

MS. WALCOFF: We left the charge, in some respects, purposefully broad because we didn't want to create an expectation of anything specific. We really wanted to get the best look, a broad spectrum look from the variety of stakeholders that represent this committee.

I think that our focus certainly would be more on the federal side because that's the area we have the ability to impact. But we would like an understanding of the intersection of what the private sector is doing, certainly public/private partnerships, and your views of where the federal government is on this would be extremely informative.

I think in terms of state regulation and state issues, I know that there's been some work

done by the committee in the past, and we will be looking at that. But I think we would be looking at a more broad federal look so that we can try to identify some specific areas where we can take action.

DR. FERREIRA-GONZALEZ: And with regard to the analytical validity and the clinical validity and utility, if you can provide us more specifics of what the Secretary is looking for.

MS. WALCOFF: Sure. As I said, this is our first outline of the charge, and I very much anticipate us continuing to work with you all as we move forward on this. I think those kinds of discussions will come out as we move forward, and I'd like an initial look at how the committee feels about the charge and I think we can further develop it from there and have some more specific discussions.

DR. TUCKSON: I think, Sheila, what we probably will do then is -- Greg, are you going to be around for much of this meeting?

DR. DOWNING: The whole time.

DR. TUCKSON: The whole time. Oh, wow. Unbelievable. Great.

So what we'll do is when we get to the discussion in the agenda on this topic, we will have a chance to engage at that level of granularity and sort of negotiate out a little bit in terms of how much of this we can get done on the timeline that is available.

I think this idea of the relationship between the public and private sector is one that has particularly engaged me intellectually. I think this is one that we are uniquely able to do something with, and I think that's going to be important.

I think your question really was important in terms of helping them to understand better -- if I understand, the charge at this level is really clearly trying to understand, when it comes to analytical or clinical validity, whether there is evidence of harm or what are the threats. What is it that we really are concerned about? I think that's really what the charge sort of speaks to, as I understand it. So we'll drill into those things.

All right. Amazingly, it's like 1 minute of. Gosh. That's why I'm going to call the question here and just say thank you again for this. And we look forward to responding back to you and the Secretary with the results of this meeting's deliberations, and we'll shape the expectations between our committee and the Secretary's office within the next couple of weeks and have something firm and a real work plan and a real sense of expectations by timeline. We'll negotiate all that out I think, hopefully, within the next two weeks.

MS. WALCOFF: Well, that sounds great, and I thank you again. While I didn't specifically mention timeline, I did leave that for a little bit of a more granular discussion. But our clock is ticking. So we are anxious to put you on a fairly accelerated timeline for this. Fortunately, you all have already done a very good amount of work on this to date. So I think focusing in on some of those specific questions that can help us in our policy process will be extremely useful.

So thank you very much and don't eat too many bunnies.

DR. TUCKSON: Well, we're all about the deliverables. So, again, thank you very much.

Right on time, look who's here. It's Dr. Kolodner and Jodi Daniel.

Now, the key we have been talking about for many meetings has been how important the health information technology infrastructure is going to be to the transformation of health care and, in particular, personalized care and particularly in the notion of genetics.

So Dr. Kolodner has stepped in marvelously to actually be the leader in coordinating across about 18 different task forces, of which I think I'm on half of them. That's why I really know that Dr. Kolodner is on his game. Believe me.

So thank you so much for joining us and giving us this background. I hope that what

the committee will get from this is not only getting the overview of what's going on in HIT, seeing some of these committees, seeing and thinking then about how this infrastructure is available to advance the interests that we have.

And thank you so much, Jodi, for joining us as well.

DR. KOLODNER: Thank you very much, Dr. Tuckson. It's a pleasure to be with you today. I look forward to not the presentation as much as the question and answer afterwards. I'll be doing part of the presentation. Jodi Daniel, the Director of the Office of Policy and Research within the Office of the National Coordinator, will be doing the second part of the presentation.

So as you know, there are multiple challenges to the advancement of the genomics. And we heard about a number of them, the issues of discrimination on the basis of genetic information that we need to protect against, that the genetic information is unique to the individual, is predictive of a person's future health, and is immutable, especially once disclosed. Unique information really does not only affect the information about an individual, but the information about other related family members. And while we had that with family history, it really wasn't as powerful as it is seen with the genetic information itself.

Finally, the challenge, that that genetic information, by then being supplemented with other types of data by non-covered entities, could be relinked, and that we need to do the protection to make sure that sort of violation of privacy does not occur.

Health IT itself, as Dr. Tuckson mentioned earlier on, can really add value to the genomics, both helping to enhance the adoption and utility -- there's a huge amount of information. In order to bring it to the forefront and to the front line clinician so that it makes a difference or to the individual themselves, we need IT to enable that. This issue of trust in the privacy and security of that information is fundamental in order for individuals, you and I and our friends and colleagues, as well as family, to allow that information to be used and to be captured now and into the future.

So there are a number of drivers for health IT adoption, and one of those that is pushing us is that rising cost of health care in the U.S., the fact that in the U.S. health care is double the GDP of any other nation and that, frankly, we're not getting the value of those dollars that we're investing. More importantly, if it continues to rise at the rate that it's going, it will fundamentally undermine our economy into the future, even as now it is challenging the global competitiveness of our corporations.

But there are also positive drivers for health IT adoption. First of all, the fact that consumers and the economy begin to see some of the substantial benefits that can come from it, and there are some organizations in the forefront having shown where health IT can help to improve care.

The administration's leadership, both in the executive branch, the President and Secretary Leavitt, as well as on the Hill, and there's real bipartisan support for the health IT agenda, which is extremely important as we move forward.

And finally, the strong endorsement from industry and commercial leaders who will be able to benefit in terms of their global competitiveness and the fact that so much of our current costs, when we go to market our services and our products overseas, are tied into the cost of supporting health care.

Now, when I talk about the health IT, there are several components that I'd like to address. At the top of the screen, you see the endpoints, the electronic health record, the personal health record, and public health information, public health systems, that are where that information gets used either by providers, by the individuals, or by the community and the nation.

Underpinning that are the standards that we need, standards for data, technical standards, as well as security standards, because without that, we have a Tower of Babel. When we have these isolated islands of standardized information, in order to get the benefit from them, we need to link

them together securely, robustly in order to flow that information among the different islands, among the different users in a way that honors the privacy and security of the individual, but also advances knowledge, advances the health of the community. That network is what we talk about as the Nationwide Health Information Network that we're seeking to foster, which is not a single network but, like the Internet, is a network of networks at the community and at a national level.

For those who aren't familiar, the President did issue an executive order in April of 2004 that established the Office of the National Coordinator. The charge to the office was to advance the vision for developing this nationwide interoperable health IT structure, as well as achieving the widespread adoption of the electronic health records, interoperable health records, by 2014, a 10-year goal.

Now, the key role for ONC is then to provide the leadership to achieve this goal and to improve the quality and efficiency of health care, as well as the ability of consumers to manage their health. By that, that's what we mean by the National Health IT Agenda.

But let me emphasize that the purpose of that National Health IT Agenda is what you see highlighted at the bottom there. It's not to achieve technology. It is about the outcome. It is about improving the quality, efficiency, safety of health care. It is about enabling consumers to manage their health.

So health IT is a critical component for a transformation to occur. The transformation is not the adoption of health IT. The transformation is in the individual and population health and advancing that, not just incrementally improving it based on what we're doing today, but bringing about a change in how we support the health of individuals and the nation.

The framework that we have builds from that 2004 charge to 2014 where there will be this widespread use of a variety of things, electronic health records, personal health records, and public health infrastructure, but also that enables other things, home telehealth, and even beyond the home, continuous monitoring of one's health. People talk about the fact that when you pick up your cell phone and you make a phone call, it's already monitoring your vital signs and using algorithms to be able to determine whether something abnormal is going on and where to record that or who to notify, you or your significant other or your primary care doc, if something is abnormal. It's really a very different way of thinking as opposed to right now where we have this episode where you have to go to a provider and you have that small snapshot where you're getting your care. This allows you to actually have a monitoring of your health in real time throughout the day and night.

We've set up four goals to support this charge that we have, things about informing the health care professional, interconnecting health care, personalizing that health management, and improving population health. Now, you can see that there is a real overlap between the areas that you are focused on as a committee and the activities that we have because the things that you're doing cut across multiple goals there that we are charged with.

We also have a federal advisory committee. It's called the American Health Information Community, and this community, this AHIC, is one that is chaired actually by Secretary Leavitt himself. It's a public/private collaboration and serves to provide input with regard to our advance towards the digital health records and the interoperability.

A lot of this is also how we assure the privacy and security of the records and how we enable the market forces because, frankly, in the area of health IT, the market processes did not work. So our role is not to replace those, but it's to set certain boundaries, to set certain targets, to remove barriers, and to provide the incentives in order for the market forces to work, in order for the creativity of the community, of the providers, of the nation to move forward and to advance us so that we achieve that interoperability and that transformation of the health arena.

Our work is done in work groups. So we have a variety of work groups that have been set up. We've been fairly busy. Last year we had over 50 meetings involving over 120 experts and stakeholders. The focus of these work groups is to make the recommendations to the AHIC regarding the policies, technical, business, and social issues so that the AHIC then, as you do, can make recommendations appropriately to the Secretary and to the Department.

We started in November of 2005 by establishing four work groups that had to do with consumer empowerment, chronic care, biosurveillance, electronic health records. Each of them had a breakthrough area. So, for example, the electronic health records established that we want to make laboratory results available to the front line providers, even if that front line provider did not order it, because sometimes that's an issue. We also wanted to make sure that consumers had available a medication profile that they could pull up and make available to whomever they chose to make it available to.

We established two other groups in May of 2006. Because each of those groups identified the confidentiality, privacy, and security issues, rather than dealing with them separately in each of the groups, we brought those together into a group that would discuss and advance those, and Jodi will be talking about that in just a little bit. We also had a work group on quality.

Finally, the most recent work group that we established in October of 2006 was the Personalized Medicine/Personalized Health Care Work Group that Sheila talked about previously.

So of these groups, you can see that there are two that are particularly relevant to the work that you're doing here.

We use the collaboration to advance our agenda, and that term "National Coordinator" is important because my role is to help coordinate the activities. We have public/private initiatives to do so.

There were three contracts that we established. The first two actually are meant to foster the establishment of organizations that will go on and have a regular role to serve the nation. The first is a standards harmonization panel referred to as HITSP. We like to make a lot of alphabet soup as well. This group is looking to take those standards in a variety of areas that exist and harmonize them and identify which ones are we going to be using as we go forward because the problem that we have, as with many standards, is we have so many to choose from. And the problem is if we're going to get beyond the Tower of Babel, we have to decide as a nation which one we're going to be using in order to make sure we're speaking the same language.

Then we have a Certification Commission to look at a variety of products that are out there, electronic health records, both outpatient and inpatient, the network services, and now we're going to be also moving forward on personal health records, in order to provide certification for those.

The reason for certification is twofold: first of all, to help push forward, to drive forward that adoption of the standards that have been identified; and secondly, to help reduce the risk for the front line provider, for example, when it comes to the electronic health record, so that they aren't having to decide does a product meet my needs, does it meet the standards. They will have the certification there to be able to depend on.

In fact, in the very first year, we already have 55 ambulatory EHRs that have been certified, and there's another round. So we expect it will get over 70 by the time we finish the first year. And that represents over 25 percent of the products on the market, but over 75 of the installed base already. Now, that's the good news.

The bad news is that the installed base of really significant electronic health records being used is only at 10 percent of the provider community, whether that's inpatient or outpatient. So we have a long ways to go. We need to help to move that forward, but that is what our charge is.

Now, the final contract is not to establish an organization, but it's actually to foster the development of that network. We started last year by issuing contracts to technology consortia to develop prototypes so that we could look at what does it take, what are the components, and what are the best ideas that we can have. We then drew from that. They actually demonstrated it to the AHIC in January. And our next round is to go not to the technology companies, but to the health information exchange communities that are out there in the regions, local and state, in order for them to then contract for the services.

But we're going to be defining certain capabilities that need to be there, particularly with regard to enabling individuals to control the information that flows over those networks. The reason for doing the latter is not to say that that is the policy, but to make sure that as this technology moves out, that the technology doesn't limit or define the policy, but that it can, in fact, support whatever policies we adopt as we move forward as a nation.

The other collaborative activities that we've been having are at the state level because the state and the communities are where the real action is occurring. It's not going to be occurring at the national level. We can foster certain things such as the development of standards and the certification, but the true implementations are going to be occurring locally. So we have a number of activities there. Two of them Jodi will be talking about very briefly.

The first on that list is the activity within privacy and security which was a collaboration at the state level to identify where the variations in state laws occurred that might act as barriers to the movement of information.

And the one at the bottom is the State Alliance for eHealth, which is a contract with the National Governors Association and is also a committee, one of those many that Dr. Tuckson is engaged in for the Department. And that's really one that has established the executive level advisory body. It's a connection in to the Governor and to the legislative levels at the state in order to develop the consensus solutions for state policy.

Then finally, another state activity that we had went out through the AHIMA and was to work and identify some of the top, leading-edge health information exchanges out there to identify the best practices and to cull them out so that others that are proceeding to establish the health information exchanges can learn from them and see what issues and strategies were addressed by those early adopters.

Now, one way of looking at this is that health IT supports transforming health care and that, like a tree, privacy, security, and confidentiality are the basis of all the activities that we're doing in transforming health care. And the health IT are activities that feed the roots of the tree. And you see a number of them there, a few of which I've talked about. There's a governance process. In this case, it's the AHIC.

But the real purpose of it is not the tree trunk or the roots, it's the foliage and the fruit of that tree. You see there adding value to patients, achieving high quality, safe health care, adding value for providers, improving public health.

But there are three of them, individuals managing their health in a safer, healthier nation, that really mean that we're not just transforming health care, but we're transforming health and the care. It goes beyond the health care sector itself.

I mentioned the AHIC. We've achieved a number of things over the past year and a half that we have been operating in terms of setting priorities and making recommendations to the Secretary. We have a number of things still ahead of us. That issue of privacy is a critical one in terms of what those policies and what those principles should be. And transitioning the AHIC, unlike what you will be doing, to a public/private entity. So there will remain a federal advisory committee behind, but the real governance will move out to an entity that is a public/private entity in the private sector. And

we're in the process of starting that movement.

You heard from Sheila about the Personalized Health Care Group and a broad charge there. I'm highlighting here the issue of common standards and the incorporation of interoperable, clinically useful genetic laboratory test data into electronic health records. The specific charge, again highlighting, establishing the standards for reporting and incorporation of these common medical genomic test data into EHRs and providing incentives for that adoption.

Health IT can facilitate knowledge management. It can help us to organize the information to improve the safety, the quality, the efficiency of the health care part. Right now I'm talking about the health care sector specifically. We do this through that establishment of common standards. Those standards will pervade through not just the electronic health records, but the databases, the repositories that we will be fostering.

We need to be managing the systems to generate that knowledge. It will give us better information on the individual differences. We'll be able to draw that standardized information so that we can do postmarket surveillance, so we can get better evidence development and advance medical knowledge. What we need to do, though, is to figure out how to do that so, again, we honor the privacy of the individuals and do this in a manner that all of us as a society can benefit from.

And we need to, in fact, move from what has been the incentive in the health care arena, which was automating the revenue side, to automating the core activities which are the delivery of care because, as you look across any industry, it's only when you automate your core processes, that you really get the benefits from that automation. And for the last 30 years in health care, we've been automating the edges, the revenue, not the health care delivery.

Health IT, again, is not the endpoint. It is the means to improve health by supporting the physician and the care provider, keeping up to date with medical information; making sure that they have access to that information; making sure they have all the information about an individual so that they can give that better care; improving the diagnosis, having the decision support at their fingertips at the point of care; and being able to know, based on the various parameters, including genetic tests and results, what the anticipated course of that illness might be for that individual.

It supports the researcher by making available a variety of tools and by providing access to a wealth of information that goes beyond what we can achieve with our normal randomized control studies where we have to refine that population in a very tight manner and where most of the individuals that we care for actually have multiple diseases, and we'll be able to draw that information from these databases.

Finally, supporting the consumer, the real beneficiary of all of this, by helping them to receive the best care possible and personalized health so that they get the right diagnosis and treatment the first time, every time.

But as I say, it's really beyond health care itself. It's transforming health and care. So not only do we deal with improving the diagnosis and treatment, the health care delivery portion, but it's really about moving to anticipate and prevent illness and, by that way, really transforming from health care to health.

With that, let me turn it over to Jodi and she will be talking more in detail about the privacy and security aspects. Then we look forward to taking questions at the end.

DR. TUCKSON: So we will do that, and let me just tell you that -- terrific -- Jodi is Director, Office of Policy and Research in the Office of the National Coordinator for Health Information Technology, fondly known as ONC.

(Laughter.)

MS. DANIEL: It used to be ONCHIT, and when you pronounce that out, it

sometimes didn't sound quite right.

(Laughter.)

MS. DANIEL: So we shortened it to ONC, and it's not a perfect acronym, but it's better than the alternative.

Good morning, everyone. I am going to just drill down on some of the specific issues related to privacy and security that Rob had touched on in his part of the presentation just to highlight a couple of things that Reed Tuckson and Sheila Walcoff have both said, that privacy is probably one of, if not the most important policy issue that we face with respect to health IT, and that really trust is the key here. If we don't have patients trusting the systems that are set up for sharing information electronically, if providers don't trust that the information is reliable and is going to be protected, then we're going to have a real problem in achieving our health IT goals. So this really is the key policy issue that I face and that we face in trying to roll out our health IT goals and our health IT initiatives.

Two things to highlight. I think the technology clearly does provide some added risks for health information to be disclosed. There's greater ability to aggregate data. There's greater ability if there is an error for a large amount of information to be shared. But it also provides really great opportunities to protect data in a way that's much more secure than in the paper world. You can build in protections that might be administratively burdensome in a paper world. There's ability to identify when there has been a breach of information, where in a paper world, you can't necessarily do that. So there are real opportunities here too, and we're trying to look at how to minimize the risks and increase the protections that are available with technology.

Rob had mentioned the executive order that established our office, and one of the goals that is set forth in that executive order is about privacy and security, that a nationwide interoperable health information technology infrastructure must ensure that patients' individually identifiable health information is secure and protected. This is a key tenet of everything that we're doing and is part of our mission of the office.

One of the things I like to highlight: there's always debate. Do we have to have the policies in place before the technology? Is the technology moving ahead of the policy? I know these are issues that are addressed in medical technology, as well as health information technology. We really see these as having to work hand in hand. These cannot develop in the abstract. The policies have to be built as the technology is being developed. The technology will provide some insights on how best the policy goals can be achieved. For instance, particularly as technology is being developed, you can come up with great policies, but if they're difficult for people to use, people will find workarounds and may, in fact, have less protections than they may have had with a different policy incorporated into the technology.

For example, I know everybody has 3,000 different passwords for every different system you have to log onto and you have to change them every day or every few months. And there are different requirements for making them more and more difficult for people to be able to figure out. But because of that, people always have their little sticky note with their password up on their computer, which in fact is making it less protective than if they had a simpler password that they were able to remember. So there's always that balance with developing the policies and the technology that fits well together.

Rob had also mentioned the NHIN, Nationwide Health Information Network, trial implementations. This is really one place where we're trying to make sure that as some of these technology architecture standards are being developed and being tried out, that we're incorporating the ability for different privacy policies to be developed and be incorporated in the technology. So we're going to require that the trial implementations have consumer control capabilities in them so that as the policy is being developed, there is the ability to work those into the technology rather than the technology

being developed without considering those at the onset.

So where does this all start? I think that when we're looking at privacy and security issues, HIPAA always comes up as the issue and the foundation for everything we're talking about. I think some of the challenges that we face with respect to health IT and genetics -- there are some similarities here based on that HIPAA baseline. The HIPAA privacy and security rules are a very strong foundation for protections. They were the first nationwide protections of health information. There's a federal floor. So they allow for state protections that are greater than those federal protections. Some of those state laws also provide greater protections for specific kinds of information, including for genetic information.

So as we're looking at privacy and security policies, we need to not only be looking at federal policies, but also some of those state policies and how those two can work together. That's why we're doing so much work with the states, as Rob had mentioned, to make sure that we're looking at both levels, both the federal and state level, to address those issues.

There are some things, though, where health IT may pose additional privacy or security risks that may or may not have been considered by HIPAA, and those are some of the things we're looking at now. Again, as I had mentioned, there are opportunities for greater data sharing. There are opportunities for greater aggregation. So these raise questions as to do we have the right policies based on these greater abilities to share information and to aggregate information.

There are also new entities that have entered the market in the realm of health IT, as well as with research and genetic technologies. We have new health information exchanges that have developed, regional health information organizations and the like, that are not necessarily covered directly by HIPAA. They may be covered indirectly through contracts with those entities that are covered, but they raise questions when those entities are sort of holding a lot of information or aggregating a lot of information. Does that raise new challenges? Does that raise new policy questions that we need to think about in order to make sure that the information is private, is secure, and that there is trust that consumers have that information flowing through those will be safe?

Same thing. Sheila was mentioning the ability to aggregate a lot of genetic information and have genetic databases. Again, these entities that are holding this information may or may not be covered directly by federal or the state laws that currently exist. And so there are new opportunities and challenges to look at those areas.

Some of these issues are being raised by the privacy and security solutions contract at the state level that Rob had mentioned. There are also things that we're looking at internally and that we've been talking with the Office for Civil Rights about. The Office for Civil Rights at HHS enforces the privacy rules. And as we're getting some new information from the states, both at a state and federal level, about some challenges that they're facing, we're taking those to heart and we're looking at how we can best develop policies to address those concerns.

So at the state level, as Rob had mentioned, we have the Health Information Security and Privacy Collaboration. This was an effort to look at a state level at the state laws. We have 34 states and territories that are working within their state but are collaborating across states as well through some regional and national meetings to look at their state privacy laws and their business practices, get folks from various stakeholder groups to identify how things really work in the real world with respect to privacy and security policies and practices. We've learned about many misconceptions about certain laws. We've learned about entities that are much more protective than those laws. We've learned about variations in those laws. And those states are each identifying variations in policies and practices and laws looking at state solutions and developing implementation plans within their own state to address any legal or policy barriers that they have at a state level with respect to privacy and security.

Where we're going with this is we now have 34 states that have been looking at these issues and they've had some cross discussions through regional and national meetings. But what we want to do in the future is to try to find opportunities where there are issues that are overlapping across the states to bring those states together to have some regional or multi-state collaboration to look at some of these challenging issues that come up at a state level or an organizational level, but that really do require collaboration across jurisdictions. As we all know, patients don't stay within state jurisdictional lines. They often will cross over to different states. People travel. People might travel to specialty hospitals for care. People from rural areas may be going outside of their state to go to cities and the like. And so we want to make sure that we don't end up with 50 state stovepipes but, in fact, that we have collaboration across those states on some of the privacy and security policy issues and legal issues.

Because the HISPC had identified this need for this cross-state collaboration, it was one of the drivers for the State Alliance for eHealth. This is an effort by the National Governors Association working with the National Council for State Legislatures, the National Association of Attorneys General, and the National Association of Insurance Commissioners to try to build consensus by state leaders. The State Alliance itself is made up of governors, legislators, attorneys general, insurance commissioners, folks from their health agencies and the like, as well as technical advisors, including Reed Tuckson, to look at these issues that are coming up in various different manners and to try to see if there's some consensus that can be drawn across the states and promoted across the states so that as the states are taking on these issues, they have a baseline to work from, they understand what other states are doing in this area, and there's some harmonization of those policy discussions and decisions.

Particularly with respect to privacy and security, there are three task forces that are providing information up to the State Alliance. One of them is the Health Information Protection Task Force, and this one really is focused on the issues of privacy and security at a state level. They will be taking some of the information from the Health Information Security and Privacy Collaboration work, as well as doing their own work and research and testimony to try to identify where there are issues and opportunities for cross-state collaboration on privacy and security policies.

Then at the federal level, one of the biggest sources of policy development we have is the Confidentiality, Privacy, and Security Work Group of the American Health Information Community that Rob had mentioned. The broad charge of this work group is to make recommendations to the community regarding the protection of personal health information in order to secure trust and support appropriate interoperable electronic health information exchange.

The specific charge is really related to those breakthrough areas that Rob had mentioned. This work group was formed by a recommendation of the first set of work groups that were focused on the breakthrough areas, the Electronic Health Records Work Group, the Chronic Care Work Group, and the Consumer Empowerment Work Group, who all identified privacy and security issues with respect to their breakthroughs. They were replicating the same discussions in all of those work groups, not necessarily having a means of coordinating them and not necessarily having the experts at the table who really understood these privacy and security issues. So they made the recommendation to have a specific work group focused in this area.

We started up this work group in August of last year. So they've been operating for about seven months at this point. So far, they've come up with recommendations on patient identity proofing. They had five recommendations for how entities would identity-proof a patient and make sure that the patient is who they claim to be. Those recommendations were advanced by the American Health Information Community to the Secretary based on their January meeting.

They're trying to now go a little bit broader and look more at some of the privacy focused issues and are looking at the implications of having some entities within health IT and electronic

health information exchange being covered by federal and state laws, whereas others that are new and emerging that are not covered by federal and state laws, and trying to figure out what the implications of that are, how to make sure that there are appropriate protections that will ensure consumer trust and the like. We've just started down this road at our last meeting a few weeks ago and will continue in our next meeting to have some more hearings on this topic this month.

The other thing that they're very focused on and interested is personal health record privacy policies. There are a lot of personal health records where the consumer can put their information in a health record that they control as opposed to the doctor's health record, and many of those personalized health records are not necessarily covered by federal or state laws because, again, they're new entities.

So the Consumer Empowerment Work Group has focused on these and has identified this as an area to focus, and the CPS Work Group will be working with them to look at privacy policies for personal health records.

So this is just sort of a summary of how all of these things work together. Underneath everything that we're looking at, all of our privacy and security policies, is the legal framework that we're focused on. We have the CPS Work Group, and then we have what we're calling phase II, which is how does the work of the CPS Work Group fit in with other activities that we're doing.

The dotted lines are sort of informational and the solid lines are sort of more of a direct link. But we see the work of the CPS Work Group feeding our certification activities for electronic health records and for networks. We see it providing some input to the State Alliance where there are state-level issues that are raised. We see a direct link with the NHIN trial implementations as we said. As there are policies that are developed, we want to make sure they're incorporated into the technology and we'll be requiring those contractors to look at those policies. Clearly, their work will infect our federal policy development and our thinking on how to protect information from a federal perspective. And then it will help with standards efforts as the HITSP group is looking at standards for privacy and security and will feed other AHIC work groups. So we see them working closely with the Consumer Empowerment Work Group, the Electronic Health Records Work Group, as well as the Personalized Health Care Work Group, and we have met with the Personalized Health Care Work Group, and I've spoken at that group as well to talk to them about the CPS Work Group and some of our activities. And Greg and I are in constant dialogue on how we can make sure that those groups are working together.

Then as Rob was saying, the goal here isn't just to have all of these activities, but really to make sure that we end up with a nationwide health information network that brings together the policies and technologies and make sure that they're incorporated together. As we start moving, we hope to see these circles get closer and closer together and eventually have a direct overlap with one another so that the privacy policies and the technologies are in harmony.

And with that, we'll take your questions and comments. Thank you very much.

DR. TUCKSON: Well, this is terrific. Thank you.

So as my colleagues begin to think about their questions, I just want to reemphasize for those of you that don't live in the world day to day of AHIC, again, the reason that this stuff is being presented to you is, from where I sit, I can't think of anything that is currently more transformative in the real life of health care delivery than what's going on in these committees. I mean, this is absolutely fundamentally redefining the mechanisms for the infrastructure of care delivery at every level. This has all the stuff that's going into an electronic record, everything that will be standardized expectations for how the electronic record will work, not only collecting information but providing the prompts for information, evidence-based scientific guidance that will affect care at the point of delivery.

So all the things on the task force's agenda around how do you educate physicians and

other professionals to know how to keep up with all of the developments in genetics around appropriate stuff -- this is one of the vehicles to dump that kind of information into a point of access care record delivery. It's how we're going to evaluate physicians' performance around are they doing the right stuff. That's what's going on in this space. It's the personal health record for the patient. It's how they're going to accumulate family history and how family history and genetic-based information gets accumulated in a way that a patient can take that from one care setting to another across the fragmented health care delivery system. That's what this stuff is essentially all about. So I just want to sort of keep in your mind that this is transformative.

So I guess the questions that I would have, as my colleagues begin to think through, are two things. One is how can we influence or at least ascertain that genetics is, in fact, a priority in the electronic record committees, in the patient health record committee. And I don't mean that pejoratively. Is it only or specifically through the Personalized Health Care Work Group that we ought to be following up? But how do we sort of say, okay, genetics is actually -- you know, because the committees are making decisions every day about what they can do and what they can't do. Certain things are more important than others on a timeline, so that this committee may need to sort of understand, all right, well, where are we on the line, our interests are where on the line.

Secondly, if you can remember a second one after that long first one, is for us to start thinking and trying to understand better the privacy and confidentiality and just the natural linkages that occur between our interests in anti-discrimination. What I'm trying to get to here is -- so try to keep both of these in your head. I know I'm killing you here. The concern around discrimination is one thing, legitimate and real. On the other hand, of all the people in health care that will require an infrastructure of support for coordination of care, it's going to be people with genetic disease. They're going to have complex illnesses requiring lots of interaction with the health care system. So the ability to have information about that person put forward into the health care delivery system in a way that allows the coordination across care settings, having that protected but used and then not discriminated, if it ever got out, are fundamental issues.

So I put both of those before you. Then my colleagues will ask you from then on.

DR. KOLODNER: Well, thank you very much. I'll take the easy question, the first one. I'll leave the hard one to Jodi.

We're balancing a lot of priorities as we move forward in this agenda. The AHIC has a lot of things that it's identified and is starting to move forward. The good thing about that is everybody's particular interest is number one. So we have a few number ones.

This, however, because it is part of that transformation of health care and health, has to be built in at the foundation as well. So the Personalized Health Group is certainly the main vehicle for connection, and Greg Downing helps to foster that as he does this one and is a direct link.

In addition to that, as with your meetings, all of our meetings are broadcast and widely available. Whether it's monitoring the AHIC meeting itself or reading the transcript, which may go faster than just listening to the meeting, or the work groups which also are broadcast, where there are issues -- you can see what we have for an agenda, and if there are issues that you think either touch on your area of interest here or should touch on the area of interest, then first of all, through Greg, you can make sure if it should touch but it's not clear from the materials that we send out ahead that it has, you get the message to Greg, and that is something that puts it on our plate at the time of the meeting. But by monitoring those things, you can see where we need to add and pay attention to something that we may not be paying attention to.

So I encourage you to kind of use all of those means, but you do have a primary channel in. The AHIC will be considering those things.

The other thing that you have is for the next 666 days, if that's the right date -- and I didn't check the calendar this morning before I came in -- Secretary Leavitt has this as a top priority. So you have an advocate both as the chair of the AHIC and in the separate hat, because it is a separate hat, in his role as Secretary for those interests.

DR. TUCKSON: Great. Well, as Jodi gets to my other question -- again, we've got time for my colleagues to be able to query you as well -- I'd like to make a specific request.

First of all, I do want to acknowledge Greg who spends a lot of energy making sure that our staff is updated on these things.

Number one is I would like you, as you consider new candidates for the Personalized Health Care Work Group, to consider someone from this committee formally to be on it. Again, I understand how complex it is populating those committees. So if you'll notice the careful way in which I phrased it, I'd like you to consider someone from this committee to be on that.

Secondly is I'd like to have, as a standard part at least for our next meeting and perhaps several to come, a formal update from the Personalized Health Group, either a member of that committee to come and brief us or staff function. However, you best decide, Robert, in your role. But somebody would come and brief us as to exactly what's going on. We will certainly monitor. My thing is I think you gave the right answer, Bob, but unfortunately, these folks are so darned busy on this committee here, with their regular lives, that I think they just need to have that going forward. So if we could do that.

I see Marc --

DR. WILLIAMS: You're too late. There are two of us that are already on the Personalized Health Care Work Group: Steve Teutsch and myself. I can't speak for Steve, but I am going to speak for him anyway.

(Laughter.)

DR. WILLIAMS: But I think we would be most interested in formally liaising with this committee and doing that.

DR. TUCKSON: I wasn't too late. I was prescient.

(Laughter.)

DR. TUCKSON: No, that's great, Marc.

So why don't we do this then? We've got a committee of the committee. You are connecting it. So we will hear from you as a team report.

I think that what we ought to do then is -- Sarah, if you could remind me -- when we get to the discussion about next steps tomorrow, let's see if we can't give our team a little sense of guidance about at least what we see as some of the issues. I think this needs to now become one of our strategic goals, and since it's basically one we can claim, since we're already doing it, we're in terrific shape.

DR. KOLODNER: We'll be glad to put the check mark next to the recommendation. It's nice to have that.

(Laughter.)

DR. KOLODNER: But there's another one that just has the box instead of the check mark, and that is, that it might be worth having the same connection to the CPS Work Group, to the Confidentiality, Privacy, and Security, so that there's somebody particularly sensitized to this area on that committee. And we would certainly entertain that if there is another member who would like to sacrifice their time and be on multiple committees as well.

DR. TUCKSON: And then I'll just sort of telegraph specifically I'm sort of interested in the connection between this stuff and the electronic -- the Certification Commission for Health

Information Technology and the connection with the personal health record crew because I think those two are very important.

Jodi, in terms of my quick question on the confidentiality and privacy.

MS. DANIEL: Sure. As Rob had mentioned, if we would be open to including more folks -- and actually, I have talked with Greg Downing trying to find somebody who has sort of a research in genetics background to join that work group. We haven't identified a particular person. So we would be at least open to suggestions.

In addition, internally Greg and I have been talking a lot about how to make sure that genetic and privacy issues, as well as health IT and privacy issues, are both considered simultaneously. As I had mentioned, the CPS Work Group is starting to look at some of these issues, you know, the landscape of having some entities that are not covered and some entities that are covered, looking at some of these entities that are aggregating data from a health IT perspective, but I think there's also the same thing happening with respect to genetic information and these databases. I think there are some very similar issues that are being raised. So we've been talking, but we would definitely be open to any input on how to integrate those together.

DR. TUCKSON: Great. The thing I want to just explicitly tee up for later discussion, especially when we get to the genetics and the anti-discrimination legislation stuff, again, it really is this extremely sensitive and specific point, that there are lots of effort being done to have information that allows you to coordinate care for chronically ill, complex people. And then the genetic discrimination stuff is clearly trying to make sure that you're, again, not able to harm or misuse that. So there's a dynamic tension, though, between how do you solve that equation. So I just want to keep that in front of the committee as we go forward.

Let's take other questions. I'm looking for hands. Yes, Francis.

DR. COLLINS: So thanks for a very interesting presentation, obviously a critical topic for the future of all of medicine and particularly for personalized medicine.

I just want to ask, in terms of the charge to the Personalized Health Care Work Group, which you outlined, it seems very heavily focused on the use of genetic laboratory tests as a means of making sure that that information is properly standardized and incorporated into the electronic health record so that it is possible for all of the communication priorities to be achievable in terms of physicians and other health care providers having access to interpretable information and using it to benefit health care.

I was a little surprised, though, not to see any reference in that charge to family history, given that family history at the present time is a very strong driver of whether a genetic test is ever going to be conducted. And of course, it is an independent predictor of potential future risk and, at the moment, probably the best genetic test we have. Plus, it's free. It's poorly collected, however, and certainly poorly represented in any kind of electronic form in most medical records. So there's a great opportunity here to optimize that part of personalized medicine.

Many efforts have been underway by several groups over several years to try to provide the kind of tools that would make that possible, including the work that's been going on with the Surgeon General and the family history tool and the work at the CDC.

So I guess I'd like to be reassured that the charge here, by focusing so specifically on genetic tests, is not missing out on the opportunity to do something that could really be quite spectacular, both empowering providers and empowering patients to take advantage of the use of family history in a much more effective way than we currently do.

DR. KOLODNER: Fortunately, the work group, like many federal advisory work groups, isn't limited by their charge. One of the first activities that they looked at, as we identified what

are the areas to focus on, family history is one of those areas that they are focusing on, and I expect that we'll have a recommendation coming forward on that which, the way that we flow, will then form the basis of a scenario of what we call technically a use case, which then we give to the standards group to identify what are the standards that should be used, which then can be put into the certification process. So the work group has corrected that shortcoming and will be moving that forward.

DR. TUCKSON: The list we have is Kevin, Marc, Chira, Joe, and Muin, and let me start with Kevin.

DR. FITZGERALD: Great. I'd also like to thank both of you for the presentation.

I'd like to thank you too for your emphasis that both of you gave on the idea that for any of these public health benefits to occur, there's going to have to be public trust. I understand that we certainly want to reassure the public that there aren't going to be any harms coming out of this.

At the same time, I'm just wondering. In order to get this public trust, we're going to have to also engage those segments of our population which, unfortunately but perhaps justifiably, already don't trust the system or the sector, however you want to put it.

So instead of just reassuring people they're not going to be harmed by this, how can we engage them in such a way as to say this is actually going to give you greater empowerment, greater control both on a policy level and also on a technology level, you know, an empowerment and control that they don't presently and haven't in the past experienced?

DR. KOLODNER: That's an excellent question, to which I can't say that I have the answer.

But as we move forward and ferret out what our policy should be and how that policy evolves over time, I think we need to think about our experience in other realms, and specifically let me raise the issue of the Internet and the use of credit card information on the Internet. On any issue that we have, we have the early adopters who take risks and we have the people on the other end who may never adopt that technology or never trust it and certainly are more risk averse. We need to figure out how to allow the population to develop that trust and for them to choose when to be a part of it and how fast we move it forward.

I think those are the challenges with the policy development because, on the other hand -- and this gets to things that are labeled as opt in/opt out. Do you opt in to allow your information to be a part of it, or do you opt out if you don't trust it? And there are pros and cons to each of those that we'll be exploring and discussing in great depth in a variety of fora.

But this issue of recognizing that there are different levels of trust, there are different levels of risk-taking, and also the fact that no matter how much reassurance I give or the Department gives today, there are people who are going to take a long time to develop that trust. And how do we address that? What sorts of policies do we do in the meantime?

MS. DANIEL: If I could just add also. I think the personalized health records can go a long way in gaining that consumer trust because it is a place where the consumers can gather their own health information and have greater control of how that information is disseminated. And that is something that's new where now a consumer's health information is basically held by their health plan and their health care provider and not by them. So I think that that could be one big driver of consumer trust and consumer involvement that can help us.

A couple of other things. We're very much including consumers in all of our different collaborative efforts, our consumer advocacy groups, both in our work groups, as well as in the work of the Health Information Security and Privacy Collaboration at a state level. We've had consumer advocates come and talk to the states about how to engage consumers, and we've required them to engage consumers and consumer advocates in their approach. So we are trying to get that consumer engagement

up front as the policies are being developed.

Many of those projects have recommended consumer education and that is part of some of those state implementation plans, which I think can be helpful. And as Rob had mentioned, again, there are some opportunities for consumer control so that if folks are comfortable with sharing some information but not others, there may be opportunities to create policies in that area. Again, we don't have specific policies at this point, but there are opportunities there to get more consumer engagement and consumer trust based on a lot of the different activities we're doing.

DR. TUCKSON: So here's what we're going to do. We're going to do real quick questions and real quick answers. This has been terrific but we've got to get a break in, and we have to be back in here at 10:15 because we've got all these important people calling in for the next part.

So, Marc.

DR. WILLIAMS: Brief comments. Just to reinforce what Francis said, we are moving ahead on family history and actually already have a draft use case to take that forward. Since that information is already available, unfortunately in unusable form in electronic health records, we're trying to say can we convert it into something useful.

The second point was the interaction between the different work groups. I think the use cases are really an excellent vehicle. As I've begun to review some of those that have come out of other work groups, I can see where pieces of what our charge is would fit into others. So I think using those as a point to be able to interact and suggest that perhaps we could include something from our work group into this that would enhance that use case could be quite powerful.

And the third is just relating to the tension that Reed mentioned about the harm from privacy violations, which for most cases, still represents a theoretical rather than a tangible harm, against the tangible harms that are resulting from the inability to use the information that we have. Again, just to take it back to the family history, this information is already in the medical record. It is already available for anybody who wants to look at the medical record. But if we could actually take that information that's there and put it into a usable form, we can prevent tangible harm that is occurring because we don't know the information.

DR. TUCKSON: Let's make sure we come back to that, Marc, in the discussions to come. I think that's very important.

Chira?

MS. CHEN: Thank you for your presentation.

I would like to find out how these electronic records are being kept. A provider A and a provider B, they are from different, separate systems, where a patient goes to two different providers and how they could be connected and how they are being protected.

DR. KOLODNER: That's at the heart of our agenda, that is, first of all, standardizing the information so it is usable within each and not just textual information, and then developing a network that is secure, how do we authenticate the user, how do we know that they are authorized to receive that information, and how do we move it across so that the systems themselves can receive the information and incorporate it as part of the thing. That is actually what we're challenged with doing. And we have examples where that is happening on a small scale, and what we're looking to do is how do we foster that widespread use.

MS. CHEN: This especially will be important for a patient that does not have insurance, that just goes from provider A to provider B just for a specific treatment and that's it, and how these are going to be connected and how they're going to be followed through.

DR. TUCKSON: So you absolutely got to the heart of the matter. You've spoken right to the heart of the issue.

DR. KOLODNER: One thing just to mention is we're working with HRSA to make sure that we don't increase the gap, but that we actually address safety net provider needs and rural and underserved.

DR. TUCKSON: That's key. That's key.

Joe?

DR. TELFAIR: Since I have to keep it short, I'll cut down on the number of questions that I had and others do too.

DR. TUCKSON: Sorry.

DR. TELFAIR: That's all right. You're the boss.

(Laughter.)

DR. TELFAIR: Just on two things, and this is an area I asked earlier. The first is if you could speak to the maintenance and sustainment of the system itself, how you anticipate that that will occur. It's a long-term issue because you have a development piece, but when you are done with the development piece, now what? How do you maintain that? That's the first question.

The second one then is also what do you have in place at the current time that addresses issues related to monitoring the policy and work group process because you have a lot of those. I know every group always has goals and objectives and that sort of thing, but how do you get a sense that they're moving in a direction that's consistent with the overall intent of the effort itself? Because that to me will have a lot to do with your outcomes.

DR. KOLODNER: With regard to the system, what I mentioned is is that our focus is to enable the market forces to work so that it isn't that we're developing a sustaining system, but we're fostering the development of that. So the electronic health records have to be self-sustainable within the provider setting.

The personal health record which, as Jodi mentioned, may in fact be the great disruptive technology, may be the thing that, when the consumer gets it and understands the value of it, may take off faster than the providers are adopting the electronic health records. It may actually push that forward. We'll see whether that happens, but it's certainly possible.

Right now there's a number of efforts, employer-based, insurer-based, or individual-based types of personal health records. Each of those will be self-sustaining. They need to occur, and then what we need to look at is how do we have a governance process. That's why we're looking and having the AHIC move into the public/private process that will oversee and foster that. There are other examples where the networks are not sources of profit but actually are byproducts.

If you look at how much we spend in health care today and how inefficient it is, if we were to take just a small portion of that, that would more than sustain the infrastructure, but we need to make sure that market forces are there so there's actually a movement of those dollars in so that we can get the value for our dollars spent.

DR. TELFAIR: But that is actually my point. There's a utility issue in regards to the actual application of this process. So I'm wondering whether or not any of your groups are actually developing a set of concrete, adoptable recommendations about them. There's the wish side of we hope this occurs. There is the side that history may play itself out. But then there is the aspect of will they actually get this done, given what we know about the way that our health care dollars and decisionmaking around those dollars are actually spent and how that information is influenced.

I guess I'm just trying to get to the point that this is a very good system. And this is for both of you all. This is a very good system, but it always falls apart when the rubber hits the road, particularly around those who are trying to assess this. And if you're talking about working with states and localities, that is pretty much what they're real concerned about.

So I'm just wondering, given everything, do you have any groups that are focusing on concrete, usable recommendations for both sustainment and then for assessment of that process?

MS. DANIEL: In almost all of the contracts that we have with the standards folks, Certification Commission, with even the State Alliance, and others, we've asked them, as part of their contract, to identify sustainable business models. With our NHIN prototype contracts, one of their requirements was to develop sustainable business models that could be used to sustain a nationwide health information network. They presented those at a public forum that we held for them to display what their prototypes were, as well as the business models for sustaining those networks.

So it is something that we're incorporating into a lot of what we're doing. We understand that that's one of the biggest challenges that we face and we're trying to make sure that as folks are looking at the technology and looking at the policy issues, that they're looking at those as well.

DR. TUCKSON: Also, I think, Joe, you've got to realize that a lot of this stuff -- and it may be a model that we need to think about or that challenge we got from Sheila a moment ago around public/private partnerships. It's going to be very difficult for a software vendor to be able to put forward a product that does not have CCHIT certification in it. It's just going to be hard to do business. So I think there are certain things that are being built it. But I think your question is appropriate.

Let me do this as I get to Muin, and Steve had his hand up. Here's the deal. This committee is in training. We're in shape. We are an in-shape committee. And I think that we can probably manage to know, you know, you need to slip out quietly to do a bathroom break or grab a cup of coffee. And we don't need no darned breaks anyway a lot of times --

(Laughter.)

DR. TUCKSON: -- because this is a hard core committee.

So since we've got four important people about to call in at 10:15 on genetic discrimination, which we have to be in for because we asked these people to stop their work to do it, we're not going to worry about the break. We're going to keep asking questions until 10:15. So that way, we get Muin in and we get Steve in. So you're in shape. It's all right. You don't need a break.

Muin, go.

DR. KHOURY: Reed, I admire your firm leadership on this. So I'll try to be very quick. But thank you very much for both of your presentations.

Actually the ultimate utility of personalized health care resides probably not only in establishing standards for how you put the stuff in the records, et cetera, but trying to connect the providers and the patients so that patient care and disease prevention can be achieved.

So in terms of genetics, there are the three areas that we alluded to: genomic tests and genetic tests; family history, which is very, very important; and then a third area which touches upon Reed's early comments about our initiative called GEDDI, Genetics for Early Disease Detection and Intervention, which goes along with this.

So right now, for example, there are many people with familial hypercholesterolemia that are missed in the medical system. I mean, these are people with very high cholesterol. They may have a family history. They have other signs and symptoms, things like hemochromatosis where people show up with chronic fatigue and maybe elevated liver enzymes.

So I think the ultimate utility of this stuff is the ability to meld in the results of genetic tests with the results of family history with the results of prompts of signs and symptoms that together will allow the health care provider to make early disease detection and then intervene in a much more effective way.

So I think the plug I have is, in addition to genetic tests, family history, add a way to code and allow for signs and symptoms to come out through the medical records, but I didn't see that

here. So that's one question.

The other is aside from transmitting the results of these things -- you know, you have a family history, a positive test -- the ability of decision support by the physicians and the health care provider to figure out what these things mean. So when does a positive family history mean anything? So, for example, in our family history initiative at the CDC, we have a classification of average, moderate, and high. So if these things can become part of the coding behind it so that you will see not only a family history, but a family history of sufficient magnitude to allow sort of a prompt to refer for genetic testing, perhaps that could be it.

So these two things are questions and maybe they're too much detail at this point. But I would encourage you to explore them, and if you have any comments on these right now, feel free.

DR. KOLODNER: Just a brief comment and that is, I absolutely agree. First of all, the linkage between the personal health information that an individual might have and the provider, bi-directional exchange is critical. That's why the PHR is really just another node on this network, and it's up to the individual how much they choose to share or not share.

But the functionality that you're talking about within the electronic health record, both for the provider, as well as for the individual, because at least certainly from my experience in VA, we're now starting to give the same reminder prompts to the individual so they can be an active part of their own health care, is important. And what you're really identifying is the edge of what is their knowledge and where can we, in fact, put those prompts. They're relatively sparse right now but will increase. We need to make sure that the functionality is there.

So that would be something -- and I suspect it will be at the next round or two for the Personalized Health Care Work Group -- that beyond family history, they may start to do a use case having to do with some prompts that would be in the clinical decision support area.

DR. TUCKSON: And one second from Steve.

DR. TEUTSCH: Yes, very briefly. We talked about trust at the individual level. There's also trust at the group level. As this information gets used for population health interventions and population health, clearly we need the trust of these groups and how will it be protected and what will be the mechanisms because, obviously, it can create lots of population-oriented concerns as opposed to those just at the individual level.

DR. TUCKSON: All right. We're going to go ahead and dial in on the phone.

Let me just say this. One thing the audience and members need to know. It's good to slip out quietly, whatever you've got to do to take the break. These damned doors are going to kill me. So if you can, let's maintain good door etiquette.

Thank you, Bob and Jodi. We really appreciate it. This is a great relationship we've established. Let's keep this going, and I really appreciate your effort today. Thank you so much.

(Applause.)

DR. TUCKSON: Now, we're going to dial in and that's going to be its own technical issue, but we're going to do that. Members of the committee, try to really be here, you know, like now.

Can you guys hear us on the phone?

MR. PETERSEN: Yes, we can.

DR. TUCKSON: Great. Wow, technology. Well, listen thank you so much and welcome to the committee meeting.

Let me just make sure that I know who we have. Kris, are you there?

MS. BRADSHER: I can slightly hear you. This is Kris Bradsher.

DR. TUCKSON: Yes, Kris. Are you having trouble hearing?

MS. BRADSHER: I've got my ear close by to the phone. So it's a little bit better

here.

DR. TUCKSON: You are coming through spectacularly.

MS. BRADSHER: Oh, good.

MR. PETERSEN: This is Brian Petersen. I'm also having a little problem. It's not that you're unclear. You're very soft.

DR. TUCKSON: And in reality, I'm screaming my head off. Let me just ask if there is a technical solution to this. Wait a minute. Our crack technical people are on the case.

So, Brian, I at least now know that you are there. I know that Kris is there. Do I know if Keith is there?

(No response.)

DR. TUCKSON: And what about Michelle?

MS. ADAMS: I'm here.

DR. TUCKSON: Thank you so much.

So while they are trying to boost my voice --

MR. PETERSEN: I think you got a lot louder.

DR. TUCKSON: Okay, well, great because I was getting a headache from shouting. So this is great.

Well, listen, first of all, let me introduce myself to you. I'm Reed Tuckson and I'm the chair of the Secretary's Advisory Committee. You are being very clearly beamed into a conference room here at the University of Maryland Conference Center. There is a table full of brilliant advisory committee members and an audience full of equally brilliant smart people.

We are really pleased that you've taken the time to give us an update on the Genetic Information Nondiscrimination Act.

For the members of the committee, as you are aware, the enactment of federal legislation to prohibit genetic discrimination in health insurance and employment has been this committee's highest priority since we were established. We monitor congressional efforts on this issue very closely. The Genetic Information Nondiscrimination Act of 2007, GINA, was introduced in both the House and the Senate as H.R. 493 and S. 358, respectively, and many people have been predicting that, after a decade of effort, the legislation will finally be passed by Congress and enacted into law.

There's been an unprecedented amount of congressional interest and activity. This bill has been approved by the Senate HELP Committee and three committees in the House of Representatives. Floor action is anticipated in both chambers very soon.

Our presenters this morning have all been at the center of congressional efforts related to GINA and they are still intensively involved in Hill business this last week before the Easter recess. We are, therefore, grateful that they were able to devote some time to bring us up to date on the bill's progress and prospects for full congressional passage and enactment.

In consideration of their hectic schedules, they're all joining us by phone this morning. So we're going to begin.

And by the way, also to our guests on the phone, somebody who I know you have seen much in this process, Francis Collins, is here with us as well.

We will begin with Kris Bradsher, who is filling in, first of all, because -- Kris is smart herself on this, but also involved with Deputy Assistant Secretary for Legislation, Craig Burton, who we described earlier in the meeting. She will be providing an overview of the legislation and the administration's stance on the key issues that have arisen during the hearing.

So let me just start there, and, Kris, thank you for taking the time.

MS. BRADSHER: You're welcome. As Dr. Tuckson has mentioned, I'm with HHS's

Office of Legislation. I work with Craig Burton, and he was called up to the Hill. So I am going to talk on his behalf.

Let me start out with the administration favors enactment of legislation to prohibit the improper use of genetic information in health insurance and employment.

Currently on the Senate side, they're working on some remaining issues.

On the House side, that's where a lot of the action came over the course of the last few weeks. I know our folks from the House can probably tell you a little bit more. On the House side, we're told they will work to reconcile three versions of the bill, with the goal of having one bill sometime after recess. Those three versions are from the House Education and Labor Committee, the House Energy and Commerce Committee, and the House Ways and Means Committee. Each have jurisdiction over parts of the bill.

Last Friday, as you know, Secretary Leavitt had announced steps towards a future of personalized health care. And I understand, Dr. Tuckson, you were there with him as the Secretary outlined a course for achieving personalized health care. Genetics nondiscrimination plays a big role in this top priority for the administration, and the Secretary has made passage of genetics nondiscrimination legislation a top priority this year. And we are working with Congress to make that happen.

Finally, the Secretary is pleased with the progress made by the advisory committee and all the work that you have done so far as we move toward this legislation. We look forward to continuing to work together on legislation and are very happy that you have made this your highest priority as well.

DR. TUCKSON: Terrific, thank you.

Before I get to our colleagues from the Congress, are you able to let us know now whether there is any plan for a statement of administration policy on this issue?

MS. BRADSHER: As you know in the course of the last Congresses, we have made statements. So seeing that as a precedent, yes, I do believe there will be a SAP coming out. I do not know when. We'd like to see what comes out of the House side.

DR. TUCKSON: All right. Well, thank you very much. Will you be able to stand by?

MS. BRADSHER: Sure.

DR. TUCKSON: Great.

Let me turn to Michelle Adams, Legislative Director in the Office of Representative Louise Slaughter. Thank you so much, Michelle.

MS. ADAMS: Oh, yes, my pleasure.

Just to reiterate, I think most of this has already been covered, but we had three committees of jurisdiction in the House and all three have finished their business as of Friday, marking up the bill and reporting it. All three, Ed and Labor, Ways and Means, and Energy and Commerce, ultimately passed the bill out of their committees by voice vote. So now we're going ahead to reconcile the three different versions before it comes to the Rules Committee, and we're hoping for floor action shortly after recess.

DR. TUCKSON: Great, thank you. If you'll stand by then and let me turn to Brian.

MR. PETERSEN: Sure.

DR. TUCKSON: By the way, Brian, Deputy Legislative Director of the Office of Representative Judy Biggert.

MR. PETERSEN: I think Michelle has covered most of the issues here in the House. I just wanted to say that we continue to push forward with a strong bipartisan effort on this in the House with Ms. Slaughter's leadership and my boss working on this legislation and trying to work in the most

bipartisan way possible to get a bill, not only to the Senate but to the President's desk, that can be signed into law. So we're happy with the progress we've made so far on this. Obviously, a lot of work has been done in the House so far, and this bill has been around a long time. So we're hoping to move it forward and get it out of the House soon.

DR. TUCKSON: Great.

By the way, again, if either of you could just give those of us who are not experts in this sort of thing -- so once it comes out of the House, what then do you see happening in the Senate, and then how do you sort of get the two of those things together?

MR. PETERSEN: Michelle, would you like me to or do you?

MS. ADAMS: Either way is fine.

MR. PETERSEN: Okay. Just for a second, obviously, after it passes out of the House, the process is one in which the Senate has two options -- actually, I guess three options. Number one, they could pass their own version of the bill and insist on a conference with the House, in which case we try to work out the differences between the House and the Senate version in a caucus between the House and the Senate. Another option would be that they could take up the House bill and pass it as is, which would send the bill directly to the President's desk. Or a third option would be they could take up the House version of the bill, make a number of changes, and send it back to the House to see if we would agree to those changes.

Michelle, hop in if you see other options than those, but those were the three legislative opportunities that we'd look for.

DR. TUCKSON: Michelle, let me just ask you then, given that you've described that the bill has gone through a variety of committees in the House -- I know it's gone through Education and Labor, Ways and Means, Energy and Commerce.

MS. ADAMS: Correct.

DR. TUCKSON: What, if any, significant changes to the original bill have been made, or did what went in come out?

MS. ADAMS: There have been a few changes mainly because, you know, this bill has been around for 12 years.

(Laughter.)

MS. ADAMS: So some of the things that we did were actually updating, so for example, the definition of family member would be consistent with HIPAA, which wasn't around when my boss introduced this bill 12 years ago. So we've made a number of changes like that to bring it up into current standards.

In each instance, the committee folks have been working with my office and Brian's office very closely, and I think trying to merge the three different versions on the bill won't be too bad because as it's gone through every committee, we've made more and more improvements, but it's kind of been consistent with what the previous committee did.

DR. TUCKSON: So actually, other than this sort of fundamental HIPAA stuff, it sounds like you're saying, if I hear you, that there are no significant changes. Let me then ask if that's true? And maybe, Brian, you could comment.

Is there any significant concern about the bill? Who's fighting against it? Is there opposition to this bill that's going forward?

MR. PETERSEN: Sure. Michelle, would you like me to handle that one?

MS. ADAMS: If you want to.

MR. PETERSEN: Sure, that would be fine.

I would say that a lot of the changes that you've seen in the three different committees,

as Michelle has said, are not that big of changes. Usually it's a situation where the changes are slightly different in each committee. So, obviously, that presents some minor problems as far as getting one version of the bill that is consistent.

As far as opposition, I would just say that the bill is widely supported by, I think it is, over 140 different groups, and there still remains what I see as some reluctance on the part of some insurers that stand behind and support this legislation. But in the past, over the last few years, I think we've seen statements from them that show this bill not only would work as intended, but would not cause problems to the way in which they manage health care.

So I'm not sure what, at the end of the day, it will look like as far as groups in opposition, but I think that it does say something that the bill in the last few years has passed the Senate unanimously twice. We have over, I think, 90-some Republican cosponsors and I think over 120 Democratic cosponsors in the House. There's just wide, wide, wide support, and I think that's kind of the message to take away, that while there might be a group here or there that we could point to that doesn't like a certain piece of it, I think to a large degree, a lot of the opposition has been muted to the bill.

DR. TUCKSON: Well, we're going to turn now to some of the members of the committee who have questions, and we're going to start with Marc Williams, then followed by Francis Collins.

DR. WILLIAMS: Thanks for the opportunity to comment.

One of the issues, as I read through it and was asked to comment, related to what I know has been an extremely thorny issue over the years and that is the definition of what constitutes a genetic test. In reading through the language, it refers to, of course, DNA and RNA, but also, I believe the language is analysis of proteins and metabolites that would also "allow detection of a genotype." That, I know, has caused some concern as that could be very broadly interpreted in terms of what do you mean by detecting a genotype. So could a cholesterol test or could a blood pressure measurement be interpreted by some as detecting a genotype?

I didn't know if that had received any attention in the markups and how that was addressed and whether that can be further clarified in rulemaking or whether it will ultimately come to a test of case law once the bill is out.

MR. PETERSEN: I guess I'll make a brief comment on that. I think I would kind of at least like to hear Kris' opinion on the regulatory side of things as it relates to that.

Number one, in the committee, you did see an effort by a number of Republicans, Mr. Stern's amendment I think being the highlight, of an attempt to narrow the scope of the definition of genetic test in such a way that I think would be rather problematic. In Mr. Stern's amendment, they attempted to amend the definition of genetic test to basically force the Secretary of Health and Human Services to create a master list. So in a sense, we're only protecting tests and information that fall under this category with master lists created and maintained by the Secretary of Health and Human Services. So I think that is kind of a huge regulatory burden for the Secretary of Health and Human Services and also not very functionally efficient as well. So, obviously, there have been some attempts to narrow the scope of the bill like that, but I would say that those attempts have been more problematic than anything else.

I'd be happy to hear what Michelle has to say on the subject or anything that Kris would have to say about how the current definition functions and whether or not they think that the Secretary of Health and Human Services will be able to provide the necessary guidance through regulation to make sure that some of the things you mentioned are properly addressed.

DR. TUCKSON: Thank you.

Francis?

MS. ADAMS: Just to add on to what Brian said. This is Michelle. The attempts to

change the definition were defeated. So we're moving ahead with the definition that's in the bill.

MS. BRADSHER: And as far as regulation goes, we'll work with Congress. We do have a regulatory process. The regulatory process usually works with public comment. So it is something that we're prepared to address, but we'd look forward to seeing what comes out of the House as a final bill after reconciling after recess.

DR. TUCKSON: Thank you.

Francis?

DR. COLLINS: Thanks. I certainly would like to compliment those of you who have taken time to be on the phone with us this morning, Kris, Michelle, and Brian, for the efforts you all have been putting into getting this bill as far along as it is. And after 12 years of trying to see this happen, it's truly gratifying to see this coming together in a bipartisan way that has real momentum. I particularly would like to recognize the important efforts of Representatives Slaughter and Biggert in the House in making that so by their strong sponsorship of the legislation and to many others who have endorsed it as well.

I'd also like to recognize the Coalition for Genetic Fairness, an organization that has come together to support this legislation. It has become a very important voice in that effort, led by Sharon Terry who's here this morning, and has, I think, brought together many different constituencies that all see the need for this particular form of protection, and in a very detailed way, I think, assisted in a process of trying to be sure that the bill is crafted and put forward in a way that's going to provide what the public needs and deserves. So a lot of people putting a lot of effort into what now appears to be a very encouraging series of events.

But we're not quite there yet, of course. There are still some obstacles that could get in the way. As you heard, the Rules Committee will have to figure out what to do with these three different versions, then will have to figure out, in terms of the House and the Senate version.

In terms of the question that was just asked, that was actually something I wanted to bring up. There was this proposal that, in fact, the definition of a genetic test might be something that would require sort of an ongoing list to be generated, curated by the Secretary. I just want to comment from a purely scientific perspective what a really bad idea that would be because the ability to define at any given moment of the day on a Thursday what has actually arrived at the point where it could be potentially useful as a genetic test in a research project is such a moving target. I don't know how anybody on the planet would have the ability to do that, especially as we are now seeing in the course of this year and a couple of years to come, we're going to have all of these discoveries about genetic risk factors in common disease, in diabetes, in cancer, in heart disease, and asthma. Each one of those discoveries, if validated -- and many of them will be -- will potentially be a useful topic for research to try to figure out how to use that information to help people in their own personalized medicine agenda, but we'd want to do that in research before you'd do it in clinical practice.

But, obviously, one of the great risks right now, in the absence of federal legislation to protect against genetic discrimination, is that research is being impeded. We have very good evidence of that at NIH, that lots of people who would like to be part of such projects opt out because of their fear of this kind of discrimination. One of the things we hope to be able to say to them very soon is that there is now that kind of protection and they need not fear participating in an NIH research study because of that risk that their genetic information might get used against them. If we had to somehow also fold this sort of ongoing curation minute by minute of what is new and exciting into a research study somewhere, it would be, I think, totally impracticable.

So as difficult and challenging as those definitions of genetic tests and genetic information are -- and they've been developed, of course, over many years -- I think probably one should

not try to impose upon that the responsibility of any person to try to say what's on the list and what is not. It just simply won't work.

DR. TUCKSON: By the way, that's very important.

I've asked Sharon Terry to come up. She was going to be quiet there in the audience. But, Sharon, I think it's so important to hear from you, especially with our legislative colleagues on the phone, sort of your response to how you see things and any issues from your point of view in terms of barriers to getting this done. By the way, let me, in doing this, explicitly second Francis' comments about not only your personal leadership, but the organization's leadership in moving this forward.

MS. TERRY: Thanks very much. And as you know, I've had many visits to this committee where I wasn't able to be smiling all the time to say we actually are moving the ball forward.

I, again, would second or third the thanks for the huge effort made, especially by Michelle Adams from Louise Slaughter's office and Brian Petersen from Judy Biggert's office. They've really worked day and night and literally day and night, sometimes through the night, on this bill especially over the last few weeks. So a huge, huge thanks to them.

I am really thrilled to be where we are. It's almost quite remarkable to me to think that this early in a session we have this number of cosponsors -- 215, 219. I don't remember exactly what today. And to be able to have gotten the bill through all three committees this quickly -- and there were many hearings, many markups over the last few weeks -- has been enormous.

It has not been easy. When those on the outside say, isn't this fabulous how this is flying through, I think Michelle and Brian will agree with me that it didn't fly. It was a big rock that we rolled up a very steep hill. It wasn't without bumps and there were certainly a lot of the special interest groups' interests along the way, including other interests that I learned. As soon as the bill started to move fast, I joked that only the beef lobby didn't jump on the bill. So we're very pleased to have it in this shape, even in this form, this far.

I think my main concerns going forward would be that we could be really clear in the reconciliation of the three different sets of issues around the bill. I know that Michelle, working with Chairwoman Slaughter will be very careful about making sure that the bill is as strong as it can be and that it does what it needs to do.

Around that, I think the issues around genetic testing definitions, for example, were worrisome throughout the process, and I think it might even be good for Francis to make another comment about the issue around the definition, particularly since the issue that Marc brought up about whether or not metabolites and proteins that indicated genotypes should be included. I think Francis made that quite clear in his testimony and he did testify twice during the time. And I think that would be good for him to comment on.

And the last thing I'd say is one thing I didn't get to say so much in the hearings because they mostly wanted to hear from me about the history of the coalition, which has been fabulous with industry and patient groups working together with professionals. But I think that we should, as a nation, think about so what have we lost. Not only the numbers of people that have been discriminated against all these years, but in the numbers of people who did not enroll in research in clinical trials and where we might be as a nation today had we not had this impediment that other countries don't have and that other countries look at us as an advanced nation and say, we can't even protect our people's genetic information. So I think that that's very significant as we move forward.

I think that both Republicans and Democrats, that insurers and manufacturers and patients can stand together when we finish this bill and say, what a great thing we did for people. It's late in coming, but here it is.

DR. TUCKSON: Before Francis engages your question, I don't know whether you

were in the room earlier when we talked about the health information technology discussion. I don't expect that you do, but in case you do, I wanted to give you the opportunity, if you have any thoughts on the privacy and security elements in that discussion and any relationship that you see. I tried to underline that issue and don't know whether you wanted to comment.

MS. TERRY: So I appreciate your underlining that. I heard Secretary Leavitt at the PMC talk at the Press Club on Friday, and he was quite clear, as were the people here today, about the importance of the health privacy issues in health IT. I can't imagine that without this bill passing, any of that can go forward. I wish we came, again, to this game sooner. I wish we had had more forethought several years ago from the Secretary on down that we really had to push hard to get this bill done and quicker. I'm glad to see that there are clearly practical issues on the table before us so that we can get real about how fast we need to make this law and implement it. So I think those things are totally married, and without it, it wouldn't be very effective.

DR. TUCKSON: Thank you so much.

Francis?

DR. COLLINS: Well, this issue of the definition of genetic tests and genetic information has certainly been a challenging one to try to put down in a limited number of words what exactly is intended, again, with the goal being to protect people against discrimination based on that kind of genetic information.

One recognizes that the ways that you detect genotypes are not always limited just to DNA and RNA, but certainly there are indications at times where one can do that using the measurement of a protein or of a metabolite. And it would be unfortunate, therefore, if you intended to protect somebody but it just happened that the test that was being used at that point was not a DNA or an RNA test but was a protein test.

For instance, if you wish to protect people with sickle cell trait from discrimination. And I think we would want to, and in fact, some of the state bills that have been in place the longest were for that very purpose. Sickle cell trait is generally not detected by DNA or RNA. It's detected by hemoglobin electrophoresis. So it's a measurement of proteins. You would want to have that under the umbrella of protection.

Similarly, a Tay-Sachs carrier. Tay-Sachs carrier testing is generally done with an enzymatic analysis to see if the enzyme is present at 50 percent of the normal level, and if it is, that essentially infers rather directly what the genotype of that individual must be without actually going to the DNA level. That kind of circumstance is covered, therefore, under the way the definition is written about what is protected.

But in terms of other kinds of metabolic measurements, where perhaps genes are playing a role but a very complicated one, such as cholesterol, the example that you mentioned, or not to use a totally silly one, your serum sodium, your serum calcium, all of those are, of course, levels that vary over time that are affected substantially by diet, by other circumstances of what's going on in your environment, the intent of this bill is not to sweep those under the umbrella of protection given that what you are measuring there, while it has some relationship to perhaps a long list of genotypes, is influenced by many other factors.

I think it will be very helpful when the dust settles on this. I think what I've just verbalized is the consensus view of all of the people who have been commenting upon the definition. It would be good to have that incorporated into report language in the bill when it's ultimately brought to its conclusion, and that will then assist the process of figuring out the regulations which, of course, have to be implemented after passage to be sure that this bill is interpretable by those who need to enforce it.

DR. TUCKSON: Terrific.

Marc?

DR. WILLIAMS: Yes, I appreciate that and I certainly am completely with you in terms of where that is.

I think the concern that I have is that as much as the genesis of this bill has been from the perspective of the harm that could accrue from the discrimination that can result from genetic information, I think there's also the realization that there are interested parties that would look to bring as much under this bill as they could possibly bring under to essentially protect all information under this rubric of genetic discrimination, which would be equally harmful in terms of the ability to do things such as quality improvement and disease management and things that we, I think, would all agree are good things. So, again, it's a tension issue and it's an interpretation of what reasonable people would consider to be the intent versus what unreasonable people on either side of the debate would consider to be how they could use the language to foster an agenda.

DR. COLLINS: So I appreciate your clarification also of some of those concerns.

I think there are two issues here. The one really is which part of information is protected under this legislation in terms of it not being something that can be used by a health insurer or an employer to make a discriminatory decision. Then there's a separate issue about will this get in the way of actual delivery of health care. As has already been touched on several times this morning, particularly by Reed's earlier question, the intent of this bill is in no way to damage that relationship.

I think the bill is written, though, with the understanding that it is health care providers who make those patient care interactions and decisions, not health insurance companies. Health insurance companies are, of course, in a great position to encourage wellness programs, to put out information about what's now available that might be valuable for individuals to take advantage of as far as personalized medicine, but not to request or require that someone actually undergo that kind of a genetic test. That really, we felt, was a conversation that ought to be between the provider and the patient. And I think the bill has been very careful to try to make that distinction.

DR. TUCKSON: Members of the committee, do you have any other questions?

(No response.)

DR. TUCKSON: Well, this is just fantastic. On behalf of all of us, let me thank Kris, Michelle, Brian not only for your willingness to be on the phone with us today, but for the efforts that you've been doing behind the scenes to make this a real opportunity to actually deliver something. Sharon, thank you again for coming up.

Any last comments from our members on the phone?

MS. BRADSHER: Thank you for inviting me.

MS. ADAMS: Yes, thanks for inviting us too.

MR. PETERSEN: Thank you very much.

DR. TUCKSON: All right. Well, then take care and let us know if there is anything that we can appropriately do from our role at this late stage to move this forward. Take care, everybody, and thank you.

As for the committee members, you see if you're disciplined and tough and you're strong, you get a reward. So the reward is you actually will get a break until 11 o'clock. So you do get that 10 minutes and there you go. So we'll see you exactly in 10 minutes and you know that if you're late, oh, my God, the sorrow that you will experience.

(Recess.)

DR. TUCKSON: All right. We're actually trying to start. We're ready to begin, if you can close the door.

Here's what we're going to do. We're going to ask Greg, who doesn't know that we're

asking him -- Greg, so we're going to ask you to come on up to the table for a sec, Greg, if you could, and help us out a little bit.

Those of you for public comment, we're going to come to you in a minute, but we're way early here. So we're doing good.

If you look on your schedules, after we come back from lunch, we are scheduled to go into our discussion on the oversight of genetic testing. We were very pleased to have gotten the guidance this morning from Sheila Walcoff. So what we want to do is -- can we put up on the slides the summary of those recommendations? -- look at the charge that we got this morning. So what I want to do, to make sure that we have a focused oversight discussion when we come back from lunch, is I want to just review with you those recommendations, those charges to us, to see whether or not there are any questions or if we have any issues there as we start to look at things going forward. I asked if Greg would be here in case we had questions that we wanted to ask him about helping us to understand intent or anything that was unclear.

So if you look at what was presented, that we develop a comprehensive map of the steps needed for evidence development and oversight of genetic and genomic tests to improve overall health quality. So if you start out with we're being asked to describe the existing pathways that examine the analytic validity, clinical validity, and clinical utility of genetic tests and then to define the responsible organizations who are, in fact, responsible for those three things -- let me stop there.

Is there any question or issue about our taking up this descriptive assignment? So it's really describing or documenting the existing pathways that examine analytic validity, clinical validity, and clinical utility and then defining the organizations currently responsible for each of those.

So, Muin?

DR. KHOURY: I mean, that's a very good question. Actually this job should be made much easier given all the work that's been done over the past few years. So it's just pulling out these old documents and looking at them.

DR. TUCKSON: Right. So that's a defining of reality.

Andrea?

DR. FERREIRA-GONZALEZ: When you say organizations, can you be a little more explicit?

DR. DOWNING: That would be from sponsors to federal regulatory agencies, research organizations, and professional organizations. That may be different, depending on where you are in the development of evidence from analytical validity to clinical utility or cost effectiveness, if one wanted to even go to that extreme. We didn't include that last parameter in there.

But there are conduits of information aggregation and analysis that we think could be useful if lined up in terms of the responsibility and the questions of what evidence is needed, in some cases resources, whether it's well-characterized specimens or reagents that would enable a certain test to be performed. We would like to see some sort of a categorization, if you will, of the types of information that are needed at various steps.

DR. TUCKSON: Kevin, you look puzzled. Oh, Steve, go ahead.

DR. TEUTSCH: This is very clinical. Is this limited to the clinical issues, or are we also looking at things that relate to the public health and population health utility of these tests? Or is this limited to the clinical side?

DR. DOWNING: If you could clarify the distinctions on how you would see those being separate, maybe it can help with the answer.

DR. TEUTSCH: I think we understand how it could be used for prevention at the individual level, but to the extent that one is going to have this information out there and you're going to

have the genetic information that's going to be used for population health that may be related to toxic exposures in the environment or recommendations for nutrition policy -- or you could think of a lot of things where these tests might have population health impact or for specific ethnic groups or geographic groups.

DR. TUCKSON: I guess, Steve, the question would be -- and Muin, I think, has some thought about it, I'm sure. But I'm just trying to make sure I understand your question. I don't think that this first question that they're raising is -- it's simply any test for whatever purpose has to have some utility and validity. So I think if you sort of put it in that context, regardless of the ultimate application of it, does this thing work ultimately is the fundamental question. So I think if you're saying that you can think of some tests that you would want to see -- tests that would be used at the level of population base, that you should, I think, think about putting that in this mix.

DR. TEUTSCH: I agree. Certainly what you're talking about deals with the analytic validity and the clinical validity. Does it measure what it's intended to do? It's really about the application. Is it limited just in the clinical sense or for population health management?

DR. TUCKSON: So in other words, you're taking a higher level view here for the minute, moving from the specific to an overarching thing, saying -- so let me just see if I can reinterpret your question, if I'm listening to you correctly.

You're saying should a generic purpose of the oversight of genetic testing be for clinical individual patient use and, in addition, tests that are used in population-based environments as well. Should it be that the oversight is both from a generic point of view? I think that, Greg, your expectation from the Department is, yes, it would be both.

DR. DOWNING: Yes.

DR. TUCKSON: Okay. So that's good.

So where I am now on querying the committee is I'm combining, as you can tell, the first and second bullets, essentially which is one thought in my mind. So, again, it is saying to us that they would like us to document and define the existing pathways for analytic validity, clinical validity, and clinical utility and define the organizations that are currently responsible for these activities.

What we've heard from Muin is his opinion that this is pretty much a fact-finding activity. There's a lot of work that's been done, and we've gotten the clarity from Greg that that would include almost all the domains of organizations that may be relevant to this, whether they're in the Academy, whether it is private sector initiatives, whether it's government regulatory agencies. It is to really try to lay out a road map that says here are all the relevant organizations and entities that are involved in this sort of oversight and definition of acceptability.

Are there any other questions on this first point?

DR. FERREIRA-GONZALEZ: We have heard this morning that the Secretary's office is actually looking very closely at the oversight issue within the federal agencies. I was just wondering, as we go through these different questions that cover not only the public sector but the private sector, how do you think we should focus our work on these issues since the HHS office is already looking at the federal issue? Should we just focus first on the private sector? I mean, what is your take-home on that?

DR. DOWNING: The bulk of the efforts thus far are looking at -- as you know, each of the agencies that play in this space with regard to genetic tests has a lot of different authorities assigned. And how those align and how they're applied, what are the intersections of them has been the focus of trying to develop more comprehensive understanding internally. One of the roles of the Department is to assure that the communications and interactions of various regulatory aspects and the deployment of their policies are clear and are understood by the other organizations and aspects of the

duties that other agencies perform are done in concert in understanding of that. So our efforts to this point have been trying to, in an exploratory way, look to see where are those intersections and where do the authorities of one agency align or perhaps intersect or not in terms of gaps or overlap of particular policies and regulations.

One element that I would like to interject here also is on the aspect of genetic tests. Whether it's the performance of them or the ways in which the information is acquired and delivered to those that use it -- there are many different types of technologies that are evolving now. And I would think that looking historically at the documents from 2000 and 2001, I realize many people have probably moved on from the committees that worked on that. One aspect that may be of interest for this group is to look at specific requirements for different types of genetic tests, whether we're simply talking about PCR or complex, multi-gene array analyses and how the information from that is developed may have some differences in terms of the clinical validity as well as the analytical validity in how that information is developed.

So we would ask that the interpretation and defining of genetic tests take into consideration the methodologies, the types of information that are developed, how it's processed and presented as information or data to be utilized for clinical applications or in population-based health.

DR. TUCKSON: Let me make sure then. We've got a couple of issues here. I want to make sure.

On the first point, Greg, then as we look at putting together the map that has public and private sector initiatives that are involved in analytical and clinical validity and clinical utility, you're saying that even while the government efforts are going forward to look at its domain, we are to be looking at this comprehensively and pointing out from our map where those gaps are and that sort of thing. So I think that's the assignment that we're being given.

Secondly, you are saying that you want us to be sensitive to the methodologies that are deriving these tests and how information is processed and disseminated as subtleties that we should be thinking about in case there are issues that are obtained there. And that's something that we would sort of add to this first mix. All right.

So this is all what I see as point one. So it's the first two hash marks there I'm combining into one assignment.

Can we move the slides, please, to one next down?

Yes, Marc?

DR. WILLIAMS: One thing on the second bullet, and this is maybe a bit of language parsing. But you're using a term that's different than the one that's up there, and I think it's an important distinction. The second bullet says "currently responsible" which implies that somebody has actually taken responsibility. The terms you're using are "are currently involved with," and I think that's better language because there's a lot of this that's taking place in a very informal or ad hoc way as opposed to a formal way. And I think we need to capture all of that informality.

DR. TUCKSON: Well then, Marc, let's try to do both points and say "are involved with," and then as part of our recommendations, when we get to the recommendations part, "should be explicitly responsible for." So if somebody can capture that, I think Marc is on to something here. We want to say "are currently involved with."

When we get to the end of the exercise, it should be that we are making recommendations as to who should be accountable for, responsible for, and take it out of the informal, unless that informality is working as it should.

Could we move, please, to the slides? I'd like to skip down to the one that says "what new models or approaches for private solely and public/private sector engagement." Could you move to

that one?

Yes, sir?

DR. TELFAIR: I apologize for interrupting, but you covered the first two bullets on that first one and you're deliberately not covering the last one?

DR. TUCKSON: Exactly, for the moment. I'm trying to make logic out of this, and because I'm not as smart as you, I can't do quantum mechanics and, you know, multiple permutations. So I've just deliberately lumped together what I see as one coherent idea, and now I'm moving quickly to a related idea as part of the first idea. I believe this question of what new models or approaches for private sector versus private/public sector engagement in demonstrating clinical validity and utility for developing effectiveness measures for use of genetic tests in clinical practice should be considered and why -- I'm trying to sort of see and sort of try to work with Greg here. I'm interpreting this -- and I may be interpreting it too narrowly -- to sort of getting to the point that Marc gets to around "responsible for." What I think this is getting to is you've got some of these things which can be -- this responsibility is government fiat, whether it's CLIA, whether it's FDA, who should be what. Some of this may be that you can work out responsible public/private partnerships and accomplish the goal. So it's not always done by government regulation. And I think what they're asking here is for us to think about a legitimate role for public/private sort of partnership as a solution to some of these problems.

So let me just ask Greg. Am I overreading the intent of this one or not?

DR. DOWNING: No. I think what we've been trying to do is to understand, much like was discussed earlier this morning, the use case scenario, is where are the information hand-offs, who needs what information to do what with. That has not been clear in some of the earlier meetings in terms of where does that information come from, how is it applied in the decisionmaking processes. And then from a standpoint of affecting clinical care or population-based approaches, what are the key analytical questions that have to be framed and answered in order to develop that information necessary to use the test and use it in a way in which there's transparency about the implications of their results.

We have seen recently published a number of models and discussions by other authors, not by members of this group, about what it would take in terms of organization, the science input, the medical input, the health systems input, in terms of the deployment of these technologies and the information necessary to make a process in which information continues to accrue. And there's refinement about the use of those tools and their applications.

So we don't have a concept in mind specifically, but we think that it's going to take more than just the federal government's role in defining a pathway forward.

DR. TUCKSON: So what I think you've clarified for me is -- the reason I wanted to engage this discussion as part of the clinical validity and utility definition was whether the challenge was more focused on the public/private partnership role for clinical validity and utility versus the appropriateness of the use of the test in clinical practice. I hear you emphasizing more the latter. It's more on the clinical use of the test and not as much on the former. Or is it both?

DR. DOWNING: It's clearly both. That's one of the intersections that we're trying to cross here. Where do those responsibilities currently fall and what are better ways to accrue that information as we go forward?

DR. TUCKSON: And I saw, Kevin, your hand.

DR. FITZGERALD: Just also for clarification, Greg, on this. So in the pharmacogenomics report, we also identified clinical outcomes as an important part of this whole sort of formula. Now, it's not in here specifically, but I'm presuming now you also mean that.

DR. DOWNING: I think that's certainly useful, if the committee can stretch to that point, to look at those efforts. Again, I think they're at various stages of technology development and

their deployment. There's more and more to learn about that. If there are insights and there's expertise of this group to deal with that, then great. If not, certainly the evidence that we're really looking for more proximally related to analytical validity in the oversight of the test kits themselves, the materials that are brought in, the performance of those tests, those things are, I think, the prominent concerns of this committee that have been debated in the last few meetings that we'd like to try to get to in terms of more clarity.

But those longer, more distal aspects of it, I think if there are insights about bodies or authorities or ways to aggregate that information -- obviously we see the future of health IT facilitating that. That was one of the reasons why we were working on that aspect of it downtown. We would certainly be eager to do that, and I know that a number of the other agencies that are here today are also quite interested in those facets.

DR. TUCKSON: So let me do this then. I mean, I get you. The logic of where my head is then is what I think that we are being asked to do -- and you guys are going to need to track this here -- is on point one, this describing the pathways that exist now for analytical and clinical validity and clinical utility and defining the responsible organizations, the people that are involved and ultimately responsibility and accountability, as a co-part of that charge, it also includes to look at the appropriateness and need for public/private activities in this space. So it's basically saying let's look and see if there are some roles there once we lay out this road map for whether or not it's all government regulation, government oversight, but also the role of public/private partnerships in this regard. So just to that point, we're putting all that together as a bundle.

If we will now go back to -- while Muin raises his comment and also -- who's that?

DR. RANDHAWA: Gurvaneet.

DR. TUCKSON: Oh, yes, good. I always messed your name up. So that's why I said it that way.

(Laughter.)

DR. TUCKSON: You are from now on GR.

DR. RANDHAWA: I'm just G.

DR. TUCKSON: Just G., okay.

While we do that, I want to scroll back up on the slides back to the Joe Telfair, who won't let me get by the third bullet of the first slide. So that's where I'm headed.

Go ahead, Muin.

DR. KHOURY: Yes, I guess I just wanted to reinforce your idea before we get to this because those public/private partnership discussions have already occurred as part of the deliberations of previous committees. I think the clinical validity and utility of tests and their oversight, as it exists right now, would never allow for the complete type-proof, so to speak, of genetic tests seeping from research to practice. So there will always have to be this kind of public/private collaboration going on. I think we discussed it at length in previous committees.

So I think part of the existing pathways discussions could be the existing pathways plus the suggested pathways that were discussed in previous committees. So that leads you into, I guess, number three in terms of this.

DR. TUCKSON: Exactly. That's where I'm headed. You hit it right there.

Dr. G.?

DR. RANDHAWA: Thanks, Dr. R.

A point of clarification. I'm reading the words, and it says, "developing effectiveness measures." So is it developing new measures, or is it just collecting measures we already know and synthesizing them appropriately? I wasn't quite sure what the intent of that bullet was.

DR. TUCKSON: I think Greg will answer that. Let me just ask you to restate that again. Reask it one more time.

DR. RANDHAWA: Sure. I guess there are two subparts to that question. One is in here it says, "demonstrating clinical validity and utility for developing effectiveness measures." The two parts that I'm getting stuck on are "developing" and "effectiveness." So in terms of development, unless we're thinking of new measures, we already know many existing effectiveness measures. So are we developing measures, or are we just synthesizing and collecting?

DR. TUCKSON: This is a very important question. I do not think that the charge to this committee is to be concerned about the adequacy or how to stimulate more measures per se. It is the oversight of whether or not new measures are being developed or promulgated appropriately, that they are rational, that there's some accountability for the oversight of it. I don't think we're being encouraged to how do you get more stuff done, more genetic testing done, more tests. It's more of a sense of being clear that there is a relationship in science to the measures that are being developed and that they are connected to science so that the public can feel confident that, just as in the test themselves, there is someone who is involved, whether it's the public or private sector, in making sure that it's not just snake oil.

Now, let me just triple check that.

DR. DOWNING: Yes. We could substitute, in your parlance, the terms of evidence development, if you would like, to use in terms of how do we know that the test is providing the kinds of information that clinicians and health care providers and consumers want and need and can trust and reliably use and under what parameters is it useful in those conditions. If you're thinking about new ways in developing that information, that would also be insightful and useful to whomever carries on those responsibilities. I'm not suggesting on a technical or scientific level that we need guidance on -- I mean, the science should carry forward and the technology evolves. We're not looking for, you know, we need more specific ways to measure RNA and that sort of thing. Is that kind of to your point?

DR. RANDHAWA: Absolutely. So that helps.

The other part was the effectiveness. Are we considering efficacy as a part of effectiveness here, or are we focusing only on effectiveness?

DR. DOWNING: No, I would combine those two approaches. I'm giving, as Sheila mentioned this morning, some latitude to how this committee wants to frame its issues that way.

DR. TUCKSON: By the way, I did a poor job of introducing this topic and moderating it. I think that that last comment is extremely important.

I think that what we are, in fact, doing here is that the Secretary's office is trying to give us a sense of what they think they need, and we're trying to get clear here. When they say that they're giving us latitude, the Secretary's office recognizes that the committee has its own ego, surprisingly. This is a pretty head-strong group. And they're trying hard, I think, to say to us -- and I should have made it this way. They're not trying to dictate to us what we do, but we asked them how could we be most helpful. So you're right.

Within sort of the terms of latitude, I think what they're trying to do is to come back to us and say respectfully to the committee, if you want to know what we need to know to move this agenda forward within the Department, here are the issues that are on our mind. And this conversation that we are now having is trying to get down to little more levels of granularity about what is it that you all really think you all need help on.

So Dr. G. raises an important question, which I hadn't fully understood. There is a subtly here that we're moving from the actual oversight of tests, which we have been fanatically on, to now introducing, in addition to the tests, the measures of effectiveness, which is sort of a step outside of our normal box, which is something that we're going to have to really start to think about whether we

want to engage. I think that we've clearly got that in front of us. So your question actually has been very helpful.

So now, we're going back to bullet three on slide one. So far, we took the first bullet, second bullet, and this last thing, and we took half of whatever bullet this was down in the bowels of the thing and brought that up into one giant gemisch. A technical term, "gemisch."

Now we're moving to topic two which is the potential pathways to communicate clear information to guide tests and treatment selection by the provider. So what we've just done is to take the second half of the stuff we just went through with the public/private partnership stuff and we're now bringing that up and grafting that half to this.

So now we're saying we understand that we're being asked, as part of this one, to sort of talk about the role of public/private partnership, and that means the Academy and professional societies and who knows what in terms of being able to communicate clear information to guide test and treatment selection by the provider. So now I'm grafting that onto this number two.

Do we have any further comments around this number two in clarifying this goal?

DR. FERREIRA-GONZALEZ: Greg, is this where you think we can look at a different technology and how we could communicate clear information to guide test and treatment?

DR. DOWNING: Can you repeat your question? I'm not hearing.

DR. FERREIRA-GONZALEZ: You mentioned earlier that you want us to look at how we not only differentiate testing but also the different technologies, how you go about looking at the different technologies and relating that information to the physicians and how that gets interpreted and ultimately tested. So do you think this is, within this number two, I guess, something that we can address?

DR. DOWNING: So I think, as mentioned earlier, we're not looking for complete inventory of every test that can be done and categorized as a genetic test and then what's needed for this. But surely some framework of understanding particularly those cases where it's not just a positive and negative result, whether we're talking about something like PCR, but where there are cognitive and sort of interpretive skills and analysis that are needed and what levels of expertise and input -- how is that result interpreted and what is the information that's passed to whoever is going to be making decisions with it.

In reflecting on some of the earlier reports, a lot was focused predominantly on the test performance, and we think that still is a very important question. Is the test performed by the protocols in which it was done and the evidence supporting the analytical validity of that instrument or the reagents that are used to perform that test?

But I think, as we're moving into more and more complex areas, that what's new since some of the earlier reports are in those cases in which there's an interpretive side of this that's provided. How is that information gauged? What's the level of evidence that the test results are benchmarked against? And if that's utilizing other data sets and things, how is that performed and what are the cognitive capabilities that are needed to make the accurate determination?

So there, I think, perhaps may be some needs for expertise that might be on an ad hoc basis outside and beyond this group that would be important in informing those processes.

I think, again, just to step up to where we're looking down on all of this, that one aspect of it is that I think Joe is going on -- we found it particularly difficult to start from the very beginnings of when a specimen hits a laboratory or someone is going to be using it or a new method is developed, all of the steps they go through in terms of developing a piece of information that a clinician or a consumer or whoever is doing the test is making decisions about it. Lining all of that up and explaining it to someone in a layperson's terms is very challenging thing to do, and I'm not sure I can do it yet. That doesn't mean that there are others in the room that can't.

But these things in the past have been sort of aligned in pieces and chunks, and what we're trying to do is say where does the information flow go that guides this clinical decisionmaking. And ultimately in terms of the public health interest, that's what is foremost and of importance here.

So I think it's difficult for me, in looking at the kinds of cases and arguments that have been made this way. To do it in the abstract and just describing a genetic test doesn't help us very much if we're not able to put it into some context of saying here are the kinds of information that were accrued, here's how the tests are performed, here are the kinds of skills and knowledge base that are used to make an important piece of information, whether it's a number on a piece of paper that's faxed somewhere or put into some protocol that is able to develop numbers and probability statements. And then long-term-wise, I guess what we're trying to get to is a world in which that information is part of a clinical decisionmaking process.

So we're certainly not getting there yet, but all of those steps require different pieces of information to line up to make the assumption at the end of the pathway that that number has passed through all of those processes and it has valid meaning.

DR. TUCKSON: And it's something we'll discuss when we come back from lunch in terms of the oversight committee, but maybe one way to get at this is to actually take a few examples of case studies, and you sort of start from the beginning all the way through and you trace it and you sort of say, okay, what happens. So some real use case scenarios might be the way to get at it. I really like what you're trying to do.

Let me move quickly to the next slide and the very first one on the top of the page. I'm thinking now that what we might want to do is to make the first bullet -- the first dash there -- the very first question and put that at the very top of the whole thing and make that number one because, at the end of the day, that's the fundamental question. What's the point?

So it's like laying out what evidence of harm exists regarding genetics. Do we have any sense that there are real harms being done because of the gap? So I think it's important to identify what the real -- and I think if I understand the question, it is identifying either what are the harms or what do we think could be the likely harm that will exist through various developments of case scenarios. So we sort of say, okay, let me show you exactly that there's a hole that you can drive a truck through that allows maniac test number three to be inflicted on the public, whether it has actually occurred or not. And I think we have to define actual harm examples and potential.

MS. BERRY: Just for clarification, are these all interconnected? To ask it another way, what if -- and I'm not suggesting we're going to find this at all -- we found there's no harm, no potential for harm, there are no gaps, currently regulatory schemes are --

DR. TUCKSON: Return to your homes. All is safe.

(Laughter.)

MS. BERRY: -- coming along, everything is great? You recommend that we still go to that third bullet under "general questions," which is what are the potential pathways to communicate clear -- I mean, are they connected? Do we have to find that there's harm and gaps and all of that to get to that, or is that a separate -- can I pull it out?

DR. TUCKSON: Great issue. I think the way that we would phrase that, if you think about where the committee is -- and we'll see what you meant. But I think, as I understand it, if you take the case scenario stuff and you drive it along, then you do have that issue still. It still exists, that middle point in your train. It still exists as an issue, and I would assume we would still have to do it.

DR. DOWNING: Right. I think this is all to the element of transparency of how information is gathered and used, and what you decide is safe to go out in the world today may change tomorrow. So we still need to know what are the processes to deal with new information as it unfolds.

I would like to address this harm issue. One aspect of this is really distinguishing -- and Dr. Collins used a number of examples in dealing with GINA this morning, underscoring the immense importance of genetic information in a lot of ways. How is that different than other kinds of medical tests? In the context for legislative purposes, genetic information is a very broad definition. We're going to leave you to decide how you want to define that, but in the context that the types of information that you get that have genetic origin is used for a lot of different types of decisionmaking processes, it seems a tenet to us that levels of risk and tiers of risk perhaps about the nature of the types of decisions that are made based on test results have some bearing on the level of oversight and the kinds of questions and evidence that's necessary in those circumstances.

So the aspect of harm doesn't necessarily mean that somebody has to be harmed in order for somebody to not be doing the analytical work. That sort of thing isn't what's intended here. It's trying to distinguish how are these types of technologies and the types of tests being performed here distinguishable from other types of medical tests. You know, CBCs. We're not talking about cholesterol levels here, I don't think, today. Again, we use those for population-based studies. What is it that's unique and definable about the types of genetic tests here that cause concern?

DR. TUCKSON: Francis?

DR. COLLINS: So I think this is a good discussion about exactly what is the point of that particular bullet. I guess maybe we ought to be a little more generous in terms of what we're looking for. We're not only looking for the evidence of harms or potential threats, but aren't we also looking for instances where public benefit has been slowed or limited, not that harms are occurring, but that benefits are not accruing as rapidly as they might, just to put a more positive kind of view on it, but also to indicate that genetic testing in general, I think most of us agree, ultimately is going to be a public good? Of course, it could be limited if, in fact, it is used in inappropriate ways to cause harm. But not achieving the public good as quickly as it might optimally happen is also something we should be concerned about. So perhaps I'm just reacting a little bit to the language.

Now, maybe you will say, well, that's a harm if benefits are slowed, but it's a bit of a different use of the word than many people would assume where they think of somebody actually being injured. Here I'm talking about somebody just not benefitting because our process for oversight of genetic tests has, in some way, retarded the introduction of highly validated, highly useful tests at an affordable cost that the public can take advantage of.

DR. TUCKSON: But there's the challenge. You were rolling and then you got to the end, and you had to make 14 caveats to explain it. So I think we'll give Greg a chance to see what he means by it. But when we come back and chat, I think it's a provocative point, Francis. I fear -- and, again, we have a whole session this afternoon to talk about these things.

First of all, I like the philosophy that you're getting at here. I mean, we make it seem as if, again, genetic tests are something to be so scared about that, my God, oh, fear for your lives, all. The original way we got into this is pretty specific. It gave the committee a real chance to make sure, hey, let's just make sure nobody gets harmed.

Now, you're adding on something that I think is philosophically terrific, really complex to define, but still important. So I'll reserve the rest of my comment for that at the end.

But what do you think?

DR. DOWNING: I think Sheila addressed this earlier in terms of looking at the aspects that don't stifle innovation and the ability to apply technologies in new ways. I think that we see a lack of clarity and transparency at this point of having some stifling effect of whether it's commercial investment or academic investigators not wanting to really go into diagnostic development in some context because they don't know what the implications of the research will be. So harm is broadly

defined here in the context of what are the implications of the results of not knowing or having that information.

DR. TUCKSON: Good.

Yes.

DR. EVANS: I just wanted to make a plea, if it's appropriate, for being appropriately narrow in this. And maybe that could be accomplished by just switching those two sub-bullets. I don't think that we probably as a committee are intended to address all of the harms that can result from problems with clinical validity, clinical utility. I mean, those are very much the same for problems that arise with the fact that we may be doing harm with PSAs and may be doing harm with whole body scanning.

I think it might be worth, if that's appropriate, defining in some explicit manner that we're looking at the types of harms that can result because these are genetic tests. Is that in the spirit of what you're getting at?

DR. DOWNING: Yes. I appreciate it. It really did not enter our discussions in framing these questions. There are many open questions relative to the appropriate clinical applications and knowledge, and you've mentioned a number that have public health implications.

I think that, at least from my perspective, there are other federal bodies that are dealing with that and you may want to describe them in a broad context, if the committee wishes to choose that path. But we don't expect that that's a necessary charge that you have to focus a lot of time and energy on.

DR. TUCKSON: So let's do this. Staff, follow me carefully on this here. I think this is what we want to do. We've been reordering the thing so we can come back and talk about this, when come back at the end of the lunch break.

By the way, public testimony is coming. Don't get scared. We got you.

Number one becomes describing the evidence of harm, and yada, yada, yada.

Number two now becomes genetic exceptionalism because we're focusing on genetics and the issue is what is it about genetic exceptionalism within the context of worrying about harm. So what's different about genetics is number two.

Then number three becomes the combined stuff we did on analytical and clinical validity and describing the responsible, you know, involved organizations and the point about the role of public/private partnerships in that regard. That all becomes number three.

Then number four becomes the notion of the models for choosing the right tests and making sure of the roles for the right choices and the right tests and all of that getting out there.

That then leaves us with asking Greg, in the last two minutes that remain, what do we mean by -- and I'm not sure I understand this point about the resource needed for proficiency testing. Maybe we could just hear a little bit about that and figure out where that goes in the flow.

DR. DOWNING: Thank you, Reed. You have a number of people here this afternoon that can, I think, address this question fairly well, and I think there's substantial talent here.

We heard, at least in the November meeting, I believe, and from others that the development of proficiency tests requires a certain amount of preparation, and how that's done in the community -- I'm not an expert in that and wouldn't want to profess to be able to explain all of the steps involved in that.

But having well-characterized specimens and the processes for splitting or sharing samples, what are the models for proficiency testing? And are there unique and common reagents or things that are used to test and provide common results from different laboratories performing those tests? I think we have not yet gotten a good handle on what that looks like, and particularly as new tests evolve

and roll out, are those things commonly available and what are the implications of that on the laboratory for everything from costs to the availability?

It would be fine to set up a perfect framework, but if it's not going to work in the real world and those things are not developed and there isn't a commercial place that one can go to to get those reagents to do the testing, then what has been achieved by that?

So if there's a menu of materials and things that would be needed, again, in a framework that addresses different types of genetic tests, are those materials necessary to provide the kinds of analytical validity requirements, if those are available commonly, it would be helpful to know those.

DR. TUCKSON: So let me do this, staff. If you would, please, in the ordering, move that proficiency up to right before describing the potential pathways to guide tests and treatment selection by a provider? So, in other words, it comes right after the clinical validity, utility, yada, yada, yada. So once you've got all the clinical validity, et cetera, then you do the proficiency. Then from proficiency, you move to, okay, now you've got all this stuff done. Now it's going to be introduced into the world. Physicians and others have to select tests. What about the guidance there? And then you end up, at the end of all of this, with the last thing, which becomes, okay, the big drum roll is, da, da, da, da, ba, boom, what else should the government be doing to do its job. What is your conclusion about your guidance to government?

DR. DOWNING: One of the examples -- and this has been borne out in this committee previously, and then Kevin's report is the -- just back up and think about this a little bit more broadly now in the context of voluntary submission of pharmacogenomics data, for example, not selectively utilizing those tests, but in the context of what can be done to foster and enhance or bring the science forward by new models of developing the evidence and the scientific framework in which to do this. There aren't very good ways -- and that works right now -- to do comparative analysis of genomic tests, for example.

So we are asking this body, I think, to be creative and think outside the box a bit in terms of the methods and approaches that we don't have perhaps on the ground today that could be developed without a great deal of encumbrances.

DR. TUCKSON: All right. Bottom line, we'll resubmit this back to you and it will become part of the discussion that Andrea will lead us through. Of course, the committee had presaged some of these questions in their work. She will be creative at being able to interweave the two together in a logical and coherent, organized, and efficient discussion this afternoon.

MS. BERRY: Am I taking it too literally when the Secretary is suggesting that we put together a map? Is that purpose of the first three? And I'm going to mess up what Reed already did because the way you outlined the questions makes logical sense and I support that. But if our charge is also to put together some kind of diagram to map out these pathways and communications and oversight, is that something that was intended here so that we should separately consider that as a task? Or is just addressing each of these questions in a logical fashion what we need to do?

DR. DOWNING: We think a tool that would help visually and graphically explain and provide some transparency that my mother could understand it in some context, that there's an overview process that goes through and the technologies are developed and performed in ways that there's an information flow that enables her physician and her clinical provider to know the right information, anything that would facilitate that I think would address Joe's issues, as well as ours.

DR. TUCKSON: I think also, by the way, you will probably see -- I'm not sure whether the staff actually had a chance to do it.

I think, by the way, it's both, Cindy. It is laying out a grid, as I see it. I think staff has

already taken a look at it that sort of graphically tries to lay out what's existing today, what isn't existing, where are the gaps so you can start to just sort of look at it and see. So FDA has this. Here's the thing that has to get done and the FDA has this part of it and CLIA has this part of it. And nobody has this part of it. I think that map is key.

I think the second map we've just heard today is using the use case, the individual cases. So you take a map and you trace it all the way through. So it's a longitudinal map, a "walk through the woods" map, which I think is going to be terrific.

So I think those are great questions.

Let me stop here.

DR. McLEAN: One quick question of clarification back to point either four or five, depending on how you arranged the sequence. The potential pathways to communicate clear information to guide tests and treatment selection. Treatment selection really has not been a focus of the oversight to this point. How do you want us to conceptualize treatment? Management, genetic counseling, pharmacologic interventions?

DR. DOWNING: Yes, that's a good question. The context that a number of these tests are now being applied in the processes for guiding or at least anticipated to be utilized in making pharmacologic choices, but treatment is in this context also more broadly in terms of either wellness decisionmaking processes or others. So interpret the context that someone is taking a test and making a decision altering some process or health function as a consequence.

DR. TUCKSON: I really think that's a great question. I think that's a good way to conclude it.

Let me just make sure that I get it. I think what I'm hearing, what I'm animatedly excited about, is if you sort of, in some ways, start at the end and you say, Mrs. Jones received guidance that was significant to her health and life and/or that of her family as a result of some information.

Now, where did that information come from? Who made the choice of using that information? Was it the right choice? Was she the appropriate candidate to get that information? So that has to do with how it was disseminated and so forth and so on. Was the information that was given about her biological processes accurate? Was the test worth a damn, da, da, da, da? So you start working your way all the way through to the back chain. So I think that's really what we're trying to get at here.

DR. McLEAN: And then you've got outcomes measures that will naturally come in.

DR. TUCKSON: Yes.

Of course, you take the question -- I think it was Marc, or I can't remember. Again, it could be level of population, that in fact the entire Asian American population of Seattle was given such and such information. Was that relevant and right based on some genetic-based testing or information? I think that's the way you sort of work it through.

All right. We're going to have to rock.

DR. FERREIRA-GONZALEZ: Is Greg going to be here this afternoon so we can continue?

DR. TUCKSON: No. This is the last we get to hear from Greg. I'm sorry.

Marc, is it real quick?

DR. WILLIAMS: Yes, this is very quick. I just want to be explicit about something. A lot of what we've talked about are decision support algorithms, those sorts of things. I think we need to be explicit relating to oversight of development of those things because there's already been some talk in other venues of clinical support algorithms that are now being scrutinized under the rubric of a device. So relating to the last bullet, which is how would additional or revised government oversight -- I want to include maybe elimination of as one of the options, that it's not necessarily we're going to keep adding

things.

DR. TUCKSON: So you guys are going to subpopulate this outline in your afternoon discussion. By the way, I have a feeling, knowing you, that you're going to augment the outline because you've probably got other things that you want to look at beyond that which the Secretary's office has asked for. You are not limited by what the Secretary's office is asking you to look at. We are informed by it.

As a conclusion, Greg -- and if you'll send it back to the Secretary and to Sheila -- we are just extremely appreciative to know where we fit into your efforts, so that we're at least being able to be responsive. Since we are the advisory committee to the Secretary, it's nice to know what the Secretary wants to be advised about. So we are pretty specific about that.

We may, in our wisdom, decide to augment and add more to it, but at least we're going to give you back answers to the questions that you have asked. It sounds like the committee is pretty well squared away on that point.

DR. DOWNING: Reed, I would just say we're agnostic about the manner in which this is prepared, whether it's a report or a series of workshops or conference calls and summary documents. There are some deliverables I think that we've talked about that would be helpful. I just want to underscore timeline is of some essence here, and we'll leave you to deal with that.

DR. TUCKSON: So what I think that means, Greg -- and even though we're rushing to closure here, I think this is important to slow down on. As you have been very engaged with us outside of the meeting day to day, we're going to have to give the committee members some sense of the timeline that you guys are rolling on. We understand your overall 600 days calendar.

The question will be to basically hear back from you, oh, by the way, there is an interagency task force meeting on, like, April 15th -- a bad day I chose -- and we're going to deal with questions one, three, and seven. If you've got anything for us by then, it would be enormously helpful to get it in. That's the kind of thing I think we're going to have to look for.

So the subcommittee is going to wind up being fluid and doing a lot of work by conference call and then you guys will join in as need be.

Thank you. You didn't expect to do that. So good job.

Let me invite Deborah Kloos, Gentris Corporation. We appreciate the public testimony and we love you to death. You know, by the way, the draconian five-minute rule.

MS. KLOOS: No.

DR. TUCKSON: Did they tell you that? Did they tell you what happens if you go over five minutes?

MS. KLOOS: No.

DR. TUCKSON: Well, you don't want to know.

So we appreciate the public testimony and we're really happy that you have come forward to us. And thank you.

MS. KLOOS: Good morning, Dr. Tuckson, and members of the committee. I do represent Gentris Corporation, a pharmacogenomics company located in Research Triangle Park, North Carolina. As one of only a few manufacturers currently focused on the emerging pharmacogenomics industry, Gentris manufactures products for predictive genetic testing, including reference controls and in vitro diagnostics.

From the beginning, we have been directed by the FDA to achieve clearance on all of our products. Such a process is not entered into lightly, since cleared products must demonstrate documented design control from the conceptual stage to manufacturing while complying with good manufacturing practices. However, we agree with the FDA that this is the best way to ensure that

consistently reproducible reference controls obtained from properly consented patients are readily available to meet CLIA testing requirements. We have met these challenges and received clearance in December 2006 for six human genomic DNA reference controls for testing of the P450 CYP2D6 gene.

Gentris chose reference controls for our first 510(k) product submission based on the fact that there was one FDA-cleared platform for CYP2D6 testing, the Roche AmpliChip; CYP450 test. CLIA requires that laboratories use controls when performing genetic testing in order to ensure accurate results. We agreed with the FDA that it would be very helpful to the genetic testing industry to provide reliable, cleared companion controls for this cleared platform. Our concern is that this committee might be unaware that non-compliant material from other sources is also being used for the same purpose. This discrepancy is very disturbing to many in the pharmacogenomics arena and calls for action on the part of those in a position to effect change.

Currently there are three main resources for labs wishing to obtain genetic testing controls: one, leftover patient specimens, with or without direct informed consent; two, commercially available research use only or research-grade products, obtained most notably from the Coriell Institute for Medical Research; and three, FDA-cleared in vitro diagnostic controls manufactured by companies like Gentris Corporation and also Maine Molecular Quality Controls, Incorporated.

There are drastic differences between types of resources. Materials sold as RUO are not required to be manufactured under GMP regulations, so they have virtually no regulated quality assurance requirements and are not subject to FDA audits. Their performance characteristics have not been established; neither are they to be used for diagnostic procedures.

In sharp contrast, a small company such as Gentris dedicates large resources of time, money, and personnel to perform clinical trials, submit products for FDA clearance, maintain stability data, and manufacture products in a GMP environment. However, we believe it is well worthwhile to produce products that are qualified for use in diagnostic procedures. We can find no justification for lowering the bar for reference controls when they are such an indispensable component of pharmacogenomic testing.

It is evident that a great deal of attention was focused by CAP, CLIA, and CLSI on providing rigorous guidelines for genetic testing since up until now, only RUO product and residual patient material were available to laboratories. We were grateful to have had a source like Coriell for research-grade reference control material. However, now labs do have other alternatives for many controls as companies like ours are ready and willing to take the baton and meet the higher standard of producing IVD controls. Unfortunately, we continue to see research-grade products or leftover patient samples being put into clinical practice without the safeguards required for IVDs. As long as labs are permitted to use these, they have no incentive to use any FDA-cleared product control. This disparity needs to be resolved before companies lose their incentive for manufacturing IVD controls. It is unreasonable to expect the manufacturer to produce a regulated product when alternatives are still available at a lower cost because they are essentially research-grade products.

So what are we asking of you, the committee? The regulatory infrastructure has not caught up with the state-of-the-art technology. The result of this is confusion regarding what the rules actually are and a failure to apply the rules evenly for all. We urge the committee to recommend to the Secretary of Health and Human Services that its office seek congressional legislation or some other means that would create parity for manufacturers and harmonize the oversight of this area of genetic testing.

We know that the FDA is doing its best to enforce the ASR rule to ensure that only FDA-cleared products are used in situation where there are life-threatening consequences. But we also know that they are seriously underfunded. We're asking the committee again to recommend to the Secretary that his office seek increased FDA funding for the oversight of this particular issue.

This committee can play a key role in assuring that the health care community has access to the highest possible level of genetic testing controls and assays. Thank you for the opportunity to bring this to your attention.

DR. TUCKSON: Deborah, first of all, is it Dr. or Ms.?

MS. KLOOS: Just Ms.

DR. TUCKSON: No, it's not just. You'll now get me in trouble.

This is terrific. Are you going to be around this afternoon, or are you going back?

MS. KLOOS: I have a flight this afternoon, but I'll be around for a little while.

DR. TUCKSON: First of all, this is very important, what you have said. The one thing that at least gets my attention -- I don't know about others -- is the committee often, I think, has to be legitimately concerned about the private sector saying that regulations stifle innovation. So you'll say, well, you know, you guys who don't run companies, you don't know that when you talk about more regulations, more regulations, what you do to stifling innovation. Now, here you are saying we run a company and there needs to be better regulation. So it's not an either/or, black/white deal.

MS. KLOOS: Exactly. What we were saying is that we were presented with a need. We've met that need, and now what we're seeing is laboratories unable or unwilling to use IVD-cleared product because they can get something else cheaper and it's not regulated.

DR. TUCKSON: Here's what I'd like to do. We're not going to be able to, as you heard from the last discussion, jump straight to legislation. The timing of your presentation couldn't have been better.

Would you be available -- outside of the meeting process, if you could provide specificity, as you've done in your testimony. One of the things that we were asked to do is find areas of harm or a threat of harm, and you have very granular knowledge here about an area. If you could provide that to the staff so that the committee can start to examine that, you will have gone a long way in advancing the committee's work.

MS. KLOOS: I'll be happy to.

DR. TUCKSON: This is just terrific. I think it's pretty much on its own. I think we can, in the interest of time -- I don't want to violate a committee member that wants to ask a question, but I think you're right on target here.

MS. KLOOS: Thank you.

DR. TUCKSON: Really, your time here was worth it for you, I hope.

MS. KLOOS: Right. I think it was for me as well. Thank you.

DR. TUCKSON: So you'll follow up. Thank you very much.

Ann Cashion, C-a-s-h-i-o-n, President, International Society of Nurses in Genetics, ISONG. And we have always appreciated ISONG's involvement with this committee and we've always learned and benefitted from everyone who has come before us. Thank you.

DR. CASHION: Thank you. Good morning, Dr. Tuckson and members of the committee. I am Ann Cashion, a nurse scientist and educator and the current President of ISONG, 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 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 nurses, 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 U.S. is slightly over $60,000.

This nursing workforce holds great potential for 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 delineates the genetics competencies expected for nurses practicing at the basic level, as well as enhanced competencies for the advanced practice nurse. In addition, ISONG is one of over 40 endorsing organizations of the Essential Nursing Competencies and Curricula Guidelines for Genetics and Genomics. ISONG members, along with nurse leaders from the American Nurses Association, the American Association of Colleges of Nursing, the National League for Nursing, and others, are actively working to implement these competencies. Articles have been published in journals, including the Journal for Nursing Scholarship and MCN: The American Journal of Maternal Child Nursing. Presentations have occurred at meetings such as the American Academy of Nursing and the American Association of Colleges of Nursing and will be also at upcoming presentations for ISONG and the National League for Nursing's Education Summit.

ISONG is committed to working towards ensuring that the nursing workforce is well prepared to serve their patients' and the public's need for genetic information. ISONG is committed to ensuring that all individuals have appropriate access to genetic and genomic health care and has approved a position statement defining the role of nurses in ensuring access.

ISONG is eager to work with the Secretary's Advisory Committee on Genetics, Health, and Society as you work to ensure access to the appropriate level of genetics care for all citizens of the United States. This includes its work to examine the impact of gene patents and licensing practice on patient access to genetic technologies. We are committed to working towards the goal that our over 2 million nurse colleagues have the knowledge and skills they need to practice effectively.

Thank you, and if you have any questions, I'm available both today and tomorrow.

DR. TUCKSON: Well, thank you very much, and I appreciate your specificity at the end around supporting and helping us on the patents and licensing. I don't know whether you were here at the beginning of the meeting when we reviewed our strategic objectives and priorities. I for one would appreciate it if ISONG would send us a thoughtful analysis on the issue of the status of professional education in genetics and whether or not you feel like from your observations enough is being done in the private sector to handle all this, whether we have a problem or not from a point of view, or whether or not there are some real gaps here. I think you're in a unique position to help us to think through that. And we keep this on our agenda as an important priority.

Any quick questions from the members?

First of all, your statement is eloquent and stands on its own. Clearly, as I said, we have enormous respect for and know that we can turn to ISONG as a resource on many things.

DR. CASHION: Thank you.

DR. TUCKSON: So thank you on that.

If staff would keep me on track on this, but I would really appreciate it if you would send us, to the extent that you feel comfortable or willing to do it, your analysis on the status of -- things that we need to think about going forward on continuing professional development of professionals.

DR. CASHION: Thank you.

DR. TUCKSON: Thank you. Great.

Next is Gail Javitt from the JHU Genetics and Public Policy Center. Gail?

DR. HUDSON: I'm Kathy Hudson. I'm filling in for Gail.

DR. TUCKSON: See, the trick is that while I ask the people their name, it is to help

to move them going to the chair. I wasn't supposed to slow her down.

Kathy, thank you very much for joining us and taking the time to present.

DR. HUDSON: Thank you for having me.

My name is Kathy Hudson. I'm the Director of the Genetics and Public Policy Center at Johns Hopkins University, and almost exactly a year ago, my colleague, Gail Javitt, appeared before you and expressed our strong concern about the inadequacies in genetic testing oversight.

Sadly, little has changed over the course of the last year, and I'd like to take a couple minutes to review what CMS has and has not done and also to respond to some of the statements that CMS has made over the course of the last year.

So briefly, to review, CMS last June told you that a proposal for genetic testing specialty creation was on its way, possibly by early 2007. Fewer than three months later, the agency said no specialty area would be developed.

CMS has given many different explanations for this policy reversal. They told you last November that there was "no evidence" that there was a problem. With respect, we differ.

On the issue of evidence, we fielded a survey of laboratory directors and asked them about their participation in existing formal PT programs. We found that fully a third of laboratories are not participating in existing formal PT programs.

When Congress passed CLIA in 1988, it was gravely concerned about the failure of laboratories to perform PT and its consequences for patient health. For this reason, Congress directed the Secretary to require that laboratories participate in PT unless the Secretary determined that an appropriate PT program cannot be implemented.

Bluntly stated, CMS is following neither the spirit nor the letter of the law. Because of the way in which CMS has implemented CLIA, in order to require PT, CMS first needs to create a specialty, and as you heard, they have now decided not to do that. No specialty. No PT.

CMS has said that the lack of a mandate for PT has no practical effect because there are so few formal PT programs available, and while it is certainly true that the number of tests far exceeds the number of formal PT programs available, to the extent that CMS could require that laboratories participate in available formal programs, it would certainly cause a shift in the situation. And moreover, I think we could predict that more formal programs would be developed. Simple market economics.

With respect to our survey, CMS has characterized our survey findings as identifying pre- and post-analytic errors in genetic testing. And unfortunately, that's an inaccurate representation. Thirty percent of the most common errors identified by labs were analytic errors. Moreover, a strong predictor of whether a lab's most common error is an analytic error is the level of PT performed by the lab. The take-home message is fairly clear: PT matters and many labs are not doing it.

Finally, on the issue of transparency that was addressed briefly in Greg's remarks earlier, in enacting CLIA, Congress directed that the Secretary make the results of PT testing available to the public. CMS has not done this, making it impossible for any external body, yourselves included, to assess the quality of laboratories. There must be more transparency on the issue of laboratory quality.

And finally, CMS has asserted that only a few organizations want the agency to issue a genetic testing specialty when, in fact, over 100 organizations and individuals representing industry, laboratories, patients, and health care providers have called on CMS to move forward. In September, we, along with the Genetic Alliance and Public Citizen, filed a petition for rulemaking with CMS requesting that a specialty be created. Six months later, we have received no response.

In your session today on oversight, I hope you'll focus on the following issues:

First, the need for CMS to move quickly. There's no need to do an inventory. It's pretty self-evident, the importance of PT, and we should move expeditiously forward.

Secondly, we need transparency so that the public can have confidence that the laboratories are performing adequately on PT and have the expertise to ensure accurate testing.

And then the broader questions of a coherent regulatory framework to ensure that all tests are clinically valid before they're offered to patients.

I thank you for your attention.

DR. TUCKSON: Well, we thank you for especially that specificity.

Will you be around this afternoon?

DR. HUDSON: Yes.

DR. TUCKSON: So you will. All right. I think you've raised some extremely important points. I don't know whether, Jim, you are prepared or want to make any clarifying comments before lunch or just let it stand on its own and we'll just grapple with these issues this afternoon.

DR. ROLLINS: This afternoon.

DR. TUCKSON: I mean, that's appropriate.

DR. ROLLINS: Also, I think that probably the persons who are responsible for CLIA would probably be in a better position to address these questions.

Also, number two, I know that in the past that you, as well as, I think, Ms. Berry, met with Mark before he left, and probably it would be a good idea to discuss these specific issues with Leslie Norwalk or her designee who could specifically address these.

DR. TUCKSON: Well, I'll tell you what we'll do then -- thank you for that. I think what I'm interested in -- other members of the committee will have their own interests -- is not so much -- although, I mean, clearly there was some animation around whether CMS has responded or not, and I think that's its own set of issues. I'm much more interested in the generic issues of the role of proficiency testing in this chain of events and whether or not those issues are being attended to appropriately. I'm much more interested in the substantive issues than in the political issues.

So I think that this is actually very important and we should come back to these questions in our afternoon discussion. We may want to draw on you for some input. So thank you for that.

I think Judy Yost will be around this afternoon as well. So we may hear some more there.

As I said, it's always painful to hear that an agency may or may not be responding, and I don't know any of the facts on that. But I'm much more interested in the substance, which I think we've gotten some important granularity in terms of the steps in the process that is worthy of our attentiveness, regardless of any other issues.

Oh, good, Sharon Terry again.

MS. TERRY: With a different hat.

DR. TUCKSON: With a different hat. It's always good to have more than one hat.

MS. TERRY: Now that we can do something besides just nondiscrimination, thank you for the opportunity to present brief comments on behalf of the Coalition for 21st Century Medicine. Though I often appear before you as either a representative of the Genetic Alliance or the Coalition for Genetic Fairness, I believe that representing this new and diverse coalition is important since it represents our commitment to collaborative solutions.

Founded in late 2006, the Coalition for 21st Century Medicine represents 22 of the world's most innovative diagnostic technology companies, clinical laboratories, researchers, physicians, venture capitalists, and over 30 patient advocacy groups, including the Genetic Alliance's coalition of 600 advocacy organizations, all linked together by a common mission to develop advanced diagnostics that improve the quality of health care for patients.

The coalition believes that innovation and quality care are the keys to 21st century medicine and that timely access to new information by physicians and patients is critical to improving the quality of care and providing personalized medicine. The coalition shares HHS's focus on personalized medicine and the Congress' and FDA's goals of assuring that treating physicians and their patients have access to safe, accurate, and reliable information to assist in decisionmaking. In light of that, we support the Congress and the various agencies striking an important balance between regulation and innovation.

The coalition is pleased to be in an ongoing and constructive dialogue with FDA. We are grateful to FDA for its willingness to exchange ideas about their initiatives around IVDMIAs and ASRs. We met with FDA leadership in December, presented at the February 8th public hearing, and submitted dozens of formal comments on specific draft guidances.

In summary, the coalition is concerned that if implemented in their current form, the draft guidances for both IVDMIAs and ASRs may result in adverse, unintended consequences. We are concerned by the ambiguities that exist under the current draft guidance and feel that labs will need more clarity moving forward. We urge FDA and the Department to continue its dialogue with patients, providers, and innovators and believe that this dialogue can influence and inform Congress' heightened interest in enacting new law in this sector. It is clear that there is a real chance that congressional action and the resulting novel or substantially modified statutory authority may ultimately supersede the draft guidance in important ways.

In the interim, the coalition will continue to educate key stakeholders about the importance of innovative new diagnostics and the role in reducing health care costs, providing new pathways to relieving the burden of disease, and personalizing medicine. Our overall goal is to help determine the most appropriate pathway for regulation of IVDMIAs and ASRs, while preserving a forward-looking innovation environment in which patient safety and access are the highest priorities.

Various legislative initiatives are being introduced and may be enacted this year that establish different regulatory provisions. Earlier this month, Chairman Kennedy and Senator Smith introduced the Laboratory Test Improvement Act. The coalition has worked with HELP Committee staff and leadership and we share Chairman Kennedy's interest in safeguarding all laboratory tests.

However, the coalition remains concerned about particular elements of the bill. As mentioned above, the coalition feels strongly that any new regulatory environment must consider how incentives to encourage innovation are affected by this bill and how that impedes access.

We believe that the Laboratory Test Improvement Act may hinder such innovation by regulating all laboratory-developed tests as class II medical devices subject to potential premarket review. While the coalition supports the registry concept outlined in the legislation, we are concerned by the provision deeming all laboratory-developed tests to be medical devices. We worry a great deal about the smaller labs and the incredible service they provide to underserved communities of patients, particularly those with rare diseases. The coalition is committed to ensuring the safety of all tests, but regulating all laboratory tests as medical devices and laboratories as device manufacturers would present enormous difficulties for labs and the FDA.

The coalition has also been pleased to work with Senator Obama and his staff on the Genomics Personalized Medicine Act. We encourage the development and use of high quality LTDs, including genetic tests, and support the flexible approach to regulation introduced in Senator Obama's bill.

As the legislation process moves forward, the coalition will continue to emphasize the importance of the Clinical Laboratory Improvement Amendments of 1988 in ensuring that patients and physicians have timely access to these diagnostics. I won't go into the issues around that act since Kathy just outlined them, but we agree very much with the details that she gave you.

In conclusion, the Coalition for 21st Century Medicine is committed to working with CMS, FDA, and the Congress to ensure that regulation of laboratory-developed tests is provided in such a way that regulation supports innovation and access to diagnostic test services for patients, as well as reliability and quality.

As a result, we have formally requested via letter to Dr. Tuckson that Secretary Leavitt convene a meeting to engage the key stakeholders, members of Congress, and agency officials to make sure that the wide range of views are heard and considered and that appropriate coordination is achieved among these initiatives before any final decisions relating to a new regulatory provision are put into place.

We look forward to working with the Secretary's Advisory Committee on Genetics, Health, and Society and all parties involved in these vital matters of public health, patient safety, and personalized medicine. Thank you for the opportunity to share our thoughts.

DR. TUCKSON: Sharon, thanks a lot. We're going to have to roll to lunch. First of all, I appreciate that. But I think the real question to get from you is when you sort of see us lay out that outline around oversight and where pieces plug in, if you could give Andrea sort of where you see it fitting in and being pretty specific there, I think you'll get involved in our deliberation in a much more effective and quick way.

MS. TERRY: Sure.

DR. TUCKSON: Ultimately, at the end of the day, we will be at the end of it sort of figuring out what do you do with it all. But I think you really need to influence us well upstream. So if you'll get with Andrea, I think it will be important to sort of fit it into the outline.

MS. TERRY: Sure.

DR. TUCKSON: Thank you so much. We really appreciate it.

By the way, Debra, can we get to you later today or tomorrow? Because I know you want to testify. We've got to get the committee to lunch and their stomachs are getting louder.

But I do want to hear from David Mongillo from the American Clinical Laboratory Association because David did sign up for this particular session early on. David, we appreciate it. We have also appreciated the fact that ACLA has provided comments to us in the past and have always been well received. So thank you.

MR. MONGILLO: Thank you, Dr. Tuckson. We appreciate coming here.

I am David Mongillo, Vice President for Policy and Medical Affairs at the American Clinical Laboratory Association. Many, if not all, of our members perform genetic testing and thus have a keen interest in the issues addressed by the committee.

You're going to hear some redundancies from the 21st Century Coalition comments, but I think it's important to hear the vital nature of these comments.

We wish to focus our comments on recent activities related to the regulatory and legislative oversight of laboratory-developed tests. FDA recently proposed new guidance on in vitro diagnostic multivariate index assays. IVDMIAs play an important role not only in current genetic testing, but will continue to play an important role in future genetic testing.

FDA held a meeting February 8th to hear public comment on the draft guidance document. Over 300 representatives were present at the public meeting, and over 30 comments were received from clinical laboratories, manufacturers, government officials, academia, and others.

Some common themes emerged from the presentations, namely, that all laboratory tests should be safe, clinically valid, and effective, a theme which ACLA certainly agrees with and endorses. But also communicated to FDA at the public meeting was that the FDA guidance, as proposed, raised concerns and questions that needed further clarification and stakeholder involvement.

Two important bills were introduced in the Senate this month. Just this past Friday, Senator Barack Obama's bill, the Genomics and Personalized Medicine Act, was introduced, and Senator Edward Kennedy's bill, the Laboratory Test Improvement Act, was introduced on March 14th. Both bills address issues associated with molecular and genetic test oversight.

ACLA was one of 25 organizations who sent a letter on March 16th to Senator Kennedy respectfully requesting additional time for more careful analysis and discussion of the bill, and I think you have a copy of that bill with your comments. The sign-on organizations represent professionals and entities comprising virtually the entire spectrum of laboratory and medical interests, including genetic disorder patient groups, genetic and molecular practitioners, genetic-oriented policy groups, pathologists, laboratory technologists, and clinical laboratories. It's interesting to note that the organizations that signed the letter may have varying views on the need for additional oversight of laboratory-developed tests; however, they are fully united in the request for more time to provide feedback and discuss pathways that will not have unintended consequences on patient care and laboratory services. The groups are further united in the opinion that any new legislative initiative in this area should be carefully crafted to focus on the specific areas of concern and not be so broad as to encompass laboratory tests that are clinically established or that are serving a valuable purpose for rare disease groups and public health needs.

Our overall message today is simple. Let's not rush to solutions without thoughtful deliberations on all the issues associated with the need for increased genetic testing oversight. This committee has the professional expertise and the understanding to contribute significantly in advising these issues as they are deliberated. I think the HHS charge this morning and the discussions that will follow this afternoon are certainly a major step in that direction. ACLA asks that the SACGHS communicate your desire to provide input on these issues before they are finalized.

We thank you for the opportunity to comment and look forward to working with the committee and the agencies on these important issues.

DR. TUCKSON: Terrific. Well, thank you so much. Again, I would continue to urge your organization, as we did just a moment ago. Try to track with us what happens this afternoon and then find places that you think you might want to comment as we get in because that's really the way to do it.

MR. MONGILLO: We'll do it.

DR. TUCKSON: Terrific.

So we've got to go to lunch. So, members, your lunch is outside. For those who are not on the committee, I am informed that the hotel serves lunch at the renowned Mount Clare Cafe, which is around the corner from the ballroom, and the Garden Restaurant, which is also well known.

Now, here's the deal. It's 12:33. We're supposed to start at 1:15, but that's not fair to you. So we're going to start at 1:20.

(Laughter.)

DR. TUCKSON: Which means that you'll actually start at 1:25. But the problem is that we've got people calling in at exactly 1:30 and we've got some table-setting to do before they call in, and they don't know that we're late and we can't reach them because they're on the beach.

(Laughter.)

DR. TUCKSON: So you have to go right now. So bye. I'll see you at 1:20.

(Whereupon, at 12:33 p.m., the meeting was recessed for lunch, to reconvene at 1:20 p.m.)

AFTERNOON SESSION (1:20 p.m.)

DR. TUCKSON: Thank you all very much. We are right on time.

Before we move forward on today's session, it's worthwhile, I think, to recap where we are since things were left in November on this issue of oversight of genetic testing.

As you recall, Judy Yost and Tom Hamilton of CMS reported to us at our last meeting the notice of proposed rulemaking on a genetic testing specialty was not going forward as planned. Instead, CMS decided to explore other avenues for strengthening genetic testing oversight that would be faster to implement and, in their view, equally effective; i.e., improving their website, providing technical training to surveyors on genetic testing, and collaborating with CDC to publish educational materials. We've already heard some public testimony today about that issue, and I'm sure we'll be revisiting it in the course of our discussion.

To our great enthusiasm, Dr. Ann Willey, Director of Laboratory Policy at Wadsworth Center, New York State Department of Health, provided us with some insights that were very useful about the New York State program. She also conveyed some concerns about gaps in the oversight system. We invited her back today and we are very appreciative that she came. We just want to thank her for that. If you can find a seat at the table at some point, we'll have you come up and be a part of this. We're very glad you're here.

In November, we were briefed by Steve Gutman on two new draft guidances from FDA clarifying the oversight of certain types of genetic tests. The first draft guidance clarified that analyte-specific reagents, which are the active ingredients in genetic tests, marketed in combination with other products or with instructions for use in a specific test, are considered test systems and are not exempt from premarket notification requirements.

Let me just read that again because that's technical and complex, and I want to make sure that you all catch that. That's why it's complex because Steve did it.

So what Steve said was that the first draft guidance clarified that analyte-specific reagents, those which are the active ingredients in genetic tests, marketed in combination with other products or with instructions for use in a specific test, are considered test systems and are not exempt from premarket notification requirements.

The second draft guidance targeted a class of devices called in vitro diagnostic multivariate index assays or, as commonly known, IVDMIAs, that use an algorithm to calculate a patient-specific result. The IVDMIA guidance clarifies that these types of tests must meet pre- and postmarket device requirements appropriate to their level of risk, including premarket review requirements in the case of class II and class III devices. There will be a quiz on that in a moment.

Later this afternoon, we would like Steve to give us a brief update on the status of these documents and the public comments that FDA has received about them.

During our oversight session, we also heard conflicting perspectives from our presenters about gaps in the oversight of genetic tests, and we struggled ourselves to define the nature of the gap. I think it is fair to say that while a gap exists, we were all extremely frustrated at the lack of a clear understanding of the specific nature of the gap and who was responsible for filling it. At the end of the first day, we reached consensus about writing a letter to the Secretary that we had identified an area of ongoing concern and we agreed to try to illustrate the oversight gap with a specific concrete example of a

problem caused by the gap.

We also agreed that we needed to find out about the upcoming deliberations on the CLIA advisory committee on the matter of CMS's decision not to go forward with the augmentation of CLIA.

On the second day of our meeting, we also decided that we needed to probe these issues more fully and understand all the elements of the oversight system to pinpoint more precisely where the main gaps lie.

We appointed a task force to draft the letter and to organize a fact-finding session for today's meeting. To our great pleasure, Andrea was convinced, arm-twisted to serve as chair. And her group has met twice since the November meeting. By the way, it's a small group. Two people. Who's on it?

DR. FERREIRA-GONZALEZ: Cynthia.

DR. TUCKSON: Cynthia and who? You and Cindy. Wow. A meeting in a telephone booth. So it's you and Cindy.

DR. FERREIRA-GONZALEZ: Maybe the new members will help us.

DR. TUCKSON: There has been some negotiation going on behind the scenes. Certain people have had their arms twisted, and Marc, if he's going to sling, will let you know that somehow or another he was convinced to join the committee. We may need another one as well, so we'll be looking as the discussion goes on for the calling, Kevin.

(Laughter.)

DR. TUCKSON: Not you. You're on another one. We just want you to facilitate the process of the calling at some point for someone to get the spirit to join in. If not, I'm spirited.

But this wonderful committee has discussed the content of the letter. They concluded that since the committee planned to engage in further fact-finding about the oversight system, it was premature to send a letter to the Secretary. They focused their efforts on developing a framework for this session, identifying speakers, and following through on our interests in CLIAC's recommendations. I think that based on the conversation this morning, the one we had just before lunch, it's pretty clear that things are now moving forward in a very organized and assertive way. So I think that's good.

So let me just thank Andrea for your effort in convening such a complex committee --

(Laughter.)

DR. TUCKSON: -- and planning this session. If you'll now go ahead.

By the way, I did my job, which was to fill until the 30-minute moment where the people should be on the phone. Is anybody on the phone? It's a videocast? I didn't know we could do that. So Wylie Burke and who else?

MS. CARR: Wylie, and Al Berg at the end of the day.

DR. TUCKSON: And Al Berg at the end of the day. But Wylie is going to be on.

Andrea, I get to do all the hard work. So before you get started, we'll make sure that Wylie is there. So what do we do?

DR. FERREIRA-GONZALEZ: Do I start the overframe?

DR. TUCKSON: Okay. She'll do the overframe.

DR. FERREIRA-GONZALEZ: Let's move to our presentations. First, we will have an overview of the oversight roles of federal, state, and private sector entities concerning the analytical and clinical validity of genetic tests. This will be followed by more detailed presentations on New York and other state systems. Finally, we will learn about private sector responsibilities for clinical laboratory accreditation, standard setting, and the development of clinical practice guidelines for genetic testing.

Our first presentation will provide an overview of the approaches in various sectors to

provide oversight of genetic testing. As many of you are aware, Dr. Wylie Burke is a noted expert on this subject. In addition to her work at the University of Washington School of Medicine, she served on the NIH National Advisory Council for Human Genome Research and was on the Secretary's Advisory Committee on Genetic Testing, which is the predecessor to this committee. And hopefully, we'll be able to connect with Dr. Burke to hear her presentation.

DR. TUCKSON: So we'll just take just a second to see if Wylie has joined yet. Hey, Wylie. Can you hear us?

DR. BURKE: Well, can you hear me?

DR. TUCKSON: We do now. You look marvelous. Thank you.

DR. BURKE: Great to be here virtually. Sorry I can't be there in person.

DR. TUCKSON: Yes, but this works out pretty well. So feel confident that you can speak in a normal tone and behave normally because you are front and center. We see you well and hear you clearly.

DR. BURKE: Great. So, Reed, I need to explain that although I sent a slide show, I don't have it here with me. So I believe the slides are not going to be projected for you. I think everybody has a copy of them, and I don't think that's going to present a problem. But I'm just going to go ahead and give my presentation without slides.

DR. FERREIRA-GONZALEZ: Wylie, the presentation is in our packet. So we have copies of your slides.

DR. BURKE: Okay. I think that will work fine for this presentation.

DR. FERREIRA-GONZALEZ: Thank you very much. Go ahead, Wylie.

DR. BURKE: Well, I was asked to kind of give an overview of the oversight system. Before I begin, let me say that particularly when it comes to details of the federal agencies involved, I am well aware that there are ex officio members who know far more than I do about the details. My effort is going to be to give you a kind of big picture of where oversight occurs and what the potential interactions of different kinds of oversight mechanisms are. And I'll be happy to be corrected on any details, if need be.

Let me just start by saying that I think the reasons for oversight are clear and have been discussed now for many years, basically for a decade. We see coming out of the Human Genome Project many new genetic tests and a lot of complexities in thinking about how best to use those tests, many different technologies, often difficulties in determining or at least complexities in determining who is a candidate for a particular test, and genetic test results can be difficult to interpret. Superimposed on that is the difficulty that many clinicians at this point in time have limited knowledge of genetics. Surveys tell us that many clinicians are uneasy about interpreting or using genetic tests. All of this leads to concern about appropriate oversight.

Sources of oversight are multiple, and I really want to emphasize four different areas where we can take actions for oversight. What I want to reflect on in particular with you is how we might think about the interaction of these different methods.

So there is statutory regulation, and I know that that's received a lot of discussion in your committee and in the prior committee, the Secretary's Advisory Committee on Genetic Testing.

There's also public leadership, and I'm going to talk a little bit about, I think, the very important role that public leadership can play.

And then, as a separate issue, decisions about health care funding, which in our society can make a profound impact on how tests are used.

And then, finally, professional leadership.

So talking about statutory regulation of genetic testing at the federal level, I think we

can say that there have been two major areas of focus. One is on CLIA certification and its implications, and the other is on the potential and actual role of FDA, particularly in premarket review.

So the well-established model for regulatory oversight is that for laboratory oversight, the CLIA system that provides certification for laboratories that provide test results for clinical use. What this oversight system does is it provides oversight regarding laboratory procedure, the documentation of it within laboratories, standards for the training of laboratory personnel, and also the credentials needed for test interpretation.

As you know -- I know it's already received discussion in your committee -- when we think about the CLIA system, which I think all agree is a very well functioning and effective system, there is a question about whether there should be a genetic specialty; that is, whether there need to be specific enhancements of the oversight with respect to genetic tests, particularly genetic tests that might involve complex technology. And I understand that that is still an issue that people are discussing.

I want to mention another issue with laboratory oversight, and that is the issue of results obtained in research. I know that this has been a discussion now for several years, and I guess I want to bring this to your attention because I don't think it's a resolved issue at this point.

Both the NBAC in 1999 and a working group of NHLBI a couple of years ago have set out criteria by which we could identify those results that should be disclosed to research participants. In general, I think there's a consensus from those statements that when research studies produce validated results that have implications for health and for which there is a health care intervention, that these are, in essence, results that have clinical utility and should be disclosed to research subjects. But what to do if the laboratory that generated those results is not CLIA-certified?

I'm well aware that CLIA offers opportunities for small labs that are primarily focused on research to develop CLIA certification, but I also hear from colleagues that this is not always a feasible way for researchers to go and that researchers are troubled basically about exactly what their responsibilities are. So I think this is a particular small piece of the laboratory oversight picture that perhaps still needs further discussion.

I want to talk now about the regulatory oversight of the use of tests in clinical care and just start with the historical note that in 1997, when the NIH/DOE Task Force generated its report -- this was a task force co-chaired by Tony Holtzman and Mike Watson -- one of the things they called for to support the safety and effectiveness of genetic testing was what they called evidence-based entry of new genetic tests into clinical practice. What they acknowledged was that there were not necessarily concerns with all genetic tests, but certainly that some genetic tests needed more attention than they were currently getting to assure the right kind of evidence base when they entered clinical practice.

And so they called for criteria to identify those tests where special measures should be taken, special measures specifically to require validation and clinical utility data before the tests entered the marketplace. They envisioned that this process would include an independent external review of tests, basically premarket, and that professional organizations might potentially play a role. They also considered that the FDA might have a role because the FDA does have a role with premarket review of test kits.

So that was a recommendation from the task force, and the Secretary's Advisory Committee on Genetic Testing, which preceded your committee and met between 1999 and 2002, took this recommendation very seriously and gave it a lot of consideration, as Reed and others can attest.

What the committee did was to try and figure out a way to categorize tests, basically building on the NIH/DOE Task Force call, and they did try and think through what are the circumstances when a test should receive higher scrutiny looking, for example, at diagnostic versus predictive tests. That, in a lot of the early discussions, seemed to be a critical distinction.

But the short version of the effort that went on for many months is that there was no simple way to categorize genetic tests, or the SACGT could not find a simple way to categorize genetic tests that enabled them, in a clean and simple way, to say these are the tests that require higher scrutiny and these are the tests that don't.

There are a few reasons for this. One of them is that many genetic tests have multiple uses. Most do, arguably. There are different definitions. If you say we're more worried about predictive than diagnostic tests, you get into the issue of what's a diagnostic test. I can remember, for example, a conversation about whether pharmacogenetic tests should be considered diagnostic, that is, diagnosing a particular susceptibility state, or predictive, that is, predicting a particular drug response. Obviously, there would very appropriately be incentives to test manufacturers to go with whatever characterization of their test was going to be least onerous from a regulatory perspective.

So where did that take the SACGT discussion? Well, in the end, the committee recommended that all genetic tests, including home brew, which is where the large discussion occurs, should undergo some form of premarket review. But the committee was very concerned that that premarket review not be onerous, and the ultimate outcome of that discussion was to create a template, a template that laid out basically, in words often quoted, "what we know and what we don't know."

And I'm not sure exactly who to attribute that quote to. I think Muin Khoury was the first person to use that phrase. Others claim that other individuals were the first people to use that phrase

But the point is the SACGT review suggested that what we would get from premarket review primarily was information about what the test was, accurate information about what we know about the analytic validity, which we assume will be well established and we believe CLIA oversight assures, clinical validity, information often limited about clinical validity at a time when the test comes to market, and clinical utility where information is often even more limited. The idea was that a premarket review would enable health care providers and patients to know exactly what they had with the test. And that was the recommendation, and the Secretary of HHS accepted the recommendation and asked FDA to consider what would be involved in implementation.

I know that you've heard a lot of testimony in your tenure around FDA activities. So I'm just going to highlight a few issues that I think have been really important in actions taken by FDA since that time.

First, there have been several draft guidance statements related to pharmacogenetics and particularly focusing on the voluntary collection and submission of data, what Steve Gutman described in testimony to the committee about the idea of creating a safe harbor in which to explore interesting data that might help to inform manufacturers and the public ultimately about appropriate uses of drugs, guided by pharmacogenetic data, potentially appropriate development, use of pharmacogenetic data in the development process as well.

More recently, we've had a statement from FDA about the intent to change the clinical pharmacology section of the drug label, and one of the points in that change is to create the opportunity to showcase pharmacogenetic information when it's relevant to the use of the test. I think these efforts on the part of FDA signal what I think is a very appropriate decisionmaking process.

Obviously, I can't speak for FDA, but what I see in their actions is the decision that pharmacogenetics is a particularly important area for the FDA to be looking at as it's looking at guidance that it can provide about the appropriate use of genetic testing. And that's important, in part, because the use of pharmacogenetic testing is obviously tightly allied to the safe use of drugs. But I think it's also important because it seems pretty clear that pharmacogenetic testing is going to be a really important early product of genomic research in terms of impact in the clinical arena.

Other FDA efforts. Well, obviously, in the past several years, FDA has approved a

few genetic test kits and that's been a very important process, creating precedents.

But also, what I think has equal importance to the efforts that FDA is making in pharmacogenetics is efforts with respect to in vitro diagnostic multivariate index assays. I'm speaking about the draft guidance that came out last fall proposing the extension of oversight to these assays. As you know, these are tests that utilize both laboratory data and analytic tools to generate results, and we're talking about things like the gene expression profiles that might predict cancer prognosis and be very important in guiding the use of chemotherapy.

What I take from the FDA's efforts is that they are identifying two areas of priority. One, as I've said, is pharmacogenetics, and the other is test complexity. I think that may be a much more functional way to think about what tests need higher scrutiny than the diagnostic/predictive kind of categorization that SACGT was working with a few years ago. So I think this is a very interesting approach.

I want to go on to the next topic and just say that clearly another area for very interesting discussion is the area of direct-to-consumer tests. The question there that's raised is, is there room for additional or different kinds of statutory regulation when we're talking about tests going directly to the consumer? And I know you're well aware of the General Accounting Office report on nutrigenetic testing in which it raised questions about whether websites offering nutrigenetic tests were misleading consumers and, in fact, concluded that this was so.

There are other potential sources of regulation around, for example, truth in advertising that might be important here, but it also raises the question whether a test that is proposed to be offered directly to the consumer should be another category, raising questions about regulatory oversight.

Let me talk briefly about genetic discrimination. For some years, there was a hope that the ADA would provide protection against genetic discrimination, and the EEOC action against Burlington Northern some years ago -- I think it was 2001. This was related to workers who had work-related claims for carpal tunnel injury and were subjected to genetic testing without their knowledge. In bringing a claim against Burlington Northern for these activities, EEOC did invoke ADA and claim protection from that bill against genetic discrimination.

But I think we have to say that when we look at how the courts have interpreted ADA claims in nongenetic cases, that it seems likely that the ADA will be interpreted as primarily providing protection against people with disabilities that actively interrupt their life and that genetic susceptibility itself is not likely to be something that would meet that standard.

So the other opportunity we have for oversight around genetic discrimination is laws that prohibit genetic discrimination, and at the federal level, as you know, GINA is now before Congress, and I know that you'll be hearing an update on the status of that later.

At the state level, statutory regulation can also be very important for genetics. In particular, some states actually have more stringent laboratory oversight than is called for by CLIA. Many states -- I think the count is now 41 -- have enacted genetic nondiscrimination legislation, although it's fair to say that this legislation has not been tested in the courts yet. So we're not really sure what the scope of protection provided by this legislation is. And obviously, newborn screening is a state function that is under oversight of states.

Let me conclude these remarks about statutory regulation by saying that I don't think the role of statutory regulation and oversight of genetic tests is yet clear. I think we see conversations that are very important going on at FDA. I think we have an ongoing concern about whether or not there should be more regulation around performance of genetic tests in laboratories, and I think we have uncertainty about certain kinds of delivery of tests like direct-to-consumer and exactly what measures we

should take to make sure that consumer safety is protected.

I do think that statutory regulation is a potential vehicle to standardize reporting and labeling of information about genetic tests, and we should think seriously about how best to use statutory regulation for that purpose. I think it's not a route to establishing a standard of practice around the use of genetic tests, and other mechanisms, I think, are likely to be much more effective. So let me talk about some of those other mechanisms.

First of all, public leadership. So in addition to the regulatory responsibilities of many federal agencies, federal agencies have the opportunity to provide leadership in a variety of ways, and I think we have many very positive examples occurring now. As I've outlined in my slides, these include promoting best practices, education and training, practice guidelines, and research, all of which are important efforts.

Just picking out a few examples, because there are many, I wanted to mention the Division of Laboratory Sciences at CDC. When we're talking about genetic testing, this particular division of CDC and particularly the Lab Practice Evaluation and Genomics Branch within that division has a variety of roles that I think are making a very positive impact. It provides leadership for quality control, quality assessment in the development both of technology and of practice. That, obviously, includes proficiency testing.

I think also as an example of very interesting work that has come from this agency, there has been an interesting project looking at genetic test reporting. When we think about the complexity of genetic tests and the fact that there are going to be many new ones and the fact that many providers are not necessarily well-grounded in genetics, this represents, I think, a very interesting kind of example of how appropriate use of new genetic tests can be enhanced simply by looking carefully at how information is provided to providers to guide them at the point of service, at the point where they need to know.

And this division has many other activities, education and training, research activities, and also does take a role both nationally and internationally in policy development, including obviously an interaction with CLIA in terms of standard setting.

But public leadership extends to other areas as well, and I want to mention the role of public leadership and the support of processes as a very important one in guideline development.

So EGAPP -- I know you'll hear more about EGAPP later today -- I think is an important initiative on the part of CDC and AHRQ to not just provide guidance about the use of some genetic tests, but really to work on establishing methodologies for evaluating genetic tests and, hopefully, also addressing what I think is a really important, unresolved question, and that is, what kind of evidence do we need, what kind of evidence is sufficient for us to be ready to say this particular genetic test is now ready for clinical use?

The U.S. Preventive Services Task Force has also provided some important guidelines, notably their guideline around BRCA testing a couple of years ago, and the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children is also active, particularly in the newborn screening area.

What I think is really important, as we step back and think about where public leadership should go, where opportunities for contributions can be made, we need to think in terms of the translational pathway. And I've shown you my diagram of the translational pathway, the idea being that we've got a huge amount of research going on that's helping us to understand with increasing detail the genetic contribution to disease, and that's one end of the pathway. And over at the other end of the pathway, what we hope are improved health outcomes.

Clearly, federal research support is a critical component in the early part of that

pathway, and NIH, AHRQ, CDC, HRSA, all make important contributions to the research enterprise.

When we think about oversight of genetic tests, what I think is important to emphasize is that there is a crucial need for educational research, research on educational interventions, what really does help providers, what really does help patients to assure appropriate use of genetic testing, the creation of educational resources, an ongoing focus on clinical utility, which starts, not least, with clarifying what we mean by that term, and as I've said, what kind of evidence we need to support clinical utility for different kinds of tests, and then also research into the ethical/legal/social implications and policy options.

I think it's fair to say that federal agencies are providing support in all of these areas. I think it's still an open question of whether more support might be provided or perhaps more focused support, identifying particular crucial areas where more work might be needed.

And now I'm going to turn to funding decisions as an alternative to statutory regulation, and I don't mean by that that funding decisions can replace statutory regulation. But I think it's really important to recognize that funding decisions play a crucial role in the use of genetic tests or, for that matter, any medical tests in our society; that is, whether or not a test is funded will have a powerful impact on whether or not that test is actually used. A test might be made available for clinical use, but if it's not funded, it's not likely to be used.

There are a lot of challenges here. What we want is for funders to make wise decisions about what they fund and what they don't fund because this will help to ensure appropriate use of genetic testing. But in trying to address this issue, the challenges that funding agencies encounter are, first of all, how they should be thinking about delivery of genetic services. For example, when is counseling essential? When should it be part of the package? And what kind of counseling should it be? When should it be a certified genetic counselor or a medical geneticist? When is the counseling appropriately given in primary care?

We do know the answer, I should say, for some tests. I think it's clear that the kind of counseling provided by genetic counselors is the most appropriate kind of service to offer, for example, with Huntington's disease testing. But as we see more and more tests coming, pharmacogenetic tests, tests for susceptibilities to common diseases, the answer to that question is not clear. But if we had a clear answer, it would be possible through funding decisions to help to ensure that services are delivered in the right way.

I think another interesting and problematic area for funders is how they should think about genetic tests which have as their primary endpoint information. So mostly we think about tests in health care as providing information for the provider and the patient that guides treatment decisions. Tests help us to manage patients in order to improve outcomes.

But in genetics, historically the majority of tests have had information as their endpoint, information that establishes a prognosis of a disease like Duchenne's muscular dystrophy or X-linked retinal dystrophy where there's a tremendous health impact on the family, where it may have very important social implications, where it may help to design the appropriate kind of supportive care to provide, but information really is the endpoint as opposed to an improved health outcome, which is what we hope for most medical testing.

How should funders think about that? In general, funders are quite willing to test the Huntington's disease type of test where we say this is a highly penetrant genotype with very important implications in terms of the information about an individual's health. Are other genetic tests that provide information, for example, about a probabilistic increase in risk for Alzheimer's disease or diabetes also appropriate for health care funding? How should health care funders think about that problem I think is quite challenging.

And as health care funders try to make rational decisions, they're confronted with a tremendous problem of lack of evidence, which gets us back to research and also to this issue of thinking through what evidence is necessary in order to say whether or not a test is ready for prime time clinically.

So let me showcase a couple of other problematic issues when funders become, in essence, the regulators of access to genetic testing.

One, of course, is that coverage of genetic counseling historically has been poor. So we have many circumstances where the patient can get the expensive test covered but not the genetic counseling that we tend to agree should go along with that. And I know you're well aware of that as a problem.

Funders also try to create rules that help to standardize use and can easily get into inflexible rules. We see this, for example, when we're looking at a potential candidate for BRCA testing. There are often family history rules that are perfectly rational; they make sense. But if they're adhered to too rigidly, certain patients that we can argue, often based on second-degree or third-degree relatives, really are candidates for testing, but they don't quite fit the rules.

Then, obviously, funding as a regulation of genetic testing doesn't address a really core problem in our society, and that is inequitable access to genetic services which comes from people lacking insurance or being underfunded, the underfunding part being a particularly important issue for genetic services because often these are kind of viewed as more marginal services that may be less likely to be funded.

Now I'll move on to the role of professional organizations and collaborations. In the same way that public leadership I think can play a really powerful role in creating standards of practice, so can professional organizations. Professional organizations can help to identify for their members the importance of genetics issue. An interesting example a couple of years ago was the American Association of Family Practice which identified genetics as an area that its membership should know about and created a series of educational videos, in partnership with federal agencies and other sponsors. They can provide education both at national meetings, as well as standalone educational programs.

We also see professional organizations playing a very important role in laboratory oversight, working with or within the context of CLIA to standardize, create proficiency testing, et cetera.

And then professional organizations play an important role in developing practice guidelines.

So practice guidelines. Practice guidelines are what most docs look for when they're faced with a new area of practice. They look for guidance and they look for guidance from sources that they can trust. This is why professional organizations play a very key role in practice guidelines.

The problem, if you look at what we have today in terms of practice guidelines, is that they're kind of all over the map. Many different bodies set themselves up to provide guidelines. They use different processes. Some processes are more transparent than others. Some processes are more evidence-based than others. We've had some reports that suggest that interests may sometimes insert themselves into the process in a way that's not good, and methodologies vary. They're not always disclosed.

Of course, with all these sort of process problems, that is, what kind of processes should we have to produce good practice guidelines, we also have the ongoing frustration, on the part of guidelines panels, that even if their processes are good, the evidence may be lacking. And I think this just speaks to the importance of both public and professional leadership, making sure that we're doing the research we need to do to get the evidence we need, but also providing leadership to ensure that practice guidelines follow rigorous procedures so that they can provide valid and legitimate guidelines.

Of course, as we do so, we have to acknowledge that standard of practice is an

evolving concept. In fact, you can make a guideline, and then there's going to be new data, which means you have to rethink the guideline. This is, obviously, a tremendously important area in genetics where technology is evolving and the quality of evidence is, hopefully, increasing over time. We've certainly seen that with BRCA testing, for example. The first guidelines came out when virtually no evidence existed, and all recommendations were made on expert opinion. We now, 10 years later, have a body of data and can, with increasing assurance, make evidence-based recommendations for people that are test-positive. And obviously, case law also will influence a standard of practice.

I will just finish by mentioning health professional education. I've already alluded to this as a very important issue at the federal level where we're looking for support for educational research and resources, at the professional leadership level, at the public leadership level as well. Health professional education has the potential to enhance other efforts by enabling health care providers to make good judgments in gray zone areas.

But there are a lot of challenges. We know that the traditional methods of calling a conference and giving a lecture don't necessarily have much impact on physician practice.

We know that many genetics curricula, as a colleague of mine said, have been created and then they sit on the shelf collecting dust. And that's probably because a lot of curricula have been created without a preliminary phase of needs assessment. We really need to go out to the individuals that we hope to bring genetics education to and talk to them about what's going to be most helpful to them. I think when people have those conversations, they discover that genetics education for health care providers needs to be intensely focused on relevance and, from the primary care perspective, ideally focused on health outcomes. That's what primary care providers see as their mission.

I'll just finish by saying that I think all of the different ways that we can provide oversight for genetic testing are complementary or hopefully complementary. They have the potential to be complementary. And I think that's one of the challenges, trying to think through what reasonably should we expect from statutory regulation and how can we make that happen, but not expect statutory regulation to do everything. What can we accomplish with a combination of public and professional leadership? What can we accomplish by working on the research agenda? What can we accomplish by making practice guidelines processes better, pushing on those standards? And what can we accomplish by education? I think that that issue of thinking through the role of different oversight mechanisms and trying to promote a complementary use of them is where a lot of attention is needed.

I'll stop there and be happy to discuss more with the committee.

DR. FERREIRA-GONZALEZ: Thank you, Dr. Burke. Right on time. That was great.

DR. TUCKSON: Dr. Wylie, as Andrea drives the train here, I do want to make you aware that we did have a -- Wylie. Well, that's fine. I messed up and called Wylie Burke "Dr. Wylie." So, you know, now they're going to write me a letter and a note and I'll get yelled at.

DR. BURKE: No problem, Dr. Reed.

(Laughter.)

DR. TUCKSON: I actually write a health column that's called "Ask Dr. Reed." So that's great. And then we have Dr. G. here, as well.

(Laughter.)

DR. TUCKSON: Anyway, just to let you know, as you participate in the discussion with us in case it comes up, we had a long session this morning with some guidance that we got from the Secretary's office regarding oversight tests and some questions they wanted us to address. Your presentation was prescient in that it anticipated a lot of the things that came in the discussion earlier. So people may refer to that.

The point I'm raising sort of with you is that the activity that we are engaged in now as an advisory committee to the Secretary is, in a way in which it has not been before, really specifically advising the Secretary around very granular issues that we had not been asked before. So, again, just giving you a sense of the importance of this activity as it goes forward.

I'll turn it back to Andrea.

DR. FERREIRA-GONZALEZ: Thank you, Reed.

Dr. Burke, thank you so much for that, and I want to echo Dr. Reed's comments earlier that it really falls within some of the discussion that we had this morning. I think you have done a very good job of looking at a comprehensive way of the oversight of the federal, state, and even professional organizations in different issues, but also to bring to the attention of our committee some of the efforts that have been occurring at the federal level through different advisory committees to these specific issues.

I think also, like you said, there is room maybe for additional oversight for specific areas such as direct-to-consumer testing, but also improving how we report the testing that we do to be a vehicle to educate these.

I really liked the questions that you have framed in the last slide because these go really well with some of the comments that we heard this morning from the Secretary and some of the other areas we'll be discussing this afternoon.

But I would like, at this moment, to open it for questions, if anybody has questions for Dr. Burke. Marc?

DR. WILLIAMS: Thanks, Wylie.

One of the issues that we touched on briefly but really haven't talked about in great detail is what might be in the drug parlance termed postmarket oversight because I think what we've surely learned, with the release of genetic testing into clinical practice, is that we learn much more after the test is out there and being used about the potential impact. I'd like to hear your take on the role of postmarket data collection and surveillance.

DR. BURKE: Thanks very much for bringing up that point. I think it is a very important point for discussion. It's, obviously, the other half of the discussion about what evidence do we need before something comes to the marketplace, something becomes clinically in use. The simple, I think, answer is the less evidence you have when it enters the clinical arena, the more evidence you're going to need postmarket to understand how things turned out.

And I think that is the reality. Most genetic tests come into the clinical realm based on partial evidence, based on a strong presumption that they can provide benefit, but not necessarily full proof.

And there are some questions that can only be answered over time because there has to be a duration of following people who are test-positive before you're certain that you know, for example, what management they should be offered or what the clinical validity of the test is.

So, yes, I do think that's a very important question, and of course, it leads to sort of the practicalities. To what extent would it be possible, for example, for premarket review to generate conditions for certain kinds of postmarket collection. That would be one question.

Another question, though, I think is realistically what kind of partnerships might we want to think about putting in place to maximize the quality of the information we get postmarket and perhaps also the speed with which we answer questions. I think you can imagine a circumstance where a partnership that included participation of the lab offering the test, or the labs, participation of some large health care systems that really have a stake in using these tests properly, and some appropriate public participation through funding. If you could create these kinds of partnerships, you might be able to create

systems where, as tests come in, you can prospectively plan on gathering certain kinds of data to be sure that you understand the uptake, outcome, and ultimate clinical effects of new tests. I think how to construct and promote those kinds of partnerships is a very important question.

DR. FERREIRA-GONZALEZ: Any other questions for Dr. Burke?

DR. WILLIAMS: The other question I had is looking particularly at your slide on the translational pathway. Having participated on a review panel for the CETT program, which I think most people here are familiar with, I've been very impressed with that model as walking through all of the pieces of that from the gene/disease association to interventions and implementation with incentives built in to translate this into the clinical arena with the caveat that there be transparency, that there be educational materials for patients and for providers, but also that there's a requirement tied to that about collecting data after the test is in clinical practice for a five-year period of time that is able to be used to answer some of the questions.

It's, obviously, a rare disease test model. Do you think there's any possibility of taking that model and translating that into something that would work for more common disease-based genetic tests?

DR. BURKE: Yes. I think you're getting to a crucial issue. I guess my short answer to it would be all the questions are going to be the same, but some of the logistic issues that arise in answering the questions will be different. And they include thinking about a critical evaluation of a genetic test versus alternatives.

So just for the sake of an example, there's been a lot of interest in the last year/year and a half, about gene variants that identify individuals with a moderately increased risk of type II diabetes. So the relative risk might be 1.5 or 2. Substantial numbers in the population will have these variants, and there certainly are some claims of potential clinical utility. These tests might be used, for example, to motivate individuals toward healthier lifestyles.

So I think when you think about the CETT model and then applying that to a test like this, not only is the potential locus of data collection much broader -- there are many more places where you might want to collect data -- I think you also have to think about collecting comparative data that will be crucial to answering the question.

So those data include just how well do we do motivating people with a healthy lifestyle to begin with. What measures work? What measures don't work? Is identification of genetic risk the best way to go versus other nongenetic risk factors like, for example, body mass index? And how do we measure the impact of different strategies for achieving the same outcome at the level of patient experience and acceptability, you know, taking into account the possibility, for example, that genetic results might have fatalistic impacts on people's motivation, and actual clinical measures of outcome and, hopefully, short-term and long-term measures of health outcome?

I guess what I'm saying is I think the questions will be the same, but how to answer them will be a much more complex undertaking.

DR. FERREIRA-GONZALEZ: I don't want to go over the next speaker's time, but I have a quick question. You touched upon a little bit about the reasons of concern about oversight. You started alluding to some of these issues.

We heard this morning from the Secretary's office, which has given very specific questions on what they would like us to be considering, and one of the questions is what distinguishes genetic tests from other laboratory tests for oversight purposes. I was just wondering if you could elaborate or give your perspective on that particular issue.

DR. BURKE: Well, yes, the issue of genetic exceptionalism. That's a really tough issue.

I think we can say a couple of things about genetics. One is that genetics certainly does provide us with a subset of tests that have extraordinarily high predictive value. You don't find medical tests that have the predictive value, say, of a Huntington's disease test. That would be very unusual in other medical arenas. So I think the notion that genetic tests require maybe a different approach to oversight starts with that fact, that there are some tests that really are by degree, if not by nature, different in the kind of information that they provide.

Clearly, as a corollary of that, genetic tests and genetic testing processes raise often questions about the family that other tests don't raise. So an example there would be testing for mutations associated with hereditary nonpolyposis colon cancer. A cost effectiveness study showed that the greatest value of that kind of genetic testing comes not at the point where you've tested the person who's affected, but at the point after that where having the positive test result, you're then able to go out to the family and test individuals within the family who are at risk and could benefit. I think you reach extraordinarily greater cost effectiveness if you're able to reach two or more relatives than fewer.

So that kind of testing paradigm is different and raises questions about appropriate use of tests and, obviously, corollary issues about confidentiality and privacy. So I think that's another reason why maybe there are some oversight issues unique to genetics.

And the third is probably a cultural one; that is, we live in a society that at this point in time accords a huge amount of power to DNA, a huge amount of power to genetic information, and people are concerned about that. I think many state nondiscrimination laws reflect that concern.

So I think those are the reasons to think about genetics as somewhat different.

And I will say, having said that, that I think we should also be extremely cautious about not pushing that concept too far. So if you look at the example I just gave you of a genetic test for increased risk for type II diabetes that predicts a 1.5 to 2-fold higher risk compared to a person who doesn't have the gene variant, I'm not sure that test should be viewed differently than any other risk factor in determining how to use it in clinical care. At the same time, I think it is true culturally that it's likely to be viewed as different, and we have to take that into account.

DR. FERREIRA-GONZALEZ: Thank you.

DR. LICINIO: A quick question related to that, which is this. I think that there is an issue with Mendelian diseases in which everything that you said is very accurate. But for a non-Mendelian specialty, I mean, if you increase the risk of the disease, like 50 percent, that's one story, but for common and complex diseases, there are many risk factors that are like 3 percent of the genetic contributor and having that marker has no predictive value in terms of whether you're going to really develop the disease in the future. It may have some, but very limited. It's not like having the genes for Huntington's disease. If you have one of the variants that gives some susceptibility to some of the common and complex diseases, you may easily have the disease, you may not.

How is that going to be dealt with in terms of this? Does that deserve a special, even different kind of protection or not? And I think the potential for misinformation there is tremendous because having a specific variant that's associated with depression, diabetes, or arthritis doesn't, by any means, mean that you're going to have the disease or not have it.

DR. BURKE: I think you're identifying a tremendously important issue. I really do worry that the variant predicting a small increased risk of type II diabetes is going to be viewed as having the same power as a test for a Mendelian disease. I think that's a great concern, and I think there is reason to be concerned about that when you look at how genetics is covered in the media, you know, where you see a headline that says "gene for Crohn's disease," but actually it's a variant that increases risk a little bit.

I'm not sure what are going to be the most effective actions, though it would seem that if we can figure out how to craft the right kind of messages, that's an area for public and professional

leadership, and if we can think about how to approach education properly, both public education, as well as health professional education, that might be where we need to put some energy. I think we really need to figure out how to communicate this notion of multifactorial disorders better than we do.

DR. FERREIRA-GONZALEZ: Thank you. I think these are very important issues that will help us later on frame up the work that we will do. Again, thank you very much, Dr. Burke, for being with us.

DR. TUCKSON: Actually, as you do that, Dr. Wylie, can I assume that as we go forward, that we would be able to draw upon you and your expertise from time to time as we journey down this road?

DR. BURKE: Certainly. I would be happy to do that, and I appreciate the chance to be here.

DR. TUCKSON: Great. You're terrific because one of the things that I mentioned I thought was prescient on your part is the request from the Secretary's office did sort of ask about looking at issues beyond the pure HHS regulatory issues. And they brought up the thing about professional societies and so forth and so on. And you sort of spoke to those issues in your presentation. So I think following up with you on some of those is going to be important.

Thanks again for doing this.

DR. BURKE: Thanks very much. I'm glad to be here.

DR. FERREIRA-GONZALEZ: After we disconnect, we can go to the next speaker. We'll now turn to the role of the states.

Welcome back, Dr. Willey, and this is Dr. Willey. We're happy to have you here.

DR. WILLEY: Actually it's Willey.

DR. FERREIRA-GONZALEZ: Ouch.

(Laughter.)

DR. TUCKSON: It's so good to know that I'm not the one that screwed that up.

DR. FERREIRA-GONZALEZ: Well, welcome back. We're happy to have you here with us again.

For those of you who are new, Dr. Willey is the Director of Laboratory Policy and Planning at the Wadsworth Center, New York State Department of Health. She's also Director of Cytogenetics at the same institution where she's responsible for genetic testing laboratories, including the newborn screening and regulatory quality assurance programs, overseeing the practice of genetic testing entities and related research activities and administration of the New York State Genetic Service Program and regional genetics network.

I'll turn the floor over to you so we can learn more about the role of New York State in oversight.

DR. TUCKSON: By the way, Marc, one of the things I try to do -- hopefully, you're feeling well introduced to the committee. Even for the people that have been here like forever, it's impossible to keep up with all this stuff. You're, obviously, sophisticated in everything that's going on.

I'm also reminding anybody that may not have been at the last meeting. I'm just using Marc as the example here. I think what we are getting at is what people often don't think about are the roles of the states as they have oversight. We think about it from the federal government apparatus, and we don't think about the state.

We did not have Dr. Willey on the agenda last time. She leaped to her feet and grabbed the microphone and educated us ad hoc. But what we also learned last time was that New York -- because so many of the lab companies have some relationship with New York, they have this extraordinary legislative clout. What we also learned is that they are doing a whole bunch of stuff that in

some ways are the models for what the federal government ought to be doing.

So I think as we all listen to this presentation now, if you in your mind are populating that map around who does what and where are the gaps, we've got to have a big, special color for states, and specifically for New York, in terms of the part that they do and then sort of seeing how that lines up. So that's what this is ultimately about.

So thanks again, Dr. W.

(Laughter.)

DR. WILLEY: Thank you. I'm technologically always challenged and I rarely speak from slides. So we'll see if this works.

I'm frequently asked how New York State got to the position it is. We have had clinical laboratory oversight statutory regulatory authority since 1964, predating CLIA 1967. We had deemed status under CLIA '67. We have exempt status under CLIA '88.

The relevant section of our regulatory program for discussions today is 10 NYCRR, part 58-1.10, that states that "all technical procedures employed in a laboratory shall be of proven reliability and generally accepted by leading authorities in the specialties of laboratory medicine" -- and the really critical potion is this -- "and/or approved by the Department of Health." That has given this program the authority to review any and all lab tests, even those approved by the FDA, as applied to New York State.

The other piece of history I should share with you is that in 1964 when the statute was passed, it was intended to limit the practice of laboratory medicine to laboratories physically in the State of New York, therefore infringing on interstate commerce. The statute was challenged in the federal courts and overturned in terms of its ability to restrict business to labs in New York State. But the same court said that the State of New York could apply its standards, whatever they were, to any laboratory doing business in the State of New York.

So we currently regulate laboratories in Iceland, the United Kingdom, Hong Kong, and all over the United States. If the specimen is drawn in the State of New York or if it is shipped to a laboratory anywhere in the world, that laboratory is subject to New York State licensure requirements.

DR. TUCKSON: Just to make sure -- again, this question may be beyond your area of expertise. Again, just to get it right, the FDA, which is pretty scary in terms of -- it's the FDA.

(Laughter.)

DR. TUCKSON: I mean, Gutman comes in here. He swaggers with such confidence.

(Laughter.)

DR. TUCKSON: FDA says this is okay. New York can say not necessarily so for the people of New York?

DR. WILLEY: Correct.

DR. TUCKSON: Wow.

DR. WILLEY: We have rarely, if ever, done that, however.

DR. TUCKSON: But you have the ability to tell FDA to go sit down.

DR. WILLEY: No. We have the ability of the marketer of the service in the State of New York that, for New York, they may have to meet additional requirements.

DR. TUCKSON: Okay. Then also to make sure, New York considers doing business in New York, meaning any blood coming out of a New Yorkian's arm --

DR. WILLEY: A New Yorker in New York.

DR. TUCKSON: If I am in New York and I get blood drawn --

DR. WILLEY: Correct. You don't have to be a New Yorker, but if you are inside the boundaries of the State of New York.

DR. TUCKSON: Anyone who is fortunate enough to be within the boundaries of the State of New York who has blood drawn, at that moment whatever company is involved with that process is then doing business in New York. Even if it's an Iceland company who makes the lab reagent and the blood goes in a tube, at that point that company based in Iceland is doing business in New York.

DR. WILLEY: Not that company. The laboratory performing the test. So if the laboratory performing the test is in Iceland or the United Kingdom, then they are subject to our oversight. They could be buying their reagents from anywhere in the world, and we do not regulate manufacturers of kits, devices, or reagents. We regulate the user, the laboratory.

DR. TUCKSON: You regulate the user. That was the distinction I needed. I'm sorry to interrupt your flow, but thank you.

DR. LICINIO: Just a question continuing along those lines. If something is regulated like that by the State of New York, let's say, for a lab in Kentucky or the United Kingdom, because New York is such a big market, do those labs then tend to follow these guidelines for everything they do?

DR. WILLEY: Absolutely, because at least in the U.S., the tort law cases, the medical malpractice cases look very dimly upon a laboratory that holds a New York State permit and meets those standards for specimens from New York, then applying lesser standards to specimens derived from other sources.

DR. FERREIRA-GONZALEZ: I will ask everybody to hold their questions for the end of the session.

(Laughter.)

DR. FERREIRA-GONZALEZ: So we can continue with the flow and let her go over some of these issues. Thank you, everybody.

DR. WILLEY: So I've been specifically asked what is expected of a laboratory in this process. The second half of this slide says, "A laboratory shall perform only those assays that have been validated or verified at the site where the assay will be performed." This applies primarily to multi-site, large commercial entities who might want to validate an assay at one site and then simply translate it or transfer it to other sites. They can do that, but they will have to reproduce the validation data at any site they intend to offer the test. Or they can simply ship all the specimens for that assay to one site.

They must hold the appropriate permit category for the test. New York State doesn't have six specialties. We have 26 and I think all of the subspecialties give us some 70 different categories in which we issue permits to laboratories. And every test falls in one or sometimes more than one of those categories.

And they must meet all of the other requirements related to personnel and proficiency testing and onsite inspection.

The point of this is our review of the validation of a home-brewed assay or an assay using certain commercial reagents is an integrated program. We know the personnel in the lab. We know that every category has an assistant director or director holding specified credentials. They are all doctoral degreed individuals with a minimum of four years postdoctoral clinical lab experience and a minimum of two in the specialty. All of their other personnel must meet other training experience. They are physically inspected every two years for their quality assurance program, their quality control, their reagents, their equipment, their physical location. And they are required to participate in New York State's proficiency testing program and they are encouraged to participate in any other relevant proficiency test.

Assays that we require specific validation review. This is for approval prior to actually offering the test. Any assay that is commercially distributed that is either labeled as research use only -- in other words, they're avoiding review by the FDA -- or any assays developed using analyte-

specific reagents. And we do thank the FDA for its recent clarification, but we think it will create some significant problems, which we have shared with Steve. FDA-approved assays or IUOs, investigational use only assays, that have in any way been modified from their intended use or IDE approval from the FDA. Any inhouse developed assays.

An intended use is anything which changes the specimen type, the type of analysis, qualitative or quantitative, the purpose of the assay -- are you doing screening, diagnosis, prognosis -- or the target populations as specified by the FDA, outlined in the package insert, or an IDE for an investigational use device.

FDA-approved assays and IUOs can be used simply by notifying the department that the lab wishes to add them.

Now, I'm frequently asked what is it we actually look at when we're looking at a validation package. We have been regulating cytogenetics labs since 1972 and genetic testing labs since 1990. But, again, I want to emphasize that our validation review process applies to any laboratory assay used in any one of the multiple categories. We do have category-specific standards by which we look at these materials, but these packages are the same whether you're doing a hematology assay, you're setting up a new cytopathology assay, you're doing microbiology, or you're doing genetics.

The materials the lab submits -- they tell us what they're calling the test, and you would be amazed at the innovation and creativity of some of the names out there. They have to tell us the manufacturer of any reagents they're using other than those they might make themselves. The majority of laboratories are not making their own reagents. They're getting them from manufacturers.

If using manufactured components, what is the commercial designation of that component. In other words, go to the manufacturer's catalog. Is it an RUO? Is it an ASR? Is it some other creative category?

What is the basic method or scientific principle behind the assay? Is this a DNA assay using PCR? Is it a cytogenetic assay using fluorescence in situ hybridization probes? What's the assay that they're proposing to do?

What New York State permit category -- and this takes great insight from the lab sometimes -- do they think this belongs in, and we'll tell them whether we think they're right or not. The implication of this is if this is a lab that was previously only doing molecular DNA assays and they want to now do a FISH assay for a chromosome rearrangement, they're going to have to qualify for a cytogenetics permit, in addition to their genetic testing permit, and they'll have to hire someone who meets the qualifications as a cytogeneticist. So there are implications as to what category of the test.

What specimen type do they intend to use? Blood, tissue, bone marrow?

What is their target population? Is this intended for individuals who are symptomatic with disease? Is it intended for general population screening? If so, what are the population parameters? Is it a diagnostic test, a prognostic test, a screening test, a predictive test? Is it qualitative or quantitative in its intent?

And how do they intend to establish its performance? Are they going to compare it to another existing assay similar to a 510(k) type arrangement for the FDA, or are they going to use clinical status of test subjects as in a new test for a rare condition? This list goes on and you have it in your slides, and I won't describe each assay.

How are they doing the test, down to the procedure manual that they would provide to the technician in the lab who would have to learn how to do the test?

They must also provide their practitioner/patient information, including their description of the limitations of the test. I think this goes somewhat to that issue of how do we disseminate information appropriate to help the clinician decide what test to do or to help the clinician

interpret the test after he's done it. We do rely on the laboratories to draft this material, but we do critique this material often to great extent.

The principle of the assay. How do they know it's a clinically valid assay? And we've talked earlier that very often these new genetic tests -- it is based on literature description of some association of this analytic marker with some clinical condition. For molecular genetic tests, we want the description of the actual gene structure, if known. But clinical validity is generally for genetic tests a literature-based observation, at least initially.

What equipment do they need? What reagents? Where are they getting them, and where are they getting their controls?

How are they going to calculate or interpret the result? This goes to that question of IVDMIAs. We don't care whether it's a single analyte simply reported as a quantitative value or a gene sequence or a chromosome rearrangement by ISCN nomenclature or it's multiple analytes taking demographic characteristics and put through a statistical equation. If it's the latter, we want to see the equation and the statistical basis on which that equation is derived. But how is the laboratory going to interpret the result?

What compounds or substances interfere?

What are the limitations of the test? This frequently goes to the issue of what patient population has the laboratory studied. Now, some of these assays are rare. Access to a known positive patient is sometimes close to impossible, and the laboratory will wish to offer the test having never seen an abnormal. We will approve a laboratory to offer an analytically validated test if they can detect the target, whatever it is, so long as they inform the practitioner who's going to order the test, prior to ordering the test and again at the time of interpreting the test, that the laboratory is reporting the result, but by the way, they've never seen an abnormal. And therefore, their ability to interpret these results is greatly limited.

We want to see their test requisition. How do they actually describe the test?

For germline genetic tests, they have to also, in New York State, document their compliance with our privacy and confidentiality statute which is Civil Rights Law 79L. It applies only to germline genetics and applies only under statute to predisposition testing, that is, nonsymptomatic testing, but most laboratories figure they'll just apply it to any genetic test.

We want to see their sample reports for both normals and abnormals, including all necessary disclaimers. If they're using ASRs, it must be the FDA-prescribed disclaimer. And we want to see their scientific references. They can simply give a list.

And finally, the critical component of this package is where's their data. How many specimens have they actually tested and what were those results and what are they comparing those results to? On what basis are they calling these normals or abnormals? How are they recording the data? But I would caution, we frequently review and approve packages in genetics that have tested 10 normal patients.

Analyte and specimen matrix stability, reagent source, quality, particularly for RUOs. If they buy an ASR, they can rely on the manufacturer to tell them it's that piece of DNA that came from that gene of that size that encompasses those sequences because the FDA has agreed that that manufacturer is a GMP manufacturer and they know what they're making.

If they buy an RUO, they can rely on the manufacturer for nothing. And if they buy a piece of DNA, primer, a FISH probe, whatever, they will have to establish some means by which they verify either the DNA sequence or the genetic component or the fluorochrome or whatever. We try to make the point to manufacturers as well, if you're going to sell reagents to laboratories that are developing clinical tests, you are not doing them any favor by being an RUO vendor. If you're a GMP ASR vendor,

at least the laboratory can rely on the product for whatever it is.

They must then establish the performance characteristics of the assay. What's the accuracy, the precision, the reportable ranges, sensitivity, specificity? And you would be dismayed to know how many genetics labs don't know what those terms mean.

Where performance evaluation is based on clinical outcome of test subject status, we need to know how they've established that. It isn't just the result of this test that tells them that they're normal or abnormal. They have to have had pathology, histopathology, clinical evaluation, symptomatic evaluation, however they're calling this a normal or abnormal patient. And when they're doing their validation, the analyst should not know who's normal, who's abnormal. It should be blinded to the analyst.

And when they get discrepant results, how do they resolve them? And how do they calculate their predictive values?

They must interpret the test. Our standards require that cytogenetics and genetics laboratories report with an interpretation suitable for a nongeneticist physician. If we bore the geneticists, well, that's too bad. They can skip it, but we want to make sure that those other physicians see something that they might be able to understand.

If there are reference ranges for germline genetics of single gene disorders, what are the heterozygote, homozygote results?

And does it predict disease state? Because a lot of assays are indicative of some risk factor, but they don't actually predict disease.

The assay data for actual runs, and what is their quality assurance plan and internal PT design? In New York State, we offer our own cytogenetics proficiency test. We occasionally test the ability of a lab to perform FISH, fluorescence in situ hybridization, but it would be for one or two target probes at any given proficiency test event. We ask all of these laboratories to have some form of proficiency assessment twice a year for every analyte. No commercially available proficiency test will provide them with materials to do every gene that they're doing, and for some of these labs, there is no commercially available PT material for the gene that they are doing. So they will have to have developed their own blinded proficiency assessment, probably using materials derived from previous specimens. The difference is that when our surveyors visit, they actually will ask to see the data and the design of that assay.

We're frequently asked about workload. Here are the statistics since we've been keeping them since 1995. This program actually started primarily for genetics, although it applied to every assay, in 1990 because there were no FDA-approved assays and there was no comparability testing.

In 1995, when we started keeping the numbers, we actually looked at eight assays. They were all genetics.

In 2006, we looked at 586 assays. The majority of them are genetics, but this includes not only genetic testing, biochemical genetic testing, DNA-based genetic testing, cytogenetics, it also includes for us the categories of preimplantation genetic diagnosis, forensic DNA technologies, paternity identity, histocompatibility, and oncology molecular markers. They just get thrown in there as genetics.

So for genetic testing workload, in 2006, we looked at 86 DNA-based, primarily single gene disorders; 5 biochemical types of assays. This would be enzyme assays, metabolites. I personally looked at 44 FISH assays. We looked at 3 paternity identity assays, 81 forensic identity assays. These would be different STRs, different markers, mitochondrial markers. And 92 molecular oncology markers for acquired changes or expression in cancer.

We're often asked what is the impact of the New York State program on testing in this country. We currently have 70 laboratories in the country, cytogenetics laboratories. Five of these are

preimplantation genetic diagnosis labs. The "genetic testing" should be bold print. I'm sorry. My PowerPoint technology is limited. And 32 of those perform biochemical genetic assays. That could be anything from quantitative amino acids to tandem mass spectroscopy for various metabolites to enzyme assays. Seventy-one molecular genetics labs, including four that perform preimplantation genetic diagnosis. I include those because that's a category that I believe only the State of New York examines their assays.

So the impact in New York State is all major reference laboratories solicit and receive specimens from New York. None of them have their primary labs located in New York. They're, therefore, subject to New York clinical lab permit requirements, including approval of inhouse assays. It has been estimated by others, not by us, that as much as 75 percent of all cytogenetic and genetic testing performed in the U.S. -- and that's in terms of numbers of specimens tested. It's not in terms of the number of labs. GeneTests estimates there are something over 300 labs. I've given you a list of about 170. And it's not in terms of number of analytes because there are lots of rare gene testing that goes on in labs that do one or two diseases or one or two genes that may not fall -- so it's not number of labs. It's not number of tests, but it is in terms of number of specimens tested -- are subject to New York State oversight. As I said earlier, tort law medical malpractice cases have not looked favorably on laboratories that are subject to New York State standards trying to get away with using lesser standards.

Now, I was also asked to review what I know about other states and their applications. There are 26 states that have statutory authority for oversight of the practice of clinical laboratory medicine in some respect or another. There is only one other state that has CLIA exempt status. That is the State of Washington. They do not, as far as I know, have specific standards for genetic testing in the State of Washington.

The State of California, through its Genetics Disease Branch out there and its newborn screening and prenatal screening program, has rigorous review of the assays related to newborn screening and newborn screening follow-up and prenatal screening that go on as part of that program. That oversight does not generally extend to other genetic testing.

The State of New Jersey does apply some personnel standards related to the American Board of Medical Genetics to their labs that perform genetic testing.

But I know of no state that actually requires validation data for individual assays to be reviewed, other than perhaps in the context of a physical onsite inspection which, at least for most state programs, does not involve peer review. It's not another geneticist visiting the laboratory.

I was also asked to address the issue of do we know about bad tests and harm that might have happened. Now, again, if specimens are going from New York to one of these labs that wishes to offer unvalidated assays or assays that we believe are problematic, we are aggressive in sending to that laboratory a cease and desist letter, and we warn them that we do have the authority to fine them $2,000 a day for continued operation or $2,000 a specimen.

Some of the recent examples have been a laboratory in New England that was offering to predict the gender of fetuses for moms when they were about five weeks pregnant. There we believe the significant problem with the assay is of analytical validity. They claim to be able to detect male DNA markers in maternal blood at the fifth week of pregnancy and therefore predict male fetus and in the absence, predict female fetus. The clinical validity -- if you could do that, you might be able to detect gender, but we've never received any validation materials from them.

The other laboratories have been those that offer to do SNP profiles and offer to provide the clinician with a CD which has the patient's entire SNP profile. And they tell you that your physician will then be able to provide interpretation and predict all of your medical needs.

(Laughter.)

DR. WILLEY: Since they've not been able to document the actual clinical validity for the vast majority of those SNPs, they are authorized in New York to market testing -- I believe at the moment it's only four of their thousands of SNPs.

We've had serious challenges from laboratories that wish to perform nutrigenomics. They will do a DNA profile primarily of SNPs that they claim are linked to particular genes that may predict your response to certain nutritional products, not unlike the survey that was done by the GAO. Again, lack of clinical validity. There's no association with disease. And yet, we would say that they are testing a specimen derived from the human body for the assessment of some component for purposes of health assessment. It doesn't have to be disease assessment in our statute. It can be health assessment. And the consumer expects to be advised as to their state of health, their response to their nutrition, and therefore, we say to the laboratory they should not be doing this.

The other area of great concern is hobby genetics. It may not be the topic of primary interest to this group. But there are entities out there who are offering profiling for your ancestry, profiling for paternity. You know, you've got the kid for the weekend. Just send us a little cheek swab. And you always wondered and we'll tell you if.

And since we regulate forensic DNA done in private laboratories, the personal private eye, you know, if you wanted to know if there was a little infidelity going around, just send us some sheets.

(Laughter.)

DR. WILLEY: And in New York State, consumers cannot legally order laboratory tests other than those which have been approved by the FDA for over-the-counter self-testing. So laboratories cannot accept the bed sheet, the cheek swab, whatever. And in genetics, they cannot accept any of those tests without the written consent of the person being tested. So we also tell the laboratories they must cease and desist on the grounds that they're violating the patient-ordered testing.

There are issues then. New York State restricts who can order tests -- it does not include genetic counselors, by the way -- and who can receive test results.

The greatest challenge to the New York State program is this is expensive. The program cost for the personnel and the expertise to undertake all of these reviews is significant. We currently have a lawsuit pending because the laboratories would like to not pay for that part of the program.

And the cost to the laboratories is also expensive. The preparation of the documentation of these validations in a format that is readily reviewed by the staff in the department takes laboratories time. Of course, the major criticism is -- there's a turnaround time. We try very hard for 45 days, but I have packages that have been in my office for a year. Very often they go back to the laboratories a couple of times before they get one approved.

So it's costly in terms of time. It's costly in terms of expertise, and it's costly to the laboratories.

The biggest problem is labs frequently ignore previously critiques. They are poorly organized submissions. So they end up going back a couple of times.

We talked earlier about postmarket surveillance. It's generally been our experience that, if you will, the health care market drives the survival of assays. If the assay isn't good or it's not predictive or it's not meeting needs of the medical community, the laboratory will withdraw its permit or at next inspection tell us they're no longer offering the test.

We do have an active program for receiving complaints and we do investigate all of our complaints. As I said, we do have the capacity to fine laboratories. If they told us they were going to follow one protocol and they're now using another one, they can be told they must cease testing until we

review the test.

There's a lot of enthusiasm for new tests. As a cytogeneticist, I would say three or four years ago the big new test was subtelomere FISH probes that were going to detect all these cryptic translocations. We only have three laboratories that are approved to perform subtelomere FISH. Only three laboratories bothered to make the effort to validate the ASRs. They're not really ASRs because they're packaged as multiple probes in five tubes. So there are three labs that are approved to do it. The assay costs about $1,000, and the numbers of assays being performed is very small.

The new test that has great enthusiasm that's sort of related to cytogenetics is array comparative genome hybridization, and there are a few labs that are saying, oh, we're getting so many positive hits, but we don't know what they mean. So after you get the array CGH result, you have to go back and verify it by conventional FISH assays on metaphase chromosomes, and we don't really know how that's going to play out. So we have four labs that are waiting to have their validation approved. None of them are yet approved.

We also have a system in New York. We don't make physicians wait until we get around to reviewing all these assays. If a physician for a medical necessity wants to order a test that is not offered in an approved laboratory or is offered only in a lab waiting in the quay to get their assay validated, they can make a specific request to the department for what we call a non-permitted lab approval. It's a one-time, that patient, that test in that lab. And the letter that goes back to the ordering physician says, you can send the specimen. A copy goes to the lab that says you can do the test -- we won't fine you $2,000 -- for this patient, for this purpose, for this time. But the letter to the physician also says we don't know anything about this lab. We don't know anything about this test. We don't know whether you'll ever see a result.

So we do handle quite a few of those requests. We have a 24-hour turnaround time on those requests. So when labs argue that this is so slow, it's keeping them out of the market, they can't offer the test, well, no, you can offer the test, put all the right disclaimers into it.

I'd be happy to take questions if there's time.

DR. FERREIRA-GONZALEZ: Thank you, Dr. Willey. This was very comprehensive, very interesting.

I have a couple of questions. In the materials submitted for review, you commented that when performed, evaluation is based on clinical outcome, and you made an allusion that laboratory testing will be compared to the histopathology of other clinical laboratory testing. Is that a clinical validation, or do you actually look at the clinical utility of the testing before you approve some of this?

DR. WILLEY: No, we do not examine clinical utility. By clinical outcome, I mean is this patient symptomatic of the disease for which you're establishing the test.

DR. FERREIRA-GONZALEZ: There's a clinical correlation.

DR. WILLEY: It's clinical validity. Are you calling this patient a known positive, or are you calling this patient a known negative when you're doing your validation?

DR. FERREIRA-GONZALEZ: So you do not cover the clinical utility of the test.

My second question is it was very interesting to see that you are able to identity the direct-to-consumer laboratories and you're able to go after them. I was just curious to see how you identify them. How do you know they're going after the --

DR. WILLEY: Our biggest challenge is the Internet, the direct-to-consumer marketing of anything, health care in general, pharmaceuticals, and laboratory tests. There are ones like the Gender Mentor that are quite obvious that it is a laboratory entity soliciting the submission of specimens.

There are also several companies out there that have established themselves as test

facilitators. They are not actually performing any tests, but they are marketing to the consumer population for a significant markup, oftentimes 10 times the money that the lab would cost. Sometimes they're using legitimate labs for legitimate validated assays. And New York State also has some lab practice general business laws regarding direct-to-patient billing. We do not allow third party facilitators. The laboratory must bill the patient and not bill through a facilitator. That's an other history.

DR. FERREIRA-GONZALEZ: One more question before we open it up. You mentioned that a company had submitted a test with a number of different SNPs. I don't know. It was genome-wide or so forth, SNPs profile. And then you only approved the use of four of those SNPs. I was wondering what was the rationale for approving only four versus the rest of the SNPs.

DR. WILLEY: For those four, they were able to document from the literature that there is a known association of that SNP in that region with a known physiologically active gene product or whatever that is associated with a particular risk or disease predisposition.

DR. FERREIRA-GONZALEZ: So you take peer-reviewed literature.

DR. WILLEY: Those four meet the criteria of being clinically valid and all of these SNPs are analytically valid. It's not hard to detect the SNP.

DR. FERREIRA-GONZALEZ: Now we'll open for a couple of questions before we have to break. Marc?

DR. WILLIAMS: You mentioned that you review reports for positives and negatives. One of the big issues with molecular is, obviously, a dreaded variance of unknown significance. Has your department begun to develop any standards about what the laboratories should be reporting back on variance of unknown significance in terms of what has been done to leave them in that sort of ambiguous classification? In other words, do you require certain steps to be done before one can stop determining whether it's a true positive or a true negative?

DR. WILLEY: Yes, for variance of unknown significance for DNA. And I'm looking at something one of my colleagues provided. I think they have to be able to describe how are they going to resolve the issue. Are they going to sequence the gene? Are they going to send it to another laboratory that can perform that? How are they going to report it and how are they going to resolve it? And are they going to put it in a data bank and follow it up at a later point, or those kinds of things?

That's not just for DNA-based. We see that in cytogenetic FISH assays, all kinds of things.

DR. TUCKSON: Terrific.

I guess the question then boils down -- were you here earlier?

DR. WILLEY: Yes. I've been here all day.

DR. TUCKSON: Terrific. So it would be great if you could help us, as Andrea and her committee of two now, the strong, the few, the proud, can pull together this map of what exists now and what are the gaps. If you could just sort of give some thought to that, it might help Andrea's team out a little bit as you sort of see the activities.

First of all, I'm going to write a letter to your boss because you're devoting a lot of extra effort to this stuff. So we need to write a letter of thank you as we ask you to do more and more and more here.

(Laughter.)

DR. TUCKSON: So you've kind of gotten roped in.

DR. WILLEY: I've been coming to these committee meetings since 1997.

DR. TUCKSON: Well, we're going to write a letter of thanks.

But if you could sort of also think how you would advise, in the best of all worlds, what we should be advising to the Secretary in terms of this so that we don't have this redundancy. We

don't want to spend the money of the people of New York and the people of the United States twice. And it seems a little bit unfair for citizens in New York to get hit twice because I assume New York still pays taxes even though you've told the FDA that they're not --

DR. WILLEY: This program, you should know, is supported by fees collected from the regulated laboratories. Unlike CLIA, we do not have a capped fee structure. We charge a very small percentage. It's currently less than .6 percent of the annual gross revenue of each of the regulated laboratories.

DR. TUCKSON: I'm sure they are still probably not pleased with that, though.

DR. WILLEY: No. They're suing us.

(Laughter.)

DR. TUCKSON: I am prescient.

So anyway, to hurry up, I think we really do want to try to lay that out and help to make sense. We can talk to you offline, but if you would be willing to do that, I think that will sort of speed this up a little bit.

DR. WILLEY: And I do think these collaborations and cooperations are very good. We rely very heavily on professional organization lab standards, the ACMG standards. When laboratories want to argue about how to go about validating an assay, we point to the documents that that professional group --

DR. TUCKSON: Let me just sort of ask it this way, and it is unfair. If you could be the head of CMS for a day, if you had a blank piece of paper and you could just do this the way it ought to be done so that it all lined up right, I'd be very interested to see what would come back from that point of view. That's what I'm looking for. If you could be in charge of fixing this, what would you say?

DR. FERREIRA-GONZALEZ: Thank you, Dr. Willey. I believe we're due for a break, and we can have a short break. Five minutes?

DR. TUCKSON: Ten-minute break, but it's got to be only 10 because she asked for 5, and I'm being nice.

(Recess.)

DR. FERREIRA-GONZALEZ: Because of the time -- we're a little behind schedule -- we will have the next three presenters going back to back. So if you can write down your questions, and at the end of the three speakers, then we'll have the questions for all of them.

Now we will take a closer look at the role of the private sector organizations in oversight, beginning with the accreditation of genetic testing laboratories by the College of American Pathologists. Dr. Vance -- I'm not going to try to kill your first name -- is a professor of medical and molecular genetics and professor of pathology and laboratory medicine at the Indiana University, Kansas Center, and Director of the Cytogenetic Laboratory at the Indiana University School of Medicine. She's also a member of the Board of Directors of the College of American Pathologists. We are privileged to have her today discussing some of these issues. Dr. Vance?

DR. VANCE: Thank you for the opportunity to present the College of American Pathologists accreditation program this afternoon to you.

I need to explain to you that I have revised the order of the slides slightly. That is the blessing and also the curse of PowerPoint. So if you follow along with the slides, there will be a few that are out of order.

As a presentation of the overview that I'm going to discuss today, I'll discuss shared goals, the CAP accreditation program as it pertains, in particular, to molecular pathology and cytogenetics, the proficiency testing that CAP offers, and conclude with recommendations.

The goals of the CAP accreditation program, as I'm sure are the goals of this

committee and other organizations, are to assure that tests being offered are analytically and clinically valid. We also wish to assure that there is patient safety and assure the public health and assure patient access to testing. We also wish to continue to allow for innovation and improvement of laboratory-developed tests.

The accreditation program is designed to assure that high complexity laboratory tests are provided by high quality labs that assure analytical and clinical validity of the tests they offer, that laboratories have a patient safety plan in place, and that there is incremental improvement and innovation in testing, and that that testing is not impeded.

Just a little bit of a background of the college. Now, as we are in the private organization session of the discussions, it is a professional organization. It's composed of approximately 16,000 board certified pathologists.

The CAP accreditation program is CMS-approved. It also, like New York, holds to a higher standard than the CLIA regs. We do have specialized inspector requirements for those inspectors inspecting genetics laboratories, and many of the standards that are created that are in addition to the CLIA standards arise through the scientists that populate the scientific resource committees.

In the College of American Pathologists, there are approximately 24 of these scientific resource committees. In the field of genetics, there are hybrid committees that are formed not only by college members who are pathologists, but also from laboratory scientists who are members of the American College of Medical Genetics. And you will hear from Sue Richards next who will be representing the ACMG.

Also, laboratories that are enrolled in the laboratory accreditation program are required to continuously report and update their testing menu. This serves for the purpose of not only knowing what they test for, but also so the CAP organization can match what the laboratory is testing for with the required PT.

A little bit of history about the CAP accreditation program. It began in 1961. It too predated CLIA. The program was initially voluntary. The first cytogenetics checklist and, therefore, inspections were offered in 1976, and 17 years later, a molecular pathology checklist was created and offered.

As a member of the accreditation program for the College of American Pathologists, laboratories are required to undergo biannual inspections. These inspections take place in the laboratory but by a team of external reviewers. So a team is formulated and they'll go to the hospital lab and inspect that laboratory. The team is usually composed of peer inspectors, and that means actively practicing scientists of the specialty which they're inspecting.

The tool that is utilized in these inspections is the checklist. Now, this checklist is not only a tool for the inspector, but it's also a tool for the laboratories so they understand the standards that they're being held to and they can utilize that checklist in preparing for their inspection.

There are approximately 18 checklists that CAP offers that consist of about 3,500 discipline-specific laboratory requirements. Over half of those requirements, approximately 1,700 questions, are in addition to the CLIA minimal standards. For example, there are special disciplines not covered by CLIA, and these include forensic testing, autopsy, histology processing, embryology, and also molecular pathology.

Sections within traditional disciplines that go beyond the CLIA standards include proficiency testing for nonregulated analytes, much like cytogenetics, laboratory computer systems, lab safety and hygiene, prenatal screening standards, and also sweat chloride testing standards.

As I said, the laboratories -- this includes the genetics laboratory -- are subject to inspection every two years. The inspection of the genetics laboratory requires special knowledge of the

science. Therefore, inspectors are chosen because they are actively practicing molecular scientists familiar with the checklist that they will be utilizing and also possessing the technical and interpretive skills necessary to evaluate the quality of the laboratory's performance.

There is training for these inspectors. Training modules are offered as live inspector training seminars or online interactive training modules. There are also audio conferences that are created for discipline-specific areas.

Also, there are requirements now for the inspector team. As of July 2006, every team leader that takes out a team must have completed mandatory testing and then must renew that testing every two years. There is also training for team members, and regulations are being put into place for a requirement of retraining as well every two years.

Some of the standards that apply to genetics that, again, exceed CLIA are everything that's asterisked here. But we do include assay validation, as stipulated in CLIA, clinical validation, use of universal and proper nomenclature, correlation with clinical information and other studies, recommendations for genetic counseling and further studies, and turnaround time requirements. And I'll be giving you some examples of that in just a minute.

Other examples where the CAP standards are beyond CLIA will include, as an example, two of the questions from the molecular pathology checklist, such as, are the clinical performance characteristics of each assay documented using either literature citations or a summary of internal study results? Another: does the final report include an appropriate summary of the methods, the loci, or mutations tested, the analytical interpretation and the clinical interpretation, if appropriate?

The molecular checklist covers most aspects of clinical molecular testing, but as you'll see, it includes not only inherited genetic testing, but also acquired genetic testing in the form of oncology and hematology, infectious disease, also inherited disease, histocompatibility typing, forensics, and parentage applications. Any testing that involves DNA, RNA, or nucleic acid probe hybridization or amplification would constitute molecular testing, and that laboratory would then be inspected by the molecular pathology checklist.

Techniques are also covered within this checklist and include compliance with requirements for extraction and purification, amplification, restriction enzymes or endonucleases, sequencing, detection, real-time polymerase chain reaction, or PCR, arrays, and in situ hybridization.

And I will mention that -- Ann was just talking about arrays -- we are now piloting a test for the CGH arrays in the cytogenetics resource committees and hope to offer that as far as a proficiency test later on, but also in addition to that, we're setting standards for analytic and clinical validity, if we can, of the CGH arrays.

There's also a cytogenetics checklist that covers cytogenetic testing, both standard G-banding and molecular cytogenetics. This covers chromosome analysis of amniotic fluid and chorionic villi, non-neoplastic blood and fibroblasts, neoplastic blood and bone marrow. It also has to deal with the establishment and maintenance of cultures, cells counted, karyotypes, band levels of resolution, and as I stated, fluorescence in situ hybridization, or molecular cytogenetics.

So what happens if the laboratory conducts its business, abides by the standards, and is inspected? So at the time of inspection, what happens if the inspector sees that the laboratory is not in compliance with one of the checklist questions or standards? Then a deficiency is cited. And if that deficiency holds -- in other words, there is a discussion with the inspector of whether there is a deficiency or not -- and if the inspector decides that there is, in fact, a deficiency, the lab must respond with corrective action to CAP within 30 days of the onsite inspection.

After receiving the response from the laboratory, there is a two-tier review process. This is composed of both a staff analyst who's a technical staff analyst of CAP and also a practicing

pathologist is designated as a regional commissioner to CAP. Between those two, they determine the adequacy of the action plan and the lab's ability to maintain sustained compliance. However, the ultimate authority or the ultimate decisionmaking resides with the Accreditation Committee of the Council on Accreditation. And this is a committee of lab experts who finally render their decision.

On an every other year cycle, in other words, on alternate years that the lab is not being externally inspected, the lab is required to complete a self-inspection and submit the results of that self-inspection. The results of that self-inspection then go into the inspector packet for the next cycle of external inspection. So that inspector will have with them the results of the self-inspection performed by that laboratory in the interim years.

Just to give you some information about how many labs that CAP accredits, we accredit both national and international labs. There's about a total of 6,600 laboratories that are accredited. Approximately 250 laboratories in the cytogenetics discipline and approximately 700 -- or that's sort of a dynamic number -- with molecular pathology discipline. As was quoted in Modern Health Care, this includes 98 of the top 100 hospitals, and the majority of large commercial reference labs, including Lab Corp and Quest, are accredited by the College of American Pathologists.

Some of the deficiencies that are cited after the inspection process in molecular pathology. There are three that are listed here, and associated with these, you can see the percent of that approximate number of 700 labs that were cited for this deficiency.

The first one reads, in the cases where there is no commercially or externally available PT, does the laboratory at least semi-annually -- that's in compliance with CLIA -- participate in external PT or exercise an alternate performance assessment system for determining the reliability of analytic testing? About 3.9 percent of the 700 or so laboratories received a deficiency for this. They must respond to CAP with an action plan in how to correct this deficiency.

Are temperatures checked and recorded appropriately for equipment in which the temperature is critical?

Is there a summary statement signed by the laboratory director or designee documenting review of validation studies and approval of the test for clinical use? And in this situation, there's about 3.3 percent of the molecular genetic testing labs that we accredit that have received a deficiency for this checklist question.

For cytogenetics, the most common deficiencies cited are: is the final report for tests requiring rapid reporting results available -- and that's the final report, not the preliminary report -- within 7 days of specimen receipt in at least 90 percent of the cases? And 7.6 percent of the laboratories inspected were cited for this deficiency.

Is the final report for neoplastic bloods and bone marrow analysis provided within 21 calendar days of specimen receipt in at least 90 percent of the cases? And 6.8 percent of the laboratories were cited for this. Again, this is a standard that goes beyond CLIA.

Are reagents and solutions properly labeled as applicable and appropriate? And there are four or five criteria that must be on the reagent that is being used. And if only one of those is missing, they are cited for a deficiency. And that's approximately 4.2 percent of the laboratories that were inspected.

So that's just an overview of the inspection process. I'd like to turn now to proficiency testing.

The college does offer external proficiency testing for genetic laboratories which allow the laboratories to regularly evaluate their performance and improve the accuracy of the results. In these proficiency tests, each laboratory is provided with unknown specimens for testing. They are told the category, but they're not told what particularly the specimen is. The participants analyze the

specimens and return the results to CAP for evaluation. The results are evaluated by the scientific resource committees or their peer groups. And statistical support is provided by CAP.

So for these proficiency tests in genetics, to my knowledge CAP is one of, if not the only, very few that offer proficiency testing for genetic testing. Some of the products that are available include chromosomal abnormality identification, fluorescence in situ hybridization using chromosome-specific DNA probes, biochemical genetics for metabolic diseases, and molecular analysis of lymphoma and leukemia.

This is an algorithm that shows you what happens when there is a PT failure in a laboratory. This algorithm starts on the left with the black arrow. So the laboratory is required to participate in PT for its analytes. If it receives an unsatisfactory PT evaluation or one PT event, the laboratory is issued a warning for testing for that particular analyte. They're also provided with some educational material on how to do better.

They are then monitored. If they receive one unsatisfactory report of the next two PT events, they are given a choice to either cease testing for that analyte or to document a plan of corrective action.

If the laboratory chooses to document a corrective action plan, they submit that. It's reviewed. And if it's acceptable, they're allowed to continue testing for that analyte until the next PT event, and at maximum, that's six months.

If the next PT is satisfactory, then they are monitored again for another PT cycle. If they are good after PT cycle, they're allowed to continue testing, and they start the algorithm all over again.

If on the following PT event for that analyte, they again receive an unacceptable response, they are required to cease testing for that analyte, and then they must sign a cease testing form and then again document a plan of action to bring that analyte up. The earliest that that laboratory could be again testing for that analyte is approximately six months.

This just gives you a summary of some data. This actually is from the committee that Dr. Richards sits on. It's the Biochemical and Molecular Genetics Committee. It's a busy slide, so I'll go through it with you.

Down the left-hand side of this slide are the different analytes. So for the first one, it's Factor V Leiden. And there are two challenges. This is 2006A and 2006B. The number of labs that were tested for this analyte was 784. The number achieving a correct response for this analyte was 99.2 percent of the laboratories.

Right underneath that is the appropriate interpretation for the value that they discovered. For 2006 for A, there were 786 laboratories that participated in that PT, and 782 obtained the proper interpretation for that analyte, with a result of about 99.5 percent of the laboratories testing. And if you read across for the interpretation, the summary for both challenges A and B was 99.6.

I won't go through all the numbers, but I will read the different analytes that are on the left-hand side there so you understand some of the analytes that are being tested. So in addition to Factor V Leiden, there's prothrombin, prothrombin interpretation, methylene tetrahydrofolate reductase, Fragile X mental retardation, Prader-Willi, hemochromatosis, Duchenne's muscular dystrophy, and hemoglobins S and C. And as you can see, if you just look down the right-hand column there, laboratory performance on these various analytes was quite good in 2006.

So in conclusion, the CAP laboratory accreditation program we believe can serve as a model in your patchwork that you're designing to improve the quality of laboratory-developed tests through the accreditation process in a way that improves patient care, protects the public's health, but yet does not stifle or impede test development, innovation, and improvement.

Our recommendations to the committee are that private organizations, including the CAP, and laboratories should continue to build on the work with CLIA that has been successful, in our opinion, over the last 15 years. CAP also believes that the goal of assuring analytical and clinical validity for all high complexity laboratory tests can best be achieved through the CLIA inspection process. But we also understand and do realize that in order to achieve this goal, that statutory changes to CLIA may be needed.

And I guess I'll hold questions.

DR. FERREIRA-GONZALEZ: Thank you, Dr. Vance. This was an outstanding presentation.

Now we will turn to Dr. Sue Richards. Dr. Richards is a member of the Clinical and Laboratory Standards Institute, Molecular Area Committee, and a member of the CDC EGAPP Working Group. In addition, she's the chair of the Quality Assurance Committee of the American College of Medical Genetics. Her research interests include the transition of molecular tests from the research setting to the clinical setting, development of genetic testing for the rare genetic disorders, and interpretation of sequence variants. She's here to provide us with some insight on standard setting for clinical laboratories.

Dr. Richards?

DR. RICHARDS: Well, thank you very much for inviting me here to represent this area.

So while I'm involved in developing standards with a number of groups, I'm primarily going to be representing the American College of Medical Genetics in this talk, and then I will try to interface these various groups that are also involved in this big, important project.

So professional guidelines are very important to us for setting standards of practice. Through ACMG, there are multiple mechanisms by which we set professional guidelines. One is through the Laboratory Quality Assurance Committee and the other is through the Professional Practice and Guidelines Committee. And then we also have the mechanism of developing special projects of commissioned guidelines. And I will try to give you examples of all of these throughout the talk.

There are three different types of statements that may come from the college that would be viewed as practice guidelines or as standards: policy statements, in which this is often a response to a single issue that needs to be addressed immediately, and this is quite short. A practice guideline is generally a clinical guideline of how testing should be done in what setting. So this is talking to the clinical roles. Then accompanying that quite often is the laboratory standard and guideline, which addresses what I think we are addressing here in this meeting in terms of how exactly laboratories should perform particular tests.

So the purpose of our standards and guidelines, while these are voluntary, they provide an educational resource to primarily the laboratory, and we want to address the quality of genetic testing, ensure quality. And to that end, we actually address technologies and procedures in the clinical genetics laboratories in all of the subspecialties.

So I'm going to turn to the Quality Assurance Committee as a resource and how this is done. This group is dedicated to evaluating new technologies as they come in use in the laboratory, monitoring the accreditation requirements, as we've heard from New York State, from CLIA, and through CAP, and monitoring laboratory proficiency testing. We have on our committee representatives that attend these meetings for the CAP Resource Committee, and when these results come in, we want to know how laboratories are performing. We use these as triggers for developing new standards and guidelines. If there is an analyte in which laboratories are performing poorly, as we might have seen in test interpretation perhaps in the mid-1990s, then we address it with a guideline and we see the

performance improve.

So our guidelines are virtually a notebook, a manual that continues to change over time with ongoing updates. We have what we initiated in 2000, the disease-specific guidelines, and I will show you examples. We also are including model laboratory reports in our guidelines, and this is also very consistent with some of the other projects ongoing through CDC in looking at reporting issues.

We function as a resource for education, and that's not just for the genetics community, but we do outreach education. When we develop new guidelines, we try to be involved with different professional groups and organizations where we can go and give workshops and make the individuals aware who are actually performing testing that new guidelines exist because getting the message out is part of the issue. So that's to identify test quality and discuss communication of test results.

So who is involved? I tried to answer your who, what, and why questions. Who is involved in laboratory standard development? We have three working subcommittees from the Laboratory Quality Assurance Committee that addresses the basic issues of molecular, cytogenetic, and biochemical genetic groups. We have a biostatistician who is involved who helps to guide us in some of the validation questions and statistical work that we need to look at. And we frequently include experts in fields of selected topics that we are working on.

The current group is shown here. It's quite a large group, and it's composed of ABMG-certified clinical laboratory geneticists in these specific areas. We have representatives that are involved in the Clinical Laboratory Standards Institute, CLSI. We have representatives to CDC in working projects of EGAPP. We have representatives that are working with the CDC reports and how that's translated to physicians in communication efforts. And we have the CAP representative. So we have a pulse on what's going on in genetic testing, and we try to address new issues as they surface.

So just to recap, how do standards ensure quality of genetic testing? They set standard of practice in the field. They're used in developing the laboratory inspection checklists for CAP as a regulatory requirement for accreditation. And they're used in developing proficiency testing challenges and test interpretations through the CAP process and as an educational resource.

So I want to give you an example of how our private professional guidelines have intersected with government. I'm going to use an example that came out of a CDC and NIH-sponsored meeting that was in May of 2004, Promoting Quality Laboratory Testing for Rare Disease: Keys to Ensuring Quality of Genetic Testing. It was the first national meeting that would address quality and availability and accessibility of genetic testing for rare disorders. It was so successful that many more participants from many more venues came to the table in 2005. And as a result, this is where the CETT project, the Collaboration, Education, and Test Translation, came out of. But there were other products from that meeting that might not be recognized.

Now, this is the chart, diagram that I believe Marc Williams was referring to as our draft framework in the process to enhance genetic testing for rare diseases. Now, you will see that only as the government can do, it was quite a complex model. But I think what it illustrates is that there is so much room for interface with various organizations, professional organizations, government organizations, in translating potential tests into service in the end.

What I'd like for you to focus on is that there is a need for the guidelines and standards to ensure quality assurance for our genetic testing. This is where we feel that we play a big role in the development of these standards, and we want to work hand in hand with you.

So this is the other product that came out of that meeting. It was a laboratory guideline developed by the American College of Medical Genetics on technical standards and guidelines for molecular genetic testing for ultra-rare disorders. There was a need recognized for that guideline. I've

listed here what the different sections address.

For example, technology guidelines, what types of technologies are specific for this type of testing, how personnel might need to be even more qualified in this area, how test validation should be done, quality control standards, and quality assurance programs that specifically apply to this type of testing, test interpretation, and so forth. We address pre-analytical, analytical, and post-analytical test issues. We even address pitfalls that could be involved in genetic testing to educate and make laboratories aware of this.

I'd just like to also reemphasize that we included sample laboratory reports in this document. We have had wonderful feedback from laboratories that this is very helpful to them both nationally and internationally. So I think this is an internationally recognized document, and it was published in Genetics in Medicine.

We have a number of guidelines that are being developed through various working groups, and this list here is shown for a number of documents recently that have come out of the Biochemical Genetics Work Group. You'll see that there are a number that are specific for prenatal screening. So a need was recognized here.

The same is true for molecular genetics disease-specific guidelines. Cystic fibrosis was a guideline, of course, that was prompted by the ACMG-ACOG recommendation to offer prenatal screening for cystic fibrosis to all reproductive couples. The technical guideline for laboratories came out shortly after that recommendation came through.

The Fragile X guideline was a guideline that was triggered because laboratories in the mid-1990s did not perform well on the Fragile X interpretation on the CAP proficiency test, and as a result of our guideline, they performed much better.

Cytogenetic guidelines are shown here. These are all approved guidelines. These are based on techniques and various tissue types that are examined whether prenatal or cancer. I'll just call to your attention we do have a recent guideline that has been approved by the board for comparative genomic hybridization, CGH, arrays. Hand in hand, that guideline goes with the practice guideline.

So not only are we developing other specialized guidelines in process, but we also have programs that we are launching through our committee to ensure quality of genetic testing.

What I'd like to call your attention to is the Quality Watch Program. It is a program for reporting and following up on adverse events that are suspected to be caused by laboratory products or reagents that would impede accuracy in genetic testing. This will be launched with our new website next month, and we're looking forward to a very interactive communication with laboratory groups.

So let me turn to how standard development is supported. Well, our committee from ACMG is comprised of volunteers. We all have day jobs. Commissioned documents that come from ACMG come through industry grant funding, and the cost of that can come at a very high price. For the pharmacogenetics standard and guideline that has been developed, it is estimated at around $100,000 per standard and guideline. This covers meeting cost, evidence-based reviews, and administrative costs as well.

And our newborn screening documents -- and you might be aware of the ACT sheets that have come from ACMG. This was such a large meeting. The cost was closer to $1 million. So standard development does not come cheap.

How are standards developed? Well, first is to identify a need and to make sure that we want to move in that direction. Once there is a go-ahead, we identify a leader for the project who really is the one that is responsible for getting that written. But a work committee is assigned of approximately five or six members to accompany that leader. And through conference calls and emails, they develop documents.

Now, I'll just impress upon you that with all the standards and guidelines we have developed through this time, there are two meetings a year face to face, three-hour meetings. And the rest of the work is done behind the scenes, and there's no funding for it. So if we are lucky and we are fast-tracking a guideline, we can get a guideline reaching draft form within six months with a lot of work and commitment from those groups. And many guidelines take much longer than that.

There's a thorough review process for this, and we are trying to emulate the CLSI consensus document review. We're striving very hard to do that through review from the work groups, the committee we send out to experts in the field. We post the documents once we are happy with them on our website. We invite member comment. We take those comments to heart. We incorporate that back in. It finally goes to the board for approval, and then if it's passed, it is posted on the website, incorporated in the standards and guidelines and published in Genetics in Medicine.

And it doesn't end then. Let me impress upon you that there is a continual renewal, revision, and either we retire, we renew, or we revise at least every three years. So the more guidelines you get, the more work you have to do.

Are they enforced? Well, in our guidelines, we say they are completely voluntary. However, you have already heard that they're used for developing accreditation standards and proficiency testing models. So I would say, in fact, they are enforced through CAP.

How do they relate to regulatory requirements? We have higher standards. The requirements we put in our standards even exceed that of CLIA requirements. We have paid attention to CLIAC recommendations. We've incorporated them preemptively in our guidelines so that we would be very much on top of it. We reviewed New York State requirements. We include many of these in our guidelines. And we also interact with our European and Australasian counterparts to try to get some harmonization in the guidelines worldwide. We are very focused on looking at nomenclature standards and reporting standards.

So how do these standard-setting organizations interact with and involve the government? We do respond to the government on guidance statements and also on legislation proposals. Whether or not they want to hear from us, we do. We include government representatives in our committee work for developing the standards and guidelines. I'll just give you an example. We utilize documents that are produced through CDC through the ACCE review and now through the EGAPP process with evidence-based reviews that will be useful in our decisionmaking process. I've shown you the ultra-rare disorder example for that standard and guideline.

How do standards keep pace with advances in knowledge in technology? As I've told you, it is a three-year renewal cycle, but if things change before that time, we're quick to make changes in our documents. This is a very big challenge with very limited resources.

So just some facts to reflect on. We have a big job to do. There are a lot of genes, and there are a lot of diseases in which clinical testing is available and new tests coming on all the time. So when you ask me to address are there gaps in current standards, I couldn't stand here and tell you that there aren't. There will always be some kind of gaps. There are more genetic tests than we can develop disease-specific guidelines for, and our resources, of course, are limited here.

But I think there is a gap that perhaps this group might want to address and that is a gap that involves an area that you're actually going to be speaking about tomorrow, which is your gene patents and licenses. I think what is happening now is we are seeing, with exclusive licensure of testing to a single entity, that we will not be able to provide the expertise for developing the standards or the expertise for doing the proficiency testing or have the resources to be able to support that.

So are there opportunities for us to collaborate? Well, absolutely. We would welcome a collaborative effort with these groups.

We do think funding is a major message, that we could use help in funding for more guidelines development. We could actually have a full-time individual doing this and still have work to do.

But we think meetings that would bring groups together, similar to the rare disorder meeting, to discuss these areas and to give input from different stakeholders and interest groups and users would be a very good step, providing more funding for evidence-based reviews on genetic disorders, such as the EGAPP model, and providing funding for filling in the gaps. For example, one piece that's missing on our guidance document for pharmacogenetics is that we need randomized, controlled trials, and this is a huge undertaking to establish the clinical validation.

Just finally, do the laboratories follow the standards and guidelines? Well, we think that they do. The CAP surveys, as you have seen from Gail Vance, show that the laboratories who are participating in the survey are doing quite well. And we believe, since we are so connected with this survey and our guidelines are connected with it, that that means that they are using these guidelines.

This is a resource that I would encourage you to look at, if you are not familiar with the standards and guidelines. It is freely available to everyone. You don't have to belong to ACMG to get the standards and guidelines. Just go to the website.

Thank you.

DR. FERREIRA-GONZALEZ: Thank you, Sue. This is a wonderful presentation.

We will move next to our next speaker, Dr. Berg. He'll be connecting with us through, I think, teleconference, Sarah?

MS. CARR: He'll be with us on videoconference.

DR. FERREIRA-GONZALEZ: So what we're going to do is start introducing Dr. Berg, even though he's not here.

Dr. Alfred Berg is here to discuss the development of clinical practice guidelines. He has been very active on several expert panels in this area. He was chair of the CDC Sexually Transmitted Diseases Treatment Guidelines Panel and member of the AMA-CDC panel producing Guidelines for Adolescent Preventive Services, and a member of the IOM Immunization Safety Review Committee. He currently chairs the CDC EGAPP Working Group, as well as an IOM panel examining evidence on the treatment of post-traumatic stress disorder.

Good afternoon, Dr. Berg. Welcome.

DR. BERG: Thank you. Should I just begin?

DR. FERREIRA-GONZALEZ: Yes. We have already done your presentation while we were waiting for the connection. If you would please go ahead.

DR. BERG: Thank you. Well, it's a pleasure to be with you this afternoon. I wanted to start with this slide that says, "When it's eternity here, it's still early morning on the west coast."

(Laughter.)

DR. BERG: I appreciate being able to do this by teleconference as opposed to traveling.

I wanted to show you where I come from. This is to illustrate. In the distance, you can see the outline of the United States. These are the five states for which there's only one medical school, the University of Washington. I spend a good deal of my time traveling around the region, and a good deal of that time is spent in the offices of physicians who are actually trying to deal with the complexity of medical decisionmaking. And I can tell you that the issues of genetic testing are a very big issue in our region, trying to figure out how to make sense of an increasingly large and confusing body of literature.

I'm going to spend just a few minutes giving an overview of clinical guidelines. My

background is actually not in genetics or genetic testing, but in the development of clinical practice guidelines. I worked with the Preventive Services Task Force for a number of years, with the Institute of Medicine on some guidelines related to vaccinations, and I'm now also chairing a CDC panel about genetic testing that I'll get to in a moment, and an IOM panel on post-traumatic stress disorder. So my background really is more in clinical guidelines than it is in genetic testing.

Guidelines have always been with us. They really are simply preformed recommendations issued for the purpose of influencing a decision about a health intervention. And we've always had them, as long as medicine has been practiced. Professors pontificate. Textbooks give us advice. Journal articles, editorials, consensus panels, and so forth.

The problem is that in the past many of the guidelines have just been wrong. They've been well-intentioned and well-advised by an expert but they've proven just incorrect in practice.

There's also been extremely wide variation in practice which not only leads to wide variation in outcome, but wide variation in costs.

Medical literature is increasingly complex, which makes it difficult for an individual clinician to get their arms around a given clinical topic and make sense of it.

Patients are interested in more participation in medical decisions, and guidelines when published and explicit are usually publicly available which allow patients access.

There is always legal pressure to help define standards in medicine.

And finally, part of the renewed attention in guidelines is simply because we've got better methods to generate them than we've had in the past.

From a clinician's point of view, no one can keep up. The volume of medical literature is enormous and growing. Guidelines help make sense out of what can literally be thousands of articles about a given clinical topic. They help clinicians deal with complex decisions, we hope improve the quality of decisionmaking, and increasingly provide justifications to patients, payors, and even the legal system about why decisions are made the way they are.

So guidelines are potentially useful to transmit medical knowledge, to assist patient and physician decisions. They're a way to help set clinical norms. They're increasingly used in quality improvement projects in hospitals and group practices. They're used for privileging and credentialing and also can be used for payment, cost control, and medicolegal evaluation.

In the past, most guidelines were constructed using what I'd call global subjective judgment. It's a technique where you basically lock clinicians in a room and tell them to figure it out. And you really don't know much about the process that went on. Nowadays, of course, guidelines are increasingly explicit and evidence-based, and there are several hallmarks of an evidence-based guideline. It should be explicit, that is, clearly laid out. It should be transparent so anyone going back to look at it can figure out how you reached the conclusions that you did, and it should be publicly accountable. So it should be published and available not only to clinicians but to all comers.

Here are some of the characteristics that the Institute of Medicine believes should be specified when developing a clinical guideline: first of all, to be extremely clear about the clinical condition; the health practice or intervention that is proposed; the target population; the health care setting, whether a specialist setting or a primary care setting; the type of clinician, nurse, physician, nurse practitioner, physician assistant; the purpose of the guideline, whether to improve clinical care or have some other purpose; and finally and very importantly, the source of the guideline and sponsorship, that is, who's paying to have the guideline constructed.

The Agency for Healthcare Research and Quality has also specified a number of process characteristics. These are things to look for when you're looking at a clinical practice guideline. How was the panel selected? In particular, what were the screens for potential conflict of interest. How

was the problem specified? Very explicitly, how was the literature strategy devised, how was the analysis conducted, how was the evidence summarized? And linking the evidence to the recommendation needs to be as explicit as possible. This is often still one of the black boxes in clinical guidelines, but as much as possible to be explicit about how you get from the evidence to the recommendation. To be clear about the clinical outcomes, and finally, the process should be sensitive to cost and practicality.

The AHRQ further described desirable attributes of a guideline. There's a separate slide on validity, but the guideline needs to be valid. It needs to be reliable so that it acts the same in each circumstance where it's applied. It needs to be practically applicable. It needs to be flexible, clear, multidisciplinary. It should be peer reviewed before publication, and it needs to be well documented.

Then finally, on issues of the clinical guidelines, here are some characteristics of validity that AHRQ recommendations. A valid guideline should be clear on projected health outcomes, on costs, on any parts that relate to policy rationale. It should be evidence-based and rigorously based on the literature review, evaluation, and on the strength of evidence.

So that's an extremely quick overview of the guidelines business. I see around the table a number of individuals who are quite expert in this who, I'm sure, could answer any questions better than I.

But I'd like to move on and discuss one particular guideline project. Again, I see a couple people in the room who are very familiar with this, and that's the EGAPP project. This is from the Centers for Disease Control and Prevention, EGAPP standing for the Evaluation of Genomic Applications in Practice and Prevention.

This is a slide that I call "Parents of EGAPP." These are some of the principal reasons I think that EGAPP was formed.

First of all, an obvious, growing availability and promotion of genetic tests. You have only to go to the Internet and put in "genetic tests," and see the many thousands of hits that you get, many of which are available to consumers without going through any sort of clinical advice.

A second parent is that clinicians need authoritative advice. This gets back to my experience with the five states for which we're the medical school. The clinicians out there in practice really would like to know whether these tests are ready for clinical use.

Finally, one of the parents, I think, is the natural evolution of these evidence-based processes that were used previously. One example is the United States Preventive Services Task Force.

Now, here are some of the challenges I see in using the standard evidence-based methods for genetic tests. First of all, as opposed to some of the conditions that the Preventive Services Task Force worked with, for example, with breast cancer or colorectal cancer, many of the conditions in genetic testing are uncommon or exceedingly rare. In many circumstances, the interventions and clinical outcomes are not well defined. The technology is evolving quickly so that the interventions -- sometimes the test characteristics change quickly, and we haven't had time to really examine the clinical outcomes in detail.

Many of the tests have inadequate sensitivity and specificity in unselected populations. They may be very effective tests in highly selected populations, but when applied in a general population, lose important test characteristics and thus have poor predictive value.

Many of the tests that we see are proposed and marketed based on descriptive evidence and pathophysiological reasoning with really no clinical trials yet.

And there is an important overlay of advocacy from various sources, but especially from industry and from patient special interest groups.

EGAPP has the CDC as its principal sponsor. It's a nonregulatory panel; that is, we don't have any inside track on any regulatory authority. We're all independent, non-federal employees

and very multidisciplinary. The panel went through an extraordinary review of its own conflict of interest to make sure that we had no one on the panel who had made up their mind about genetic testing or who had financial interests at stake in any of our decisions. And we're trying very hard to make the panel evidence-based, transparent, and publicly accountable. We do have public sessions.

Our goal is to establish and evaluate a systematic and sustainable mechanism for pre- and postmarket assessment of genomic applications in the United States.

And we've spent a good deal of our first couple of years working on the methodology. Here are some of the characteristics of the methodology. Devising a method for choosing the topics was in itself a major task, given the many hundreds of tests out there. Devising a methodology for constructing analytic frameworks for our literature search strategies and for our assessment of the evidence. This particular domain of genetic testing adds analytic validity to the other common kinds of validity that you look for in testing, which has presented its own particular challenges to the panel. And finally, a methodology to properly specify clinical outcomes. Many of the clinical outcomes in genetic testing are different from the clinical outcomes that one would look for in other domains of medicine.

We've actually gone fairly far, I think, advancing the field of clinical outcomes. We're pretty far in a manuscript for potential publication that outlines four general categories, one category being the diagnostic thinking or health information impact.

Another, therapeutic choice, impact on patient outcomes, and finally, impact on the family and society.

Our work plan is to select topics, define the outcomes, and conduct reviews, and then to test the methods. The first several topics that we're examining are CYP450, HNPCC, and screening for ovarian cancer.

We also are experimenting with brief reviews where the data are quite limited. We may not be able to cover all the components in a full clinical practice guideline so the scope is narrower and not in as much depth. And our first review is a UGT1A1.

We're midway into year three of a three-year project that's extended to four, and rumor has it that it may end up being five. We hope for three to five major reviews, two to three brief reviews, publications about our methods, and finally, rigorous evaluation.

I thought I would just conclude by walking you through one topic which is fairly far advanced with EGAPP to give you a sense of how the panel works. This is the clinical scenario that we specified for our review of CYP450 testing.

The question: does testing for CYP450 polymorphisms in adults entering SSRI -- that's selective serotonin reuptake inhibitors -- treatment for nonpsychotic depression lead to improvement in outcomes, or are testing results useful in medical, personal, or public health decisionmaking? So this is the question that we hope to provide useful advice to clinicians and patients and others.

The methods that we've used were, first, to develop an analytic framework. Out of that framework, we extracted a series of key questions; around each of those key questions, then conducted an explicit search using a standard abstract, full text, and two reviewers; assessing the quality of evidence; and putting together evidence tables, when there was enough to put into a table, which wasn't often.

And these were the key questions. First of all, the overarching question: does testing improve outcomes? A second, derivative question: what are the characteristics of the tests? What are the correlations of the tests with metabolism, efficacy, and adverse effects? Are there any known effects on management, clinical outcomes, or decisionmaking? And are there harms associated with testing?

We're not ready to release the recommendation yet, but here are some preliminary

observations from our discussions so far. We found some data on sensitivity and specificity, but no studies -- and I would underline "no studies" -- directly linking testing to clinical outcomes. The studies that we have are small, poor quality, mostly cohort studies. We found no studies that directly compared alternative testing strategies, and many of the studies fail to account for all of the relevant genotypes, making it extremely difficult to combine the studies into a single clinical recommendation.

So you can tell from that that this has been quite a challenge. The panel is meeting in about three weeks to finalize our clinical recommendation out of this data source.

Here are the other topics that are currently in review: tests for ovarian cancer, HNPCC for patients with colorectal cancer. I mentioned the brief review of UGT1A1 for patients treated with irinotecan for colorectal cancer, and we've just begun gene expression profiling in breast cancer, genomic profiling for cardiovascular disease, and CYP450 profiling for pain management.

So I'll conclude with two slides. This is kind of my summary of the apparent gaps in evidence, given my experience so far in this domain. There's a gap in evidence about the prevalence of some of these abnormalities in the general population, a gap in evidence regarding the penetrance of the abnormalities into something that's clinically recognizable. There's an absence of clinical trials that compare testing and intervention strategies, an absence of studies that fully assess all the relevant outcomes, very little attention to harms, mostly just attention to potential benefits, and very little literature regarding cost and feasibility of these technologies.

Then my concluding slide, which are my personal observations. This is a large and growing question for clinicians here in the United States, both for clinicians and for consumers on how to make sense of this. We tend to be in a national attitude where more is always better and that technology is always good. I just recently returned from a meeting of the German Genetics Society in Bonn, Germany, and it's just always fascinating being elsewhere and finding such a completely different view of technology and how it fits into the social good.

We have an environment here which is relatively hostile toward regulation.

There is potential using these technologies for both benefits and harms and, unfortunately, finding limited evidence. And I'd have to say that I knew that this was going to be a problem getting into it, that our evidence base was going to be limited, but I didn't realize how limited it would be. We've chosen some very important topics for our initial few reviews which are supposed to be about as good as it gets, and yet, we're finding major gaps in the evidence in all the reviews that we've undertaken so far.

So I apologize for zipping through this, but I know that the discussion is always more interesting than a presentation. So I'd be happy for comments or questions. Thank you.

DR. FERREIRA-GONZALEZ: Thank you, Dr. Berg. This is very timely with some of the tasks that we're going to be undertaking.

I would like to ask the other two speakers to come up front, please, Dr. Vance and Dr. Richards. If you can sit at the front of the table.

I will open the committee for questions. We have a limited amount of time. So if we can have a specific question from the committee. James?

DR. ROLLINS: Dr. Berg, this is a question for you. On one of your slides, you talked about the gene expression profile for breast cancer. Currently a number of insurance companies are paying for a mamoprint, as well as oncotype dx for gene profiling for the occurrence of breast cancer. It seems like maybe the cart was put before the horse because a number of insurers are currently paying for it, but yet, this is one of the proposed studies that you're going to be looking at in the future in terms of the EGAPP goal?

DR. BERG: Yes, and thank you for that question. One of the reasons that this area

particularly interested me is that I spent 10 years with the Preventive Services Task Force where the horse was long out of the barn before we got to any of the topics. There are many things that are out there that are being routinely promoted and used for which the evidence base is actually quite thin, and I was hoping that for this domain, we might have a crack at getting to some of these things early enough to help clinicians and consumers make the decision before it becomes the standard of practice without evidence.

So we're not very far into that particular assessment, but I'm hoping that we can move quickly enough to actually get ahead of it and help clinicians and consumers decide whether it's a good idea, and if so, in what circumstances, and if it's not a good idea, what are the circumstances that we should be wary of.

So I think it's an excellent question that relates to this domain in particular. There are many things out there that are being marketed that would be nice to have an assessment done before the horse is out of the barn.

DR. FERREIRA-GONZALEZ: Reed?

DR. TUCKSON: Well, thank you, all three of you, for your involvement.

Dr. Berg, I'm going to try to catch you up real quick in 10 seconds on some important conversations that occurred prior to your joining us. Earlier today, the Secretary of Health's office gave us a specific challenge to respond to some specific and relevant questions regarding oversight. One of those actually was very relevant to your point, and that was to provide some guidance on how tests are selected by providers as part of our oversight responsibility. I think that you've sort of spoken to those issues in some ways today.

Again, because I'm the chair, I get to be the bad guy to ask all the terrible requests. It's kind of like if you haven't given enough. We have our advisory committee, and that advisory committee is chaired by Andrea who asked you to join in today, all three of you. And it also has Cynthia Berry and now Dr. Marc Williams. I would like to ask all three of you -- and you don't have to say yes or no today because you may not want to and you don't want to do it in public -- to join the committee. And also, by the way, Dr. Willey, if you are still here, I'm going to ask you to join the committee, and I think we're going to probably ask Dr. Burke to join as well. I think we're starting to get a terrific team together.

So I'm going to ask you all to see if you would be willing. Again, like I say, I don't want to put you on the spot -- ha, ha -- today. But if you would join in with us and we'll sort of ask you to help us to think about these issues because the work will go like lightning because of you.

Then in the interest of time, not to take up the time of the committee today, I think each of you made very wonderful presentations. The point I think, because it wasn't your assignment to do, is to point out what's missing, what are the gaps, what needs to be done that you're not doing.

Secondly, I don't know whether or not, as proud as you are of each of the components that you presented, if you really became designated in our schemata as the deal for your part of it, could you actually sustain the work. Do you have enough scale? Can CAP actually scale this -- but I just want to make sure that as part of the committee, you speak to the issue of sustainability at scale going forward.

So I think the two things I would sort of challenge you with are you've told us all the wonderful things. Now tell us what's not wonderful, what's missing. And secondly, for the parts that you are responsible for that you are so legitimately proud of, can you sustain in scale? And then would you join the committee? I think that's what I would sort of look forward to.

DR. FERREIRA-GONZALEZ: Any other questions?

(No response.)

DR. FERREIRA-GONZALEZ: I have a question for Dr. Vance. Earlier in the day, we had a public comment from the Genetics and Public Policy Center which states that two-thirds of the laboratories are involved in PT testing and a third is not. You presented some data from 700 molecular

pathology laboratories, and the most frequent deficiency on the PT program accounted to 3.9 percent of the laboratories. I'm still trying to figure out the discrepancy for this.

DR. VANCE: What I can say is not all labs adhere to CAP. It's a voluntary program and not everyone enlists in the CAP accreditation program. So I think that's where the commentary comes from.

The other thing that you need to remember, though, is that number, as I told you earlier, is a dynamic number. It's a moving target. There are labs being gobbled up by larger labs. There are new labs coming out in the market all the time. So I think it's very difficult, number one, to keep tabs on all those laboratories, but also to make sure that those laboratories are involved either in a CLIA inspection process or a CAP inspection process.

DR. BERG: If I may make one comment.

DR. FERREIRA-GONZALEZ: Who is that? Oh, Dr. Berg, go ahead.

DR. BERG: Just a quick comment that a number of the tests that are out there and are being promoted are single source tests, which presents problems not only in that many of the data that might be relevant to the issue of their usefulness in practice are proprietary. Secondly, a further result is that there's very little in the peer-reviewed literature that allows us to look at them. It also means that these tests are not subject to the proficiency testing kinds of mechanisms that we have in place for other kinds of tests. So this particular domain has some special challenges in helping laboratories do a good job because of the nature of the tests and who is providing them.

DR. FERREIRA-GONZALEZ: Any other questions for the speakers?

DR. TUCKSON: Dr. Berg, I would also make one other request of you. One of the things just to think about on a go-forward basis, if in fact you are willing to go forward on a basis with us, is we are interested in the idea of sort of developing some case studies that allow us to sort of see in the continuum of activities from analytic and clinical validity and clinical utility, all the way through to how tests are chosen for clinical use by a clinician. If you sort of think about a whole longitudinal chain of events, we're trying to think about some of those kinds of test cases, and I just want you to think about maybe using your CYP450 example as one. So if you were to sort of start at the end of the chain where a patient actually gets the test and work your way all the back to clinical utility and validity, yada, yada, and the oversight of those steps along the way, that might serve as a pretty interesting one of our examples that we might use. It may not be the best one, but I just want to get your brain to kicking around the idea if you were to look at all the steps along the continuum from clinical application all the way back through, you know, does the test actually do what it's supposed to do for the people that's supposed to do oversight, sort of how you might think that through. But I appreciate your offering an example.

Again, your presentation seemed to really predict much of our discussion.

DR. BERG: Sounds very interesting. Thank you.

DR. FERREIRA-GONZALEZ: I have one more question for Dr. Vance. With enacting CLIA, Congress also directed the Secretary to make the results of proficiency testing performance available to the public. Is the College of American Pathologists taking any steps to have this actually happen, or if that's not possible, can we as a group have some of those results?

DR. VANCE: I know that the college renders its proficiency testing results to CLIA, but I don't know if they would render them to the public. I can't speak on behalf of that.

DR. FERREIRA-GONZALEZ: So CMS has results of the proficiency testing.

DR. VANCE: Yes, they do. Yes, they are reported to CMS.

DR. FERREIRA-GONZALEZ: The other question I have -- and then Muin goes after me -- is that you have showed a diagram of the different laboratories that perform a proficiency testing

program and when they fail, what you're supposed to do or not do.

DR. VANCE: Right.

DR. FERREIRA-GONZALEZ: Now, who is responsible for checking that laboratories that fail the proficiency program actually follow the steps that they have to follow? Is it up to the laboratories, or is the CAP keeping a tally on this?

DR. VANCE: That's a very good question. Actually CAP has gotten much more involved in that and has recently spent about $9 million to bolster its accreditation program particularly with monitoring and has created an entire new council called the Council on Accreditation. One of the subcommittees of this council is called the CCC, or a continuous monitoring committee. It is the responsibility of that committee then to monitor the PT results.

So it's a two-pronged review: one, to make sure that we're reviewing the laboratory testing menus to see that the laboratories are, in fact, enrolled, as they're required to, in appropriate PT; and then the other part of that is to make sure that they're performing adequately or successfully in the PT.

The other thing that I might mention in that regard -- so the Continuous Compliance Committee does monitor, and they're the ones that send the cease testing letter. Then they, again, follow that algorithm.

The other part of that is then the inspector too, when that inspection process comes along every other year, will have the PT results of that laboratory for the last two years as well. So the inspector will then be able to target their PT results and look at the evidence for their PT results and also their plan of action, if they have been unsuccessful previously.

DR. FERREIRA-GONZALEZ: Muin and then Steve.

DR. KHOURY: I don't have a particular question in mind but I'm taking this opportunity to thank Dr. Berg for his leadership in moving EGAPP forward. EGAPP has been a process that came out as sort of the product of the previous advice of different committees that came out in the '90s, the NIH/DOE Task Force, and then SACGT. I think, for the first time, we're beginning to see a little bit of a road map for how we can move forward. I think EGAPP and the EGAPP Working Group -- by the way, many of them are here, Sue and Steve Teutsch -- and did I miss anybody? And Deb Leonard has been on it -- have provided us with a really good leadership model to evaluate how we can move forward with this.

And I would like to acknowledge too that EGAPP is not only a CDC process. We have a very tight partnership with AHRQ. Gurvaneet has provided a lot of the raw material, so to speak, and the use of the evidence practice centers to do some of our work. We have an amazing steering committee that has FDA, NIH, and a whole lot of other partners. Obviously, nothing would happen without Linda Bradley, our secret weapon, who's sitting back in the audience.

(Laughter.)

DR. KHOURY: So thank you, all, for your hard work.

DR. FERREIRA-GONZALEZ: Steve?

DR. TEUTSCH: While we have Al on the phone, you've talked a lot about getting guidelines out. One of the issues, of course, is then getting guidelines into practice and all the quality improvement and translational things on that end. I'm not sure if that's going to be within the scope of some of the things that we're going to be having to deal with as part of the oversight, but it's, it seems to me, one of the real issues that goes beyond sort of how do you get from the laboratory to recommendations.

And I wonder if you've had any reflections about the complexity of getting this translated into practice beyond sort of what we've talked about with a health information infrastructure and decision support.

DR. BERG: Well, when talking about the Preventive Services Task Force, I often make the comment that the work that the task force does is the easy part. Although working through the methods and the science of these kinds of tests can be complicated and tedious, in the end, it's not rocket science. It's fairly straightforward when you're evaluating evidence against established standards. The real challenge comes exactly as you state: when the recommendation is out there and it's available, how do you get it into practice?

Those of us in primary care are extremely happy to see the NIH Roadmap leading towards the CTSAs and the T2 translation which is moving things. T1 is bench to bedside, and T2 is bedside to the community. And there are a lot of us very interested in that particular translational step, moving things from things like clinical guidelines and clinical trials into actual practice into the hinterlands of Alaska that I outlined on the slide.

So it's an excellent question. The EGAPP panel isn't likely to address that, but we hope that other groups will be able to help with that.

DR. FERREIRA-GONZALEZ: James?

DR. ROLLINS: I have a question for the EGAPP committee members, as well as Dr. Berg. We talk a lot about analytic as well as clinical validity, and then we also talk about clinical utility. But from an insurer's perspective, in terms of making sure that a particular test does have some desirable outcome for the population, or from a population perspective, for some reason it seems like there's not much emphasis being placed on clinical utility.

Now, earlier Reed asked you about a case where you might start from the beginning and go to the very end. As an insurer, as I say, how can I be sure that this EGAPP initiative, in terms of some genetic test, is going to result in certain outcomes at the population level or result in decreased cost or better management of patients?

DR. BERG: Well, I would encourage others to respond. But I would not want to be misunderstood that EGAPP is not interested in clinical utility. In fact, we've spent a huge amount of time trying to figure out how to take the methods of, for example, the Preventive Services Task Force in the community guide, which are ultimately focused on utility and apply them in genetic testing where there's so much more emphasis on analytic validity. In the Preventive Service Task Force, we almost never examined issues of the analytic validity of measuring blood pressure, for example, or measuring hematocrit. Those aren't issues. In genetics, it's a huge issue.

So the panel is absolutely committed to saying as much as we can about clinical utility because that's where clinicians live, that's where patients live, that's where insurers live, that's where employers who pay for insurance live. So we're absolutely committed to go there, if we can, recognizing that the evidence probably will fall short in an unfortunate number of cases.

DR. FERREIRA-GONZALEZ: Correct me if I'm wrong too, but a member of the EGAPP Working Group is a member of the Blue Cross/Blue Shield Technology Assessment Group. So then you'll have that component of the third party insurer into that group. But I think it makes a very key component to that work group to address the specific issues you're bringing up.

DR. BERG: That's correct. Maggie Piper is a wonderful addition to the group.

DR. FERREIRA-GONZALEZ: We have no other questions. We all put on our thinking caps, and we're going to move forward. Before we do, I will thank the speakers for very thoughtful presentations and hope that we can count on some of you joining our committee. So maybe we'll go from two to expanding significantly.

DR. TUCKSON: Not some of them. We're hoping that all of them will.

(Applause.)

DR. FERREIRA-GONZALEZ: But before we move into our discussion, I would like

to close some of the issues that Reed brought earlier from our November meeting on oversight. We had requested CLIAC to provide a report back about their discussions with CMS about the specialty. In our package, in tab number 5, there is a summary of the committee meetings that occur in February, and I'm only going to read part of these just to have closure from our discussions in November.

So an update on the committee on the outcomes of the CLIAC meeting in February. At our November meeting, we learned that CLIAC was meeting in February to discuss CMS decisions not to go forward with the notice of proposed rulemaking for genetic testing specialty under CLIA. Given the complexity of the oversight issue and the questions that remained for us as a committee, we felt it was important to get an update from CLIAC after they held their discussion.

I want to thank CLIAC chair, Dr. Lou Turner, and Joe Boone, Associate Director for Science in the Division of Public Health Partnership of CDC, for providing us with a summary of their deliberations. Again, a copy of that is in your tab number 6. Let me just highlight the main points of the meeting, and the rest, please go back to tab 6 for the complete report.

"Judy Yost shared CMS's plans for strengthening genetic testing oversight, which were the plans she presented to us in November, that is, improving their website, providing technical training to surveyors on genetic testing, and collaborating with CDC to publish educational materials. CLIAC members expressed support for CMS's efforts to improve its website, provide technical training to surveyors, and collaborate with CDC to disseminate information.

"However, several members of the committee disagreed with CMS's decision not to go forward with establishing a genetic specialty under CLIA. These members questioned the agency's rationale and pointed to concerns in the genetic testing community about laboratory quality, particularly regarding the qualifications of laboratory personnel and the interpretation of genetic test results, two important measures of quality that are not being captured in CMS survey data because CMS surveys are not routinely inspecting genetic testing laboratories."

There's a number of other key points, again, that are in your tab number 6 that I would recommend you go back and check.

DR. TUCKSON: I was trying to make sure that Kathy Hudson she was hearing what was being said as well. Let me just try to see if we can nail this issue down here because I'm a little confused, and I appreciate this.

So this issue was teed up by public testimony from Kathy Hudson who was pretty specific about a number of these issues. And I'm trying to understand where we are.

So what you just read was from -- who was that from?

DR. FERREIRA-GONZALEZ: CLIAC.

DR. TUCKSON: That was from CLIAC. And it specifically addressed this issue of why the decision was made by CMS not to do a specialty. And they concluded at the end of the day -- what was their conclusion again? That it was okay?

DR. FERREIRA-GONZALEZ: They "expressed support for CMS's efforts to improve its website, provide technical training to surveyors, and collaborate with CDC to disseminate information." So they were in agreement with CMS that those are the plans for strengthening genetic testing oversight.

DR. TUCKSON: And I think I want to just restate it again. Again, you're trying to report not justify. I'm just trying to make sure.

So do you get the sense that as a result of the discussion that CLIAC said we are okay with CMS not doing a specialty and that their strategy of these other tools is acceptable? Or did they say that the other tools are good, but you also need to deal with the specialty issue? I'm trying to make sure which. Are they completely endorsing the whole strategy and saying it's okay not to have the specialty

issue?

DR. FERREIRA-GONZALEZ: That's my understanding, but I don't know if Joe Boone is in the room to further confirm this. I mean, there was an endorsement of the activities that CMS has decided to put in place to strengthen the genetic oversight. There were some concerns among some members of the committee that it was not sufficient.

DR. TUCKSON: I see Steve has got his hand up.

DR. GUTMAN: Yes. I was present at that meeting. It was certainly my sense of the meeting that the package that Judy put on the table as the surrogate for the genetic specialty sold, and I'm not sure it was unanimous, but that the sense of the committee was that this would be an acceptable substitute.

DR. TUCKSON: Well, let me ask then of Andrea and your committee, Andrea, as you go forward.

First of all, I think Judy Yost and the CMS people are terrific people, and they're hard-working and well-meaning to get after what they're trying to do.

I don't know what to do with some of the testimony that we heard earlier from Johns Hopkins, in that they were very specific about some points regarding the relationship between the specialty designation and the proficiency testing. I'm somewhat concerned about one-fourth. Again, I don't think that the presentation from Hopkins was designed to say this is a definitive probability of .008, New England Journal of Medicine study. They didn't oversell their presentation. But I think they made an observation that in one review, one-fourth of the labs are not doing proficiency testing as perhaps they should be doing. I think there were some issues raised around analytical errors that may be resulting.

So I just think that I would ask us to tighten down -- if we could sort of take that testimony that we've got there from Kathy Hudson and sort of look at these issues carefully. If the CLIAC people have reviewed this thoroughly and, as Steve has said, they have bought off on it, I'd just like to sure I know what parts of Kathy Hudson's presentation they have bought off on. And if it doesn't need to be redone and if I'm doing something to add to bureaucracy and stagnation and redundancy, then please overrule me quickly at the beginning of your next meeting.

DR. WILLIAMS: I mean, I think the presentations we heard today present a prima facie case that there is a need, and the reason is that all of these people that presented would not be spending the time, money, and effort that they're spending if there wasn't a need to do oversight. I think we wouldn't even be having an argument about whether it's needed or not if people had not taken the ball and run with it to say, well, we think we need to do this.

And if the College of American Pathology and the American College of Medical Genetics hadn't created their guidelines and their proficiency testing, I think we would be in a terrible morass regarding having any standards. And I think there would be a huge hue and cry. So in some sense, there's an ability to not take ownership in the sense that so many people are doing it voluntarily that we are being prevented from the scope of a problem that could be much larger. But ultimately the problem comes down to that this is all being done voluntarily, and as a consequence, there's the ability to opt out.

DR. TUCKSON: First of all, well stated and well articulated.

Just to drill a little deeper, in terms of what I'm trying to get at, because your comments are right on, it's the specific part around the specialty determination because I think what I'm curious -- that issue was apparently clearly presented then to the CLIAC around this need for a specialty determination and it decided that it wasn't necessary. Kathy raises the issue, if I understand her testimony, about the relationship between that and the proficiency testing. And I'd like to just make sure that the subcategory of proficiency testing is actually going on and that the CLIAC committee's

discussion, if it did not explicitly deal with the frequency of proficiency testing, then let's add to that. That's just my subcomment within the overall framework.

DR. FERREIRA-GONZALEZ: Well, this is something that we can take and look at what CLIAC, which is an advisory group to the Secretary, made the decisions and what these other individuals presenting today have brought to our attention.

DR. TUCKSON: The other thing, by the way, just to complete the thought -- I apologize -- is I also want to make sure that the committee explicitly nails down this question of -- Congress had directed the Secretary to make the results of the proficiency testing performance available to the public. Apparently this may not have been -- and I note the careful use of the words -- "apparently may not have been done." I just think we need to look into this and see whether or not this is an issue that needs to be addressed. It's like once a committee like ours has been informed of these concerns, it is not easy for the committee to ignore them. And we just need to, without saying yes, just check into it and make sure everything is cool.

DR. ROLLINS: A quick comment? Representing CMS, I think that because of the conversation which took place this morning in terms of possible deficiencies on CMS's part, I do think, as I said, some type of dialogue or some type of meeting should take place between the representatives of Johns Hopkins, as well as CLIA representative Judy Yost.

Number two, in terms of, I guess, some follow-up, since we're talking about CMS, some of the recommendations which were made in terms of things that this committee wanted CMS to perform, essentially the recommendations have been reviewed by the different divisions of CMS. Most of those recommendations are feasible and favorable. Some of the recommendations there will be some more discussion on, but in terms of specifics, because the document has not been cleared, we couldn't present it today, but by the time this committee will meet again, that document will be cleared so that we can, as I say, address the recommendations made by this committee.

DR. TUCKSON: Let me just note then -- and I want to be careful here since I'm the one that raised all these things. I'm trying to walk a very deliberate and a very transparent and a very public fine line. So, number one, again, I want to be very careful on this.

I am trying very hard not to be critical or put CMS in a defensive or negative posture here. It's very important to not do that. So we are not going to be, at least as far as this chairman has anything to do with, attacking or putting CMS in a negative posture.

Let the record state the ex officio from CMS has leaped to a cooperative posture and a willingness to engage in conversation to clarify these issues. And that's an important principle that I think we want to acknowledge and underscore.

The ex officios are not members of the subcommittee that we're creating, but I'm sure that they'll be called in to be supporters. No, the ex officios don't get to be on the subcommittee this time.

But anyway James Rollins has really stepped up and been really supportive of that. So I think that's important. Given the spirit of your comment, Dr. Rollins, whether you work with the Hopkins people or not, I think the real issue is more the generic issues that have been presented. It provides a certain focus to make sure that these are part of the work of the subcommittee, and whatever happens has to occur in that environment. And this is not an adversarial kind of thing. It's trying to understand it.

So I hope there's no difference of opinion where I am. This is all on the high road, high ground, trying to accomplish things which everybody has the same interests, and that is to do right by the public. There are no bad guys here. There are no enemies. There are no adversaries. We're just working on behalf of the American people, and let's keep it right there.

DR. FERREIRA-GONZALEZ: Now, with that comment in mind, looking at these

issues, maybe we can put back up again the framing of the questions that were put forward to us this morning. There were seven questions.

As we go through those seven questions, there's another set of questions at the oversight task force we came up with. It's a framework for moving forward, and you can find them in your document under tab number 5. There are actually six questions there.

So maybe we can actually discuss these more in detail. As Reed was saying this morning, we can look at the questions that the Secretary has put forward and see what we want to add or want to delete from these.

Now, we can use these six questions that the task force has come up with to see where are commonalties and where we have moved forward and even actually add or delete some of these.

Any comments from anybody?

(No response.)

DR. FERREIRA-GONZALEZ: If you look at our the task force's question number 5, I think there is an issue here. I will read that for everybody. "What would be the impact of these solutions on the accuracy and quality of genetic testing; investment and innovation; availability and cost of genetic tests; and patient/consumer health and health care decisionmaking? How might these effects vary for different categories of genetic tests, for example, direct-to-consumer, predictive, diagnostic, pharmacogenomics? What would be the effects of leaving the system as it is?"

So what we were trying to look at in the work group at this point is to see what are the consequences of some of these issues. And I think we need to look at these, and I would like to add this into the area where the Secretary has added.

Any comment from any members?

(No response.)

DR. FERREIRA-GONZALEZ: So the idea will be to -- Joe?

DR. TELFAIR: Let me just make a general statement about the questions. There are a lot of compound questions that you have in terms of the way they're written. So if you were looking at how you're going to assess or get the answer to a specific one, I would recommend actually for your committee that you consider is there a way that you look for comment as across the questions, or do you look at a way to demarcate the questions to be more discrete? It just is going to make your process a lot easier because you do have questions where you can answer the question, but you're not quite sure what element of the question you're answering. It's just that it's hard to follow, as a committee member, when you have this. That's a general comment.

Specifically for this one, it seems something was mentioned earlier by the CDC. Is there an evidence base already to answer some of the parts of this question in terms of can you review what is already written or can you get it through other sources and then address that issue? I would say maybe that could be something that you could do as a task force, and then you have it open-ended. I know that's the process we engaged in when we were doing the large scale testing issue, and in another committee that I sit on, it was the same thing. What can we answer with the existing information, and then what can we not answer?

So an approach -- I guess what my contribution would be because I'm not a laboratory person -- would be to consider looking at that question because it's a good set of questions. So to repeat, one is to make them a little bit more discrete. Secondly, to look at existing information that you can gather from the experts themselves, and then look for the holes, and maybe there are other sources. That's just a recommendation.

DR. FERREIRA-GONZALEZ: Thank you.

Any other comments? Is there anything that we want to add to the seven questions

that were posed to us this morning?

(No response.)

DR. FERREIRA-GONZALEZ: One of the things that struck me today, one of the public comments from Gentris Corporation, was the use of controls and the FDA/CLIA controls. So maybe when we look at the proficiency testing materials, we can also add about controls for the testing. That's something where we can address some of the concerns of from the public comment.

Marc?

DR. WILLIAMS: I would just like to comment on that. This is something that has come up in the CETT process quite frequently. In the public testimony, they indicated that they had six cleared controls. We've seen evidence that there are 937 genetic tests that are currently being offered. I think the perspective is if we are going to move controls to the level of what are FDA-cleared, do we in fact have a system by which we will be able to have controls for all tests, even the ultra-rare disorders where we've essentially had to rely on patient samples, or whether there would be certain exemptions relating to that. So I just was struck that this was a relatively narrow view of the control issue when one looks at the broad perspective of testing.

DR. FERREIRA-GONZALEZ: I think this is an excellent point because not only is this a limited number of FDA-cleared controls from these two different companies, but at the same time, there's a cost associated with running these controls, and with the current reimbursement state, I mean, it becomes very difficult.

But at the same time, I think we might be able to have some kind of exception where we can still use already characterized specimens from patients which have been run with FDA-cleared testing, for example, to get the right result. But I think something that we can consider and look at different ways where we can actually look at these controls when there are FDA-cleared controls or not and so forth.

Thanks.

Dr. G., I guess.

DR. RANDHAWA: Thank you.

Just responding to your comment about is there anything else we can add potentially to this. In my reading of question number 5, there's a subpart B, which is investment and innovation. It's a fairly broad category. Again, I don't know if Steve will actually want to comment on this. We'll be hearing from him tomorrow about economic impact and looking at it more globally. But if you are going to be discussing investment in innovation and the economic aspects thereof, then do we also need to consider the downstream effects of the public health impact and the economics of that on the other side, so just to maintain the entire economics and not just only one part of it?

DR. FERREIRA-GONZALEZ: That is a very good comment. Thank you.

Does anybody else have any other comments?

(No response.)

DR. FERREIRA-GONZALEZ: Where's Reed? There are no other comments? They don't want to add anything else to what we currently have.

DR. TUCKSON: So you're saying that's it? We've got the charge to the committee? We're going to respond to the Secretary's requests as is? You just left all of them there. All right.

So here's the deal. We're going to break for dinner in about 10 seconds. Andrea, here's the deal. You've got to stop for a minute, Andrea, because I've got to say thank you.

(Laughter.)

DR. TUCKSON: You've got to get your award, your applause. The committee of Cindy and you put on -- first of all, clearly you identified the right people to be before us. I mean, it was

just extraordinary. And we got all the stuff we needed done. You predicted what the Secretary was going to ask us and you had all the right people to answer all those questions. So can we get a round of applause to the committee?

DR. TUCKSON: Marc, thank you for, in addition to all the other things you're going to do, joining that. Let's go ahead and make sure that we get the other people that we asked. Let's do not lose anyone. Sylvia is joining? Steve is joining?

MS. CARR: Kevin.

DR. TUCKSON: We've got too many people now. All right. We've got a lot of people then.

MS. CARR: Kevin, Steve, Sylvia, and Marc.

DR. TUCKSON: Andrea, did you hear that? Kevin, Steve, Sylvia, and Marc, and then the external people that we are going to try to get.

MS. CARR: Ad hocs.

DR. TUCKSON: They're ad hocs. All right. So we've got a real good thing going forward. This is now a terrific issue.

There's a committee meeting tonight here. Who is that?

MS. CARR: The Task Force on Patents.

DR. TUCKSON: The Task Force on Patents is meeting here tonight. Everybody else, first of all, you're more than welcome to join them. And then the full committee comes back here at what time? 8 o'clock?

MS. CARR: 8:00 a.m.

DR. TUCKSON: And what time is breakfast?

MS. CARR: Before 8:00 a.m.

DR. TUCKSON: Before 8:00 a.m.

So gavel at 8 o'clock. You all really should feel good about a very productive day. Thank you very much.

(Whereupon, at 5:15 p.m., the meeting was recessed, to reconvene at 8:00 .a.m. on Tuesday, March 27, 2007.)