U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

Eleventh Meeting

Tuesday,
November 14, 2006

Fort McHenry Room
Inn and Conference Center
University of Maryland
3501 University Boulevard East
Adelphi, Maryland

IN ATTENDANCE:

Chair

Reed V. Tuckson, M.D.
Senior Vice President
Consumer Health and Medical Care Advancement
UnitedHealth Group
MN 008-T902
9900 Bren Road East
Minnetonka, MN 55343

Members

Sylvia Mann Au, M.S., C.G.C.
Hawaii State Genetics Coordinator
Genetics Program
Hawaii Department of Health
741 Sunset Avenue
Honolulu, HI 96816

Cynthia E. Berry, J.D.
Partner
Powell Goldstein LLP
901 New York Avenue, N.W., 3rd Floor
Washington, D.C. 20001

Chira Chen
1315 5th Avenue
San Francisco, CA 94122

James P. Evans, M.D., Ph.D.
Associate Professor of Genetics and Medicine
Director of Clinical Cancer Genetics and
the Bryson Program in Human Genetics
Departments of Medicine and Genetics
University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7624

Andrea Ferreira-Gonzalez, Ph.D.
Professor of Pathology and Director
of Molecular Diagnostics Laboratory
Virginia Commonwealth University
403 North 13th Street
Clinical Support Center, Room 246
Richmond, VA 23298-0248

IN ATTENDANCE:

Kevin T. FitzGerald, S.J., Ph.D., Ph.D.
Dr. David P. Lauler Chair in Catholic Health Care Ethics
Research Associate Professor
Department of Oncology
Georgetown University Medical Center
4000 Reservoir Road, N.W.
Washington, D.C. 20057

Barbara Burns McGrath, R.N., Ph.D.
Research Associate Professor
Box 357263
University of Washington School of Nursing
Seattle, WA 98195

Joseph Telfair, Dr.P.H., M.S.W., M.P.H.
Professor
Public Health Research and Practice
Department of Public Health Education
University of North Carolina at Greensboro
437 HHP Building
Greensboro, NC 27402-6170

Huntington F. Willard, Ph.D.
Director
Institute for Genome Sciences and Policy
101 Science Drive, CIEMAS 2379
Box 3382
Duke University
Durham, NC 27708

Ex Officio Members

Administration for Families and Children

Martin Dannenfelser
Deputy Assistant Secretary for Policy and External Affairs
Administration for Families and Children
370 L'Enfant Promenade, S.W., Suite 600-W
Washington, D.C. 20447

Agency for Healthcare Research and Quality

Gurvaneet Randhawa, M.D., M.P.H.
Center for Outcomes and Evidence (COE)
Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, MD 20850

IN ATTENDANCE:

Centers for Disease Control and Prevention

Linda Bradley, Ph.D.
Office of Genomics and Disease Prevention
Centers for Disease Control and Prevention
4770 Buford Highway
Atlanta, GA 30341

Department of Commerce

Michael Amos, Ph.D.
Scientific Advisor
Chemical Science and Technology Laboratory
National Institute of Standards and Technology
100 Bureau Drive
Gaithersburg, MD 20899

Department of Defense

Lt. Col. Scott D. McLean, MC, USA
Chief of Medical Genetics
59MDW/MNP Wilford Hall Medical Center
Department of Defense
2200 Bergquist Drive, Suite 1
Lackland AFB, TX 78236-5300

Department of Veteran Affairs

Sherrie Hans, M.D.
U.S. Department of Veteran Affairs
810 Vermont Avenue, N.W.
Washington, D.C. 20420

Equal Employment Opportunity Commission

Peter S. Gray, J.D.
Senior Attorney Advisor
Office of Legal Counsel
U.S. Equal Employment Opportunity Commission
1801 L Street, N.W.
Washington, D.C. 20507

IN ATTENDANCE:

Food and Drug Administration

Elizabeth Mansfield, Ph.D.
Office for In Vitro Diagnostic Device
Evaluation and Safety
Food and Drug Administration
2098 Gaither Road, HFZ 440
Rockville, MD 20850

Health Resources and Services Administration

Denise Geolot, Ph.D., R.N.
Director
Center for Quality
Health Resources and Services Administration
Parklawn Building, 5700 Fishers Lane
Rockville, MD 20857

National Institutes of Health

Alan Guttmacher, M.D.
Deputy Director
National Human Genome Research Institute
National Institutes of Health
Building 31, Room 4B09
31 Center Drive, MSC 2152
Bethesda, MD 20982

Office for Civil Rights

Robinsue Frohboese, J.D., Ph.D.
Principal Deputy Director
Office for Civil Rights
200 Independence Avenue, S.W., Room 515F
Washington, D.C. 20201

Office for Human Research Protections

Michael A. Carome, M.D.
Associate Director for Regulatory Affairs
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

IN ATTENDANCE:

Office of Public Health and Science

Anand Parekh, M.D., M.P.H.
Senior Medical Advisor
Office of Public Health and Science
Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

Executive Secretary

Sarah Carr
Secretary's Advisory Committee on
Genetics, Health, and Society
NIH Office of Biotechnology Activities
6705 Rockledge Drive, Suite 750, MSC 7985
Bethesda, MD 20892-7985

C O N T E N T S

C O N T E N T S

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

DR. TUCKSON: Good morning. How is everybody today?

Those of you who did not make it to dinner last night, oh, what a time you missed. We flew airplanes. We played World War One. We went to France. We got lost. We followed Sarah. Sarah blocked the highway. People blew their horns. We hid under the front seat. You don't ever want to miss another one of those.

We had a long and very productive day yesterday. It was, I think, a very, very good discussion in a number of areas. We've got some really important work to do. Not only did we have great pharmacogenomics stuff, but the oversight issues were, I thought, pretty intense actually for a while there. I think we came out with a plan that was a pretty good consensus. The amazing thing was your ability to be thoughtful that late in the day after having gone through all of that. It just was amazing.

Well, let's get right to it.

By the way, if you haven't ordered your lunch, you've got to do it by 10 o'clock. So what you need to do is to go out there and find Abbe and Abbe will take care of you, but if you don't do it by 10:00, you don't eat and there you go.

Everybody has got to fill out their FACA survey, which I always forget, but it's like technical, and return it to Abbe. You will find it in your briefing book. So make sure you've crossed your T's and dotted your I's on all your ethics stuff.

We also recognize that there are several of you that are going to be leaving at the 3 o'clock break or so to get back to the West Coast and even further west. So we're going to really rock and roll through our session. I don't think we have any real vote stuff near the end of the day, so I think we're going to be all right. The agenda was thoughtfully designed by Sarah and team for that reality.

Today's first session will focus on the report to the Secretary on the policy issues associated with the undertaking of a large population cohort project on genes, environment, and disease in the United States.

At the time of our meeting in June, the draft report had been released for a 60-day public comment period. The Large Population Studies Task Force carefully considered the comments and revised the draft report to incorporate this feedback. The final draft is in table 7 of your briefing books.

Let me also point out that the IOM has kindly provided each of us with a copy of the report, "Genes, Behavior, and the Social Environment," which focuses on the importance of including behavioral factors and the social environment in studies of gene/environment interaction. So our work is clearly a centerpiece with a lot that's going on.

Today we need to come to consensus. Today we need to come to consensus on the final draft report and whether it is ready to be submitted to the Secretary. So we really do want to get this thing in front of the Secretary. We've allotted a full five hours for this important work, and I am so happy that I will turn this over to Hunt who will lead us through five hours of a discussion of changes that have been made to the draft report in light of the substantive public comments received and the recommendations that the task force would like the full committee to adopt as part of this report. So he's really going to take us -- and Hunt and I have been through this ourselves in pre-meetings. So we're pretty clear about how this is going to go. It's very structured conversation, very specific. It's timed out to get us from here to there in time to finish. So you guys just keep knowing that as you make your comments, which we want you to do, keep trying to find a way to listen to your colleague and get to consensus around stuff that people may disagree on, and then we can just keep on moving right through and get it done.

With that, Hunt Willard.

DR. WILLARD: Thank you, Reed. Good morning, everyone. I apologize for missing yesterday, but one's day job occasionally gets in the way.

To Reed's point of this being a five-hour marathon to discuss this, I would point out what my students always tell me, which is that there's no penalty for finishing early. So if we reach consensus, so much the better and we can move on to other business.

So what I'd like to do today is to give a little bit of background on where we are with the large population study report of the task force, which hopefully will become the report of the committee, for the benefit of some new members of the committee and the folks watching us at home, as they say, and then quickly get to some of the substantive changes that have been integrated into the report by the task force after what actually was a very extensive and useful process of getting public comments which were dutifully collated and considered by the group.

It was a yeoman's effort, as this whole thing has been, by staff, particularly Yvette Seger, who has been tireless in pulling all of this together and keeping most of us on task.

Let me move forward without any other delay. For those who are new to this, the issue at hand is to examine issues relevant to a possible United States large population study which we define in this report as an approach to learning more about relationships among genes, the environment, and common disease. And the goals of the studies, both ones ongoing and ones planned both in this country and elsewhere, are to determine mechanisms underlying common complex diseases to inform treatment and prevention strategies and ultimately, of course, to improve health in this country and elsewhere.

So the purpose of this session is to review the public comment process and the comments themselves and to go through the changes that have been introduced into the draft report as a result of those comments, as well as a few other changes and, hopefully shortly after lunch, to get to a point where we have reached a consensus among the committee and we can finalize and thus approve our report for submission to the Secretary shortly after the new year. Goals are good and hopefully we'll achieve that, and I think we can.

So what I want to do is to summarize the major revisions that have gone into the draft report since last we met, and then after I introduce all of those, I'll sit down and we'll be able to go through more on a point-by-point basis the different sections of the report, ultimately the recommendations that the task force has come up with and that this committee has seen in draft form at a previous meeting, and then address the question at the bottom of this slide in terms of readiness of the report for submission to the Secretary.

Let me acknowledge the members of the task force. This list is more complete than the one that you have in front of you. So you should look at the screen, if you will. There are some new members to SACGHS and thus new members to our task force: Barbara Burns McGrath and Steve Teutsch. Others are old veterans whose involvement in this task force and on the phone calls that I'll describe in a moment was really a remarkable commitment I think to this process of trying to work with the public comments to take them seriously and integrate those comments into the report. The ex officios on the right side of the slide also were critical and really make this, I think, a broad-based task force draft which we're bringing to the full committee here.

So because we were all much younger when this process started, it's worth, I think, going through some of the events in history that led up to the report that we now have in front of us.

We were first contacted three and a half years ago by NIH, invited to weigh in on the value of a possible large population study. Coincident with that, our own prior-setting process that we went through for a number of meetings in 2004 listed the issue of a large population cohort study or project as one of those issues that required in-depth consideration. Thus, accordingly, in October of 2004, the task force that I just described was formed.

We had sessions in 2005 at the March and June meetings, and the draft report was begun in June 2005 under guidance from the NIH Director that I'll be more explicit about in a moment.

We had more presentations at our October 2005 meeting. You all saw the first draft of the report at our March meeting. That was the draft that then was sent out for public comment in May, June, and July of this current year.

Those public comments were then collated by staff and considered by task force members in two quite extensive teleconference calls in September and October, which leads us to today with a revised draft, hopefully the final draft report, which we'll consider today and hopefully approve with whatever modifications we decide we need in order to achieve consensus.

So it's worth pointing out, I think, the specific request from Director Zerhouni regarding what our committee was being asked to do and, perhaps equally importantly, what our committee was being asked not to do.

So we were asked to identify the key policy issues related to a potential large population study and specifically those policy issues that should be addressed before undertaking such a project.

We were asked to outline the approaches that could be used to address the issues that were identified, but specifically we were urged not to address the issues themselves. We were to outline the issues. We were to describe processes that the Secretary might put in play in order to address those particular issues, but we weren't being asked as a group to address those issues ourselves.

Lastly, we were to recommend mechanisms that might best be used to address those identified issues. This is very much in the spirit of the draft report that you have in front of you in order to keep with the request from Dr. Zerhouni.

What we weren't asked to do was to come to a conclusion about whether or not a large population project should move forward in the United States. That, of course, is the 900-pound gorilla sitting in the corner. On the other hand, we're essentially remaining silent on this issue, and I'll describe that particular point a little more thoroughly as we're going through the draft report. So the final report that you have in front of you has the intent of appearing to be -- and you all will have to decide the extent to which we've succeeded in this -- entirely neutral on this question, simply to say that it is an open question of whether a large population study should go forward. And in order for the Secretary and others to address that question, there are a number of issues that ought to be tackled first. There are other issues that might only be tackled after such a decision has been reached. But here are those issues and here are some of the mechanisms that might be used in order to address those issues. So that's the position we've tried to take as a task force in coming up with the final draft that you have in front of you in order to maintain the type of neutrality that I believe we were urged to do.

So what I'm going to do now is to go into some of the public comments, the process, as well as the specific comments themselves, leading up to the final draft report that you have in front of you. Then I'll sit down and we'll roll up our sleeves and begin to go through the specifics of those changes and the specific recommendations.

So as I just said previously, the draft report was released for its 60-day public comment period at the end of May of this year, and that period ended at the end of July, this past summer. The report was posted on the SACGHS website. There was a substantial targeted email outreach to a variety of different groups. There was media outreach via the NIH Office of Communication. It was posted in the Federal Register and in the NIH Guides for Grants and Contracts. And then there was a "Dear Colleague" email that was sent out to a whole variety of listservs. In total, about 48,000 individuals were informed that the draft report was ready to be viewed and commented upon, and I think we have every reason to be confident that anyone who was interested in it then knew about it from at least one, if not multiple, sources and, thus, had an opportunity to offer their comments.

From that list of 48,000 -- obviously, many people were busy -- 69 returned comments, but those were, as you'll see in a moment, very substantial sets of comments and very useful. There is a

summary in tab 7 of your briefing book that goes through literally in summary form. Then you were sent to your home offices this booklet, which some of you brought but many of you may not have, which is a compendium of all of those comments and makes for enlightening reading, if anyone is interested.

There really were some very salient comments and, more importantly perhaps, some very consistent comments that came through repeatedly from very different kinds of groups, and those were the ones that I think we felt especially that we were either not clear in our intent in the draft report or made us wish to provide more background information, as I'll describe shortly.

So the 69 comments that we received represent a number of different sectors that had received notice of the draft report. And the vast majority, about 60 percent, of the comments came from three groups highlighted on this slide: about 25 from academically based researchers, as one might expect; 19 percent from professional societies. There was a typical Macintosh to PC handoff glitch here. That's the professional societies that should be boxed at the bottom, not the individual box. And then various government agencies provided 17 percent. So those three groups, academically based researchers, the government, and professional societies, offered about 60 percent of the comments that came in, and then a variety of other constituencies and sectors made up the remaining portion.

So even though there were only 69 individual comments, many of them were quite comprehensive, and there were a total of about 600 comments that address specific issues somewhere in the draft report. The wonderful staff developed a coding system which was developed to categorize the comments into the four major policy issue categories that we had already decided on when we viewed the original draft, as well as public engagement, and those comments were then viewed within each of those kinds of categories.

Various of the task force members, usually two if not three, were assigned to each one of those sort of bins of comments in order to go through those and analyze them individually in terms of whether they were particularly substantive that we needed to address, whether they were requests for clarification, or whether they were someone who just misread what we said or what we intended to say, in which case a little bit of word-tweaking perhaps was sufficient. But those task force members then identified the major themes that came through those piles of comments and decided on the comments to be incorporated, as we discussed in full during two teleconference calls in September and October of this year.

And so it's those comments, integrated and discussed as part of what probably was another five hours' worth of telephone conversations among a fairly large group of people to decide exactly which changes should be made, how we ought to make those changes, and how we can best position the draft report that you have in front of you.

So there were some major themes from the public comments that I want to go through because I think it gives you a sense of how the report might have shifted from the original draft report that you saw to the final draft report that you've had for the last week or so.

One of the major comments was that the tone of the original draft report was decidedly not neutral, that most people read our draft to say that we were very much behind this, and in fact, to some people's reading, it appeared it was a foregone conclusion that this was going to go forward and we were simply providing guidance on how it might go forward. Accordingly then, the role of SACGHS and the charge that we received clearly hadn't been understood, and that was our fault. We just hadn't laid that out as clearly as it needed to be.

So the task force decided both to clarify explicitly what our charge had been, along the similar kind of points that I made a number of slides back in introducing these changes. And then we went through carefully in order to examine the tone of the report and make sure that we, in fact, were being neutral in our language and making sure that we were covering essentially all points of view that might be relevant to the Secretary as he reaches a decision on a possible large population study.

Another major theme was that more information needed to be included on the already-existing cohort studies of various sizes and shapes that are already being funded by HHS and other groups both in this country and elsewhere. And more information needed to be included on the types of interdisciplinary research that would be necessary to mount a large population study. And those changes have been made and we'll go through the details of those changes in a bit.

A number of comments pointed out that we had not sufficiently addressed issues of socioeconomic status and economic factors that were relevant to how costly and what kinds of issues would be relevant to a large population study. So sections on those have been introduced into the final draft that you have in front of you.

We were urged to expand our discussion of what is obviously a series of complex ethical, privacy, and confidentiality issues that we perhaps gave short shrift in the original report. And that section has now been significantly expanded, and we'll describe that in a moment.

There were specific suggestions among the public comments that the task force thought were quite good in terms of mechanisms for greater ethical and independent ethical insight that would be necessary for a large population study, were one to go forward.

Then lastly, we were urged to be clearer on the extent to which that public engagement was being emphasized. So we made a significant rearrangement within the report, not so much the content, but a rearrangement in order to provide what we think is a more appropriate emphasis on the importance of public engagement both before a decision is reached and after, should such a large population study go forward.

So that, in a nutshell, is the essence of the major changes and the processes that have gone on since last we viewed the draft report. I'll stop at this point if there are any questions specifically about what I've presented thus far, and if not, then I'll move back to my seat and, as I said, we'll roll up our sleeves and begin to go through some of the specific changes with an eye towards not wordsmithing per se, because none of us will live long enough to get through it if we do that, but rather to reach a consensus that the changes that the task force made are appropriate or not appropriate, deal with major issues of language and text where there are some major issues, but move our way through to reach a consensus on what the final report should look like. And then we'll go into the recommendations both that the committee saw last time and that the task force has, in a few cases, modified.

So any points or questions at this point before we move on?

(No response.)

DR. WILLARD: Great.

Since I'm sitting where I'm sitting, if the people in the left field seats, if you're waving your arms and I don't see you, just do something a little less polite than waving your arms and we'll go from there.

So throughout everything I'm going to present now, I'm referring to line numbers, rather than page numbers, since the draft report is organized in that way. So you can follow along in your hymnal, if you want to, as we go through this.

So the major revisions in terms of the overall organization that I just alluded to were that previously there had been two different sections on public engagement and the importance of public engagement. One was in the beginning and one was at the end. Obviously that, in terms of the public comments, failed to convey the importance that we attached to this particular issue. So we have now integrated that into a single chapter within the report which hopefully improves, as this says, the logical flow of the report, eliminates some redundancy, and increases the emphasis for any reader, including the Secretary. So the content hasn't changed very much. It simply is merging those two sections and putting them together so that it has more emphasis.

The other major revisions are in terms of the tone of the report. We've made a significant effort to change the language to be more neutral and balanced in response to the public comments. In the spirit of the request from the NIH Director to raise issues for exploration and not to either endorse or discourage efforts to pursue a large population study, we've attempted to go through this, because of these public comments, and change language, most of which has been relatively modest changes in words simply to reflect this neutral perspective, the example here being that we would say such a study would do something as opposed to the study will do something, which is the type of language we had before that many of the public commenters responded to. So for those of you who have read through it or do read through it on the fly, you'll see many examples of that as we go through.

So the introduction. The introduction has been significantly expanded and I think clarified in response to the public comments. First of all, more background has been added on the role of SACGHS and the specific charge related to this report.

We provided more background information related to the Design Considerations report that had come out from the NIH, principally from the NHGRI-led effort to examine design considerations. That's now summarized in an extensive section.

And then there's an overview of the public comment process and the type of input we received from various stakeholders, all within that introductory section.

So any comments on the introductory section?

(No response.)

DR. WILLARD: Seeing no waving arms, we'll move from there.

The second section, the second chapter is on the scientific background. Some of you will recall that began in the previous draft with an immediate description of the International HapMap Project with sort of glossing over the Human Genome Project. The task force felt that even though the Human Genome Project is ancient history now, it's not that much ancient history, and so perhaps it warranted some discussion and we have included that now before description of the International HapMap Project.

And then in response to public comments, we very substantially expanded the section on already existing cohort studies in the United States, listing them and going through with a brief description of each of the ones that we were aware of and included. That was a very consistent comment from a number of the public comments, and so we introduced that change as well.

Any discussion on either of those two changes?

(No response.)

DR. WILLARD: Either the caffeine hasn't kicked in or we're on a roll. This is good.

The third chapter. Now we get into the meat in terms of the various policy issues, in terms of overview changes. We first expanded a section beginning at line 931 entitled "Capacity to Conduct Interdisciplinary Science," incorporating a number of concepts that were raised by the public commenters, and then we specifically mentioned two of the existing cohort studies, the Women's Health Initiative and the National Children's Study, as potential models of the kind of interdisciplinary research that would be needed in a large population study.

Then a little bit later, there's an expanded section on the need for partnerships to address a recurring theme in the public comments about the wide range of stakeholders and the potential for a large number of different potential partners to lead this large population study, were the decision made to go forward.

And then there's an expanded section on access to data and materials, beginning at line 1037, again incorporating concepts raised by the public comments that the task force members felt were important.

Then lastly under "Research Policy Issues," we added a section on the recently announced --

and I believe later this afternoon we'll hear more information on this on the NIH Genome-Wide Association Studies Initiative. We included that.

Then in what I think what the task force felt was an important addition, to expand the discussion of what we meant or what people who consider large population studies mean by the word "environment." Previously this was a small footnote in the introduction, and we felt and public commenters felt that that was not providing suitable emphasis to this. So that was pulled into the main text and we incorporated significant feedback from public comments to make sure that we had a broad and workable operational definition of "environment."

Yes.

DR. AMOS: You have in here biological factors. Is that environment? Physiology? Is that the innate physiology of the individuals? Is that really environment?

DR. WILLARD: Now you're making me remember who on the task force had raised that issue.

I think it relates to in infectious disease, for example, that the infectious agents are biological on the one hand, as well as --

DR. AMOS: Okay. So the way it's written, when you say physiology, it implies the innate physiology of a person that is a reflection of their genetic makeup, obviously.

DR. WILLARD: But the task force felt it was also a reflection of the environment.

DR. AMOS: Sure.

DR. WILLARD: So it's the output of the combination.

DR. AMOS: I'm just saying you may need to explain it a little better in the way that you actually meant it.

DR. WILLARD: Okay. We'll flag that and give a more extensive example under "e.g."

Any other points on this? Because this actually is an important change in terms of the balance of the report. Joseph?

DR. TELFAIR: On the task force, we actually had an extensive discussion on this set of issues related to the environment. One of the reasons why it's a little broad was it was a deliberate effort to leave it broad because in a lot of the public comments, the specificity was leading in one direction, but besides asking us to explain it more, the point was made that we actually did not provide any kind of breadth to the discussion. So that was one part.

The other part was, as Hunt has said before, that we wanted to make sure that we provided at least some examples that could actually be used when the decisionmaking process came along too.

So being a little bit broad was actually a deliberate effort, if I remember correctly from our discussions, because they were extensive. And the other committee members could chime in on this.

DR. WILLARD: Yes. As the report says, this actually is an issue which would presumably have to be discussed. So we are, in a sense, suggesting that this lands in the Secretary's lap or NIH's lap or any other group's lap in order to determine what, in the context of a large population study, is meant by "environment." We know what genes mean, but it's less clear what we mean by the environment.

DR. KOVACS: I just wanted to say I applaud the task force for looking at the breadth. So I think it's very good to think broadly here.

But I do agree with Michael that if you look at all the other factors, they're clearly external. And if you look at physiology and say, well, there are genetic underpinnings of physiology, it's a little bit different from the other. So that's a good point.

DR. WILLARD: We'll flesh that out. Thank you. That was useful.

Yes, Barbara?

DR. McGRATH: I had two thoughts. One was under the second bullet about capturing diversity, adding geographic diversity to the recruitment strategies.

And then under the social factors at the bottom of the half a dozen bullets, gender is not included there, and that was one comment from public comments that I think we might have missed. And I would add my own of cultural under social.

DR. WILLARD: And you think gender should be added as well as a social factor, as opposed to sex which is obviously not environmental. You're making that distinction? Am I reading that correctly?

DR. McGRATH: Yes.

DR. WILLARD: Other comments on this particular point?

(No response.)

DR. WILLARD: Thank you.

So that is the research logistics section and the changes that were made there. Sorry. That was research policy. Now we're into research logistics. That's the second area.

In this area, we again changed the definition of the environment and pulled it up into the text for clarity and expanded the section on recruitment and enrollment, adding information both that came from a report by Charles Rotimi to this committee and added another section on socioeconomic and lifestyle factors which was not in the previous one.

Also under research logistics, we added a section on multidisciplinary research teams, repeating the theme that we also hit on earlier, and then added a section on coordination across multiple institutions and healthcare systems, beginning at about 1355, again in response to public comments.

Any questions on research logistics and those changes?

(No response.)

DR. WILLARD: The third area is regulatory and ethical issues. We significantly expanded the section on privacy and confidentiality and incorporated a number of comments which we received from the World Privacy Forum, as well as a number of other comments from some of the other commenters, and addressed specifically the need for a privacy officer which needs consideration, the need of a privacy impact assessment, third-party use of project records, and identifiability. So, in essence, this section is now going through in more detail the kinds of issues that would fall under privacy and confidentiality, which both from a public standpoint, as well as stakeholders who might be involved in such a project, are obviously critical ones.

Also, under regulatory and ethical issues and, again, in response to a theme among the public comments received about the need for ethical oversight, we added the suggestion of an independent ethics review committee. That becomes a recommendation of the task force, which we'll describe as we go through all of the specific recommendations. But the text for this begins at 1760 to 1789. But that is new text, and so it's worth everyone considering that.

So discussion or questions on any of the changes under regulatory and ethical issues?

(No response.)

DR. WILLARD: Thank you.

The fourth area, which actually is an integration of what had been the fourth and the fifth areas, is now entitled "Public Health, Social, and Economic Implications." It's a merger of what had been public health and social sections separately. We've added to that integration of those two previously separate sections language on the potential economic impact of a large population study, as well as, of course, as I just said, adding the word "economic" to the title of this section.

Relevant to the social implications is adding a text box to emphasize our previously announced support for and continuing support for the genetic nondiscrimination legislation, lest the Secretary lose focus on that particular issue, which we keep reminding him of. So that box reflects again both population comments in the sense that were one to consider going ahead with a large population study,

the kind of legislation already proposed under the federal Genetic Nondiscrimination Act would need to be in place for a large population study to go forward. The task force felt that it would be unlikely that there would be public support for such a study in the absence of nondiscrimination legislation. So that's now described in this section.

Questions on that point or on this section? Jim?

DR. EVANS: Yes. I was just wondering. From the standpoint of economic impact -- and maybe it's elsewhere -- discussions of the kind of balance with regard to the costs and economic impact on existing research endeavors, et cetera. So this describes the economic stimulus that might result. Are issues addressed that many have concerns about regarding --

DR. WILLARD: You mean the cost of the project per se?

DR. EVANS: The cost of the project and its impact on the research infrastructure.

DR. WILLARD: That's in an earlier section I believe. There is a section somewhere, Jim, and I'm trying to remember where it is where the cost of the project and its impact on the rest of the biomedical research enterprise is discussed. But I think we'll flag that and, if nothing else, in this section --

DR. TELFAIR: Line 2007.

PARTICIPANT: Page 66.

DR. WILLARD: I'm hearing two different things here.

DR. WILLARD: Page 66? We don't have a page 66.

DR. TELFAIR: It's line 2007 as part of that discussion.

DR. EVANS: Yes, and page 25.

DR. WILLARD: So it may be that it's worth -- because what was discussed in the beginning, the $3 billion figure, which is in the paragraph that begins on line 913 -- that paragraph we might refer back to in the later section so there is a balance of the two economic issues. Good point. Thank you, Jim.

Any other points on this? Barbara?

DR. McGRATH: Did we pass by line 1894, health disparities section? Sorry. Maybe I'm a little slow.

DR. WILLARD: 1894? Is that what you said?

DR. McGRATH: Yes, the section on health disparities.

I'm still a little uncomfortable with that because I think most people, when they think about a large population study, feel that it would detract money from health disparity research, which mostly is social and economic and environmental factors. I think there's something to be said for the research, and this could contribute to that. Maybe some acknowledgement that there is that tension between the competition for funds in the areas of health disparity research that might be addressed more directly. Do you know what I mean?

DR. WILLARD: Do any other committee members have an opinion on that point? There's certainly no harm in pointing out that kind of tension, if that's a widely perceived --

DR. FITZGERALD: I agree with you, Barbara, in the sense I think it actually will add to the amount of research that could come out of it. Is that what you're saying? You want a flag in here that this, in fact, could be an impetus for increasing that social research. Right? Because we have to look at the ramifications of the project, and in doing so, that should lead to additional research, ELSI research, in that area.

DR. McGRATH: I actually don't know, but I think most people, which is a dangerous beginning of a sentence, feel that research in the genetics area pulls money away from old-fashioned public health researchers looking at health disparities in terms of social determinants of health. Here we're sort of just jumping to the middle of the argument by saying it will, indeed, increase our knowledge

of social disparities. And, indeed, it might, but I think there's a perception on the other side more strongly. So if we really feel that it might contribute to understanding health disparities better, maybe address that tension a little more directly, because I think it's kind of down-played in here, and it sort of opens itself to criticism I think.

DR. WILLARD: I think I understand the point now.

Sylvia?

MS. AU: I don't know though, Barb, because the public comments -- we're trying to respond to public comments and evidence that we have. And I don't think that that's something that's been expressed in the public comments or in any evidence that we've received, that they think that it might decrease funding. I mean, it might decrease funding in all areas of research because if you're going to put a lot of funding into a large population study, across the board they might decrease research. So I don't know if we should add something into a report where we don't have some evidence for it or we haven't received strong public comment on that issue.

DR. WILLARD: Other opinions on this point? Joseph?

DR. TELFAIR: I think I understand. This actually came up in our conversation. It came up in a general discussion regarding if this goes forward, how will it affect looking at funding in similar type of areas. My understanding was that the wisdom of the task force was to highlight, in as much of a diplomatic way as possible, the issue itself and knowing that it probably will come back to be reviewed. It wasn't a perception that what you're discussing and that your perception is off-base. It was just that it was looked at in the context of concerns across the board of similar types of work, particularly in the social and behavioral sciences where this type of research would play a role.

So I think it was felt very strongly and put forth that this whole section be included to begin to at least have the dialogue but provide some basis for discussion and decisionmaking and to kind of leave it at that. I think some of us tried to push a little bit harder for more, but I think it was the wisdom of the group to try to leave it at this level.

I do have a comment. Actually, it's a correction in one of the lines.

DR. WILLARD: Before we leave this point, and then I'll come back to you, Joseph --

DR. TELFAIR: I just wanted to let you know.

DR. WILLARD: -- I think what we could do, Barbara, and I'll make this proposal to the committee, is that in that paragraph on page 25, when we are discussing the impact of a large population study on the funding of other biomedical research, that we expand that to flesh out what we mean by biomedical research to include behavioral research, health disparities research, et cetera, and make it clear that we're not just narrowly talking about what we often mean by biomedical research because that's the appropriate place. I think that's very much consistent with the general sense that we had before.

DR. McGRATH: Great. That makes sense.

DR. WILLARD: All right. Joseph, over to you.

DR. TELFAIR: Thank you. I have two corrections, if I can. It's on line 1914.

DR. WILLARD: Yes.

DR. TELFAIR: It should say "socially defined."

Then on line 1921, at the end of the sentence, it should stick with vulnerable groups because you have racial/ethnic groups, and if you look at the examples you're giving, those are both social and other groups as well. So sticking to vulnerable groups.

DR. WILLARD: You mean drop the word "historical"?

DR. TELFAIR: No, no, no. At the end of the second sentence, where you said these included racial/ethnic groups, and then you list a number of groups. Some are socially defined. Some are not. But all of them are not ethnic and racial groups. The second sentence.

DR. WILLARD: Yes, but I'm not reading that sentence to suggest that the women, gay, and lesbians are social and ethnic.

DR. TELFAIR: I'm sorry. What? No, no, no. I'm saying that these are racial, ethnic, and socially defined groups. I mean, what I'm saying is that the way you define the groups is not correct.

DR. WILLARD: I don't think we are defining them in that sentence. So what's the exact correction you would have us make?

DR. TELFAIR: All I was just saying is that you should stick with "vulnerable" because that better defines the groups. That's all I'm saying.

DR. WILLARD: So you want to delete the second sentence?

DR. TELFAIR: No. What I'm saying is you should include groups such as and then keep the rest of the sentence as is.

DR. WILLARD: So drop out the "racial/ethnic."

DR. TELFAIR: Yes.

DR. WILLARD: You want to delete that.

DR. TELFAIR: Yes, sir.

DR. WILLARD: Okay.

DR. HANS: Don't you have concerns, Joseph, that some others reading that would feel that there is a glaring omission?

DR. TELFAIR: Yes. I think whenever these sentences and stuff that we have done before, whenever you've written things this way, people have always said, well, there are other groups that would go here, et cetera. And it's more straightforward, if this is an example, to have it that way. But just in experiences that we've had in putting reports like this together, people have always said something is left out or something is included that shouldn't be there.

DR. WILLARD: But if I'm following you correctly, you're proposing to leave out racially and ethnically defined groups.

DR. EVANS: We wouldn't want to leave out a historically vulnerable group. Right?

DR. TELFAIR: No. Never mind. No. Forget I said it.

DR. WILLARD: I don't want to forget what you said. I want to make sure everyone agrees.

DR. TELFAIR: I realize now what's being said, and I guess I was reading it slightly differently than that because I was trying to read it from another lens. But I'm fine with that part. But I will stick to my earlier comment, though.

DR. WILLARD: Changing the word "culturally" to "socially."

DR. TELFAIR: Yes.

DR. WILLARD: That seems appropriate from my vantage point.

Other points? Kevin?

DR. FITZGERALD: I just have a question. As you mentioned, because of the public comments, we're highlighting the genetic nondiscrimination legislation. But in the table of contents, it isn't flagged, and I imagine there are going to be quite a few people -- the first thing they're going to look for in the table of contents is where is that addressed. Is that intended to be in the table of contents somehow?

DR. WILLARD: We can certainly take a look at that.

DR. FITZGERALD: Yes, because I know some people are going to immediately go to that and want to know where that is in the report.

DR. WILLARD: I'm taking this as a sign that we're actually pretty close to consensus when we're worried about the table of contents.

(Laughter.)

DR. WILLARD: Anand?

DR. PAREKH: I like the discussion on the economic impacts, and clearly the paragraphs highlight the importance of looking into the potential economic costs of this large population study. Did the task force feel that there should be an actual recommendation to the Secretary that there should be some kind of independent body or something that could provide some estimates of how costly such a population study might be to provide some kind of basis for resource allocation to ultimately make a decision?

DR. WILLARD: Well, we certainly didn't make a specific recommendation to that point. I think when we go through the recommendations that we've drafted, let's sort of look for opportunities where that would be covered. Clearly, someone has to come up with an estimate as part of any process to go forward or not. So that's the intent. We didn't single that out as one particular recommendation that said put a price tag on this. But as we go through the recommendations, I think that's a point.

Sherrie?

DR. HANS: I was just going to comment that in the task force discussions, actually the question of whether that discussion should be included in the report at all -- sorry. My comment was specifically in response to your question. In the task force discussion, there was a great deal of debate about whether that discussion should even be included in the report. So there was certainly not overwhelming support for its inclusion at all. So the question of a recommendation then I think is one that is worth a great deal of discussion.

DR. WILLARD: Other comments on this section? Joseph?

DR. TELFAIR: Just a point of order, if I can. The reason why I just sort of stopped the conversation on my point is that I think it will take a little longer discussion. I was wondering if I could indulge a little bit of your time to explain a little bit more and see whether it's relevant or not.

DR. WILLARD: We're doing well. So, please, go ahead.

DR. TELFAIR: No, no, no. I don't want to take up the committee's time. Trust me. It's a little bit broader expansion, and I want to make sure that when I make the recommendation, in terms of wording, that it is correct because I just don't have the wording right now.

DR. WILLARD: Yes. I think we all know what we want to say. We just want to make sure the words are not subject to misinterpretation by some other reader.

DR. TELFAIR: That's correct.

DR. WILLARD: So it's an issue of clarity of language more than the actual intent.

DR. TELFAIR: Okay, thank you. I appreciate your indulgence.

DR. WILLARD: Anything else on public health, social, and economic implications?

(No response.)

DR. WILLARD: The final chapter is on public engagement which, as I said previously, merges what had been two separate sections in the original draft specifically here. Then we've now added a section on one example of public engagement, the Moderated Focus Groups and the National Children's Study. We've added a section on the Public Consultation Initiative recently funded by NHGRI to describe that project. And then we've added a section based on recent survey data based on the presentation that was made to this committee. That's all now in this section.

Comments or questions about what this section is doing?

(No response.)

DR. WILLARD: So that takes care of the text. Now we have what, I'm sure, will be a little less easy and straightforward, and that's to actually look at the specific recommendations themselves. As a sort of preamble to this, let me say that what I think we're looking for is to achieve consensus on what the committee would like to recommend and move to consideration of approval of that content. If there's

specific language that some of the committee feels needs to be improved or is unclear or is inappropriate or what have you, this is the time for us to do that. Minor wordsmithing of change this word to that word and this section and add a comma here, that kind of thing we can deal with outside of the context of a committee meeting and just do that by sharing information by email with Yvette and Sarah. But I do want to make sure we get to a consensus here on the intent of these recommendations so we all go away with a sense of what it is that we're all recommending.

So there are now 18 recommendations in the report. These are what were previously called "options" which the task force felt, from the original draft, was sort of a weak word and not particularly responsive to the NIH Director's request that we actually make some recommendations. So we now have 18 recommendations divided into the different sections, as you see on the slide, and then one beginning, overarching recommendation that the task force felt was necessary in order to put into context all the subsequent recommendations.

Now, this table that is on the screen and you have in front of you, I think, is fairly important because it really makes two points. The first point is the vast majority of what we're about to look at you've seen before. Most of these recommendations are essentially unchanged except for some minor wordsmithing from a version which we all saw before and largely stood behind. But there are three specific recommendations here that are either entirely new or substantially new wording, and those we'll want to take a closer look at as we go through this.

You have in your packets two documents that are relevant to this. One is called "Public Comment Draft Versus Final Draft: Changes in Recommendations." That sort of gives you the Reader's Digest abridged version of the changes that I'll be describing.

You also have another sheet that's called "Revised Final Draft" that replaces page 31 in the report. There was one recommendation that was left out by pure glitch on our part, and this now puts that back into your report. I'll give it to you on the slide as we go through. So you're not going to be missing it there, but just so you have a page that you can substitute into the final draft in front of you.

So I'm going to propose to go through all 18 of these recommendations, spending most of our time, I suspect, on the three that are totally or substantially new and probably less time with the ones that we've all seen and supported before. But, obviously, I want to invite comment and potential changes if members of the committee feel that we should do that.

So the first new recommendation is this overarching principal recommendation that the task force felt needed to be in place in order to put all of the subsequent recommendations into context and to allow them to be presented with some clarity about what we intended.

Some of these recommendations overall are for issues that the Secretary would need to address prior to making a decision about a large population study. Other recommendations wouldn't need to be addressed at all unless there were a decision to go forward with a large population study. And this recommendation is intended to sort of provide the context that would tie those two different types of recommendations into place.

So let me read this, not that you're not capable of reading yourselves, but let me read it anyway.

This recommendation reads: "As part of the process for determining whether to undertake such a large-scale research project -- and prior to a decision being made -- the Secretary should initiate a thorough consideration of the full range of policy issues outlined in this report. The Secretary should consult and engage the full range of potential partners for such a project during this decisionmaking process, including the public at large, the full scientific community, a wide spectrum of government agencies, and the private sector."

So this recommendation intends to make two points: one, that this entire group of policy issues needs to be addressed prior to a decision being made, that it would be inconsistent with the fact that these

issues are being raised and that there are processes that one would need to go through in order to address those issues to sort of make a decision about a large population study absent a thorough consideration of those issues; and then secondly, that as part of doing that, that there was, in fact, a very broad range of potential partners in the public and the government and the private sector. And the task force felt it was important to sort of articulate that within this recommendation.

So let me open it up then to the committee, both those on the task force and not on the task force, for their input. Emily first.

DR. WINN-DEEN: Well, I just noticed, if you look ahead on your slides to recommendation number 2, that you state that we should also consult with Congress to get their buy-in basically, but that consultation is left out of this overarching recommendation.

DR. WILLARD: Because they're not an agency you mean.

DR. WINN-DEEN: Right. So I don't know if you want to think about putting them somehow into this because they definitely would have to appropriate funding for it, and you would want to engage them early on as well.

DR. WILLARD: So you're suggesting that the advice of the committee would be that not just as part of the appropriations package, but as part of actually deciding whether to go forward or not, that you would bring --

DR. WINN-DEEN: Right. I think if you don't have buy-in from Congress, that you're not likely to get the funding that you need, and you want to get that buy-in early. Or you at least want to educate them that this is coming, why it's coming, what the rationale is, and keep them informed about this whole pre-decision process so that when the decision happens, it's not a surprise to the guys that have to write the check.

DR. WILLARD: Right. So without worrying about how we would actually word that, do other members of the committee have an opinion on that point? Sylvia?

MS. AU: Let's just add policymakers to the list. That includes state level, local level, federal level.

DR. WILLARD: Without specifying Congress per se.

MS. AU: Yes.

DR. WILLARD: I see a red light down there. Yes.

MR. DANNENFELSER: I'm thinking maybe at the beginning of this overarching recommendation, we should say as part of the process for determining whether to recommend that Congress undertake or recommend to Congress the undertaking of such a large project, something to that effect, that you put Congress in there, but that the Secretary do all the other outreach in order to decide whether to make that recommendation to Congress because I think he needs to make a strong case to Congress in order to do that. He probably does want to get Congress involved at some point, but I think that it does perhaps make sense to get Congress up there in that overarching recommendation at that point.

DR. WILLARD: I have Reed and then Joseph.

DR. TUCKSON: Yes. I want to be careful I don't open up a Pandora's box here. You did allude earlier in your early comment about the tone and to make it neutral. So clearly, you all have wrestled with this. This is a neutral statement. So there is no way that anyone can read this that I can see that shows the committee has any particular interest in doing this. It just reads that if you decide to go play in traffic, look both ways and don't get hit, as opposed to go play in traffic.

I just want to make absolutely sure that we have no intention to be pushing as to whether this is actually a good idea to do with the appropriate caveats as we are going to describe in great detail.

DR. WILLARD: That's an invitation to the committee to address that point. I think the sense

of the task force was that until one had the answer on a number of those issues and knew what the answer was, that we wouldn't want to necessarily recommend either for or against a large population study until we had all the data in.

DR. TUCKSON: Let me just ask it this way then. And I'm being careful here, extremely careful I hope. But what I'm saying is that there must be some reason why you would want to have all these things done because, at the end of the day, there is some potential that this might be a reasonable thing, a good thing, if all these caveats were checked off.

So what I'm sort of wondering again is the subcommittee saying -- it's hard to tell whether you're being dragged, kicking and screaming, into this recommendation to do all these things or this actually could be good and it's important to do all work, or let's don't do this thing and I'm going to show you a whole lot of work you've got to do before we even think about it. It's like which way are we coming.

DR. WILLARD: Kevin, I saw your light.

DR. FITZGERALD: Now I'm completely confused by Reed.

(Laughter.)

DR. FITZGERALD: I thought we were on the same page, and I'm not sure now anymore. But I think the idea was to be completely, if that's at all possible, as neutral as possible on this. And I guess I'm still now trying to see -- are you saying that this isn't neutral? Are you reading this as non-neutral?

DR. TUCKSON: I'm saying if I am a person from outside of this, I could read in any which direction I wanted. So you're right. If you want to be absolutely neutral, this is a neutral as you can be. You can't determine whether you are interested -- I'm asking. I don't think you can determine whether this committee is saying that this kind of a large population study is actually a reasonable thing to try to aspire to if it meets certain tests, or this isn't a very good thing, but if you're going to be so unwise as to pursue it, you need to meet these tests. I can't tell which way. Are you part of the group, I guess, that is saying this large population study is actually a good thing for the country under certain conditions or it's not? I just don't know how people will read it.

DR. FITZGERALD: I think that's all right.

DR. WILLARD: Jim?

DR. EVANS: Well, my feeling is that is all right. I like the neutrality of it, and I think that for those people who are interested in looking at the more nuanced take, the report does lay out clearly I think in the prose that if certain conditions are met, this could be a good thing, but there are caveats. I think to come across in the overarching recommendation in a partisan way is probably exceeding our mandate. I like the neutrality.

DR. WILLARD: Emily?

DR. WINN-DEEN: I'm just listening to this dialogue and I think what I'm hearing is does this committee want to make a recommendation that at least the funding to explore whether this is a good thing should be coming forward in terms of moving to the next level of decisionmaking. Is that really what the committee is interested in recommending, that at least that much investment be made by the government to determine if this is a good thing to move forward.

DR. WILLARD: But isn't that what the recommendation says? It says, "The Secretary should initiate a thorough consideration of the full range of policy issues outlined in this report."

DR. WINN-DEEN: Right.

DR. WILLARD: You can't do that for free.

DR. WINN-DEEN: So to Reed's point, it's not exactly neutral from that point of view because it is recommending, at least to some extent, an investment of government dollars in the exploration, you know, phase I or phase 0, whatever, of the project.

DR. FITZGERALD: I would argue that, in fact, that's what makes it neutral because if you don't recommend the initiation of a thorough consideration, you are, in fact, making a decision because without a thorough consideration, this doesn't go forward. So the idea is in order to achieve that neutrality, you really have to understand what's involved in choosing either to do or not do this because there are consequences either way. And you can't really know those consequences unless you do this thorough consideration. So I think that was built into our idea of how one does achieve a sort of neutral position on this because you have to say we can't answer this question until we do a good consideration of it.

DR. WILLARD: I have Alan.

DR. GUTTMACHER: If I understand Reed correctly, which I think I do, I would agree with him. I would think that, for instance, we might put something in here because the potential benefits to health of such a study are so great but the issues underlying it are so complex, that there should be this kind of -- I mean, this group has spent a lot of time and has a lot of expertise, has gotten a lot of community input. To come out and just say absolutely nothing, I think personally, is not benefitting the American public to the degree of -- without saying, you know, go out waving flags and say go do this. Unless we say, you know, there really is something here, then it may fall under the weight of here's some large, sort of bureaucratic report that says there are 18 different ways of looking at this, et cetera.

I think earlier, several meetings ago, we had sort of a hands-up show around the table, and there was a fair bit of excitement, et cetera, of the group for the potential of this kind of thing, understanding that there are many reasons why maybe it should never go forward, but that it had real potential. I think somehow that has been lost as we've gone through all of these changes, and I think overall, the changes have been good. They've added some depth. They've added some nuance. But I think we still at some point need to say there's a reason for thinking about all of this.

DR. WILLARD: Point heard, although I do recall that the public comments were pushing us to be completely neutral, and so that's what we've tried to do. Now, the committee can, obviously, decide differently today.

DR. GUTTMACHER: Not all the public comments said that and the public comments did not represent the vast majority of the American people, et cetera. I think we need to record the public comments. We need to take them into consideration, but I think it is this committee forgetting its duty to just say, well, gee, whatever happens to come across the transom, we'll take sort of the general consensus of those comments and just make that the report.

DR. WILLARD: Other comments? Yes.

MR. DANNENFELSER: Looking again at this language and prior to a decision being made, I think that perhaps subtly that helps reinforce the point that Reed is making, that that sounds extra-cautionary almost to have that language in there. In a way it almost looks a little bit condescending that you're saying to the Secretary -- you're already saying you should initiate this process, but prior to a decision being made -- I mean, I think that's kind of a given that you would go through this process before making a decision. And I'm just wondering if that language would come across almost a little condescending towards the Secretary.

DR. WILLARD: I think the intent was not to be condescending.

(Laughter.)

DR. WILLARD: The intent was to anticipate that one perhaps reasonable response would be to go ahead and start a small-scale sort of first phase of the project itself, while simultaneously going through all these other issues. And the task force, at least, felt that, no, that probably wasn't the right way to do it, that in fact, the issues needed to be addressed first before initiating or considering initiation of a project. So if there's another way to word that -- if it appears condescending to one person around the

table, chances are it appears condescending to others.

Yes.

DR. AMOS: I'm just wondering. I actually think the overarching recommendation is really good. You're just saying, look, go figure out whether it makes sense to do this or not and then move forward.

But I was wondering, you know, like the Senate does, when they're not ready to put money into it, they create a statement of the sense of the Senate. So could we as a group put a statement in here somewhere in the preamble or introduction as the sense of the committee? Is that appropriate?

DR. WILLARD: Well, recall a slide that I showed very early on today which is that we were specifically asked not to say, yes, we should go forward or, no, we should not go forward. We were asked to simply outline the issues that are relevant to appropriate people making that decision.

DR. AMOS: Well, maybe it could be in a separate document. I'm hearing people say that this is something that the committee has sort of shown hands before and said we should do it. Just an idea.

DR. WILLARD: Well, we have to know what "it" is before the committee could reasonably decide that that was appropriate or not.

Jim.

DR. EVANS: I'm going back to the slide that very specifically says what we were not asked to do, and we were not asked to come to a conclusion about whether this should move forward. If I understand our charge right, it would violate our mandate to do so. And moreover, I don't think we're qualified to decide that. We were asked a very specific task.

I think this neutral statement is very good, and I think the nuance is supplied with the rest of the report. I guess certainly it wouldn't change the tone to remove the hyphenated clause because, as part of the process for determining whether to undertake such a large-scale research project does, indeed, imply that that would be done prior to a decision being made. So some degree of wordsmithing might be appropriate for this overarching recommendation, and I don't think it would be unreasonable to get rid of that if people find that somewhat insulting or condescending. But I like the neutrality of this.

DR. WILLARD: I've got Joseph, and then Reed, and then Kevin.

DR. TELFAIR: I think it's important -- and the rest of the task force can correct me on this -- the order in which the overarching statement was written. It was one of the last things that was done after a full review of all the work that had been done. That's where it was coming from. It was in light of what we can and cannot do, given what we have already done. I think it's important that those that are reading this, even though it's first, to realize that it came pretty much at the end of a very long, very arduous review process that took into account many, many things.

I say this more for clarity and to not reinforce because, you know, a sense of this -- and I guess in my neck of the woods we call it the wimp factor -- there is that did we or did we not wuss out on this. I think it's critical for us to know that the committee worked really hard to come to this point. I think it's important for people to realize that where this overarching comment was is more of an introduction, and I think taking a real good look at this set of recommendations to me will answer a lot of the questions that people are bringing up and a lot of concerns people are bringing up. It won't answer everything because those things don't, but I would suggest not to say move forward, but I just want to put it in perspective.

DR. WILLARD: Kevin?

DR. FITZGERALD: I guess, too, what I would like to make sure doesn't get lost, as we wrestle with this, is the sense that I don't think the task force or this committee would recommend to the Secretary to initiate a thorough consideration of something if we didn't think there was potential benefit there. I mean, why would one bother? So, obviously, the more rigor one decides a topic is worth investigating, the greater potential that topic must have. Otherwise, why bother?

So I think inherent in this, from a perspective, one could read that there's a great deal of interest, there's a great deal of possibility for this sort of thing. I don't think we need to overstate then. I understand one can look at this from a variety of perspectives, but that's the whole point of the neutrality in a sense or the openness in a sense of this statement, that people coming from a variety of agendas can read into it what they want and also all see that it's either too optimistic or it's too pessimistic. And I think we would get that from this reading.

DR. WILLARD: Reed, I apologize for skipping you before.

DR. TUCKSON: I'm actually glad you did. I wouldn't have missed that for the world.

(Laughter.)

DR. TUCKSON: Kevin, I was with you all the way till just like when you jumped off the bridge, but I was right there holding your hand. I think, though, that you were speaking very specifically to Michael's legislative history point, which I think is actually pretty right on target there.

First of all, I think this is such a contentious issue that we do, I think, deserve to be clear to people about where we are. I mean, I think the wuss factor, Joe, is absolutely right there. It's not fair to the people participating in this debate to not be very clear.

I think that the legislative intent that Kevin said is right there. And if everybody agrees to that, which is why would anyone ask the Secretary to spend money and all the trouble of going through this if this did not have the potential for promise -- so, in other words, if you thought that this was the dumbest idea known to man, you would say, stop now, screw it, and go do something else worthy. And if that is the sense -- because I need to know how to represent your sentiment in external bodies. So I've got to be really clear that I know how to speak for you.

So if that is what you are saying, then I think people need to sort of acknowledge that through our committee chairman that we are saying that it has the potential, therefore, do all of these caveats. And that's as far as we're prepared to go. But I need to be real clear that that's what you are saying. I will take off my moderator role, neutral role, and say as a member of the committee, I am voting but more than prepared to submit to consensus that that is, in fact, what we are saying. I am urging some degree of clarity that says this is important enough to let's get at it and figure this thing out.

DR. WILLARD: I've got two people in the queue, but let me remind people this is simply a recommendation. This is not our grand statement of final conclusion. This is simply a recommendation that one needs in order to make sense of the other recommendations. There will be an executive summary. There will be a conclusion that hasn't even been written yet.

So I think there's plenty of room for language if in fact we want to say something similar to what Alan was addressing earlier, which is that there seems to be enormous potential for terrific things to come out with respect to both science and health. That is in the text itself and presumably there are ways of pulling that out into the executive summary and conclusions without it being in a recommendation like this which already is contorted English language. I'm not sure I'd want to make it any worse than it is.

So I've got Robinsue and then I have Alan.

DR. FROHBOESE: I'm just curious at the outset to find out the task force's thinking behind recommending that the Secretary undertake this extensive process as opposed to SAC's serving in its advisory capacity to actually collect the information from the various sources. I'm wondering what the mechanism is for the Secretary to go out and to get this wide public input as opposed to this being a continuing function of SAC.

DR. WILLARD: I think the task force was responding to Dr. Zerhouni's charge which specifically said identify the issues but don't make an effort to actually address those issues. So that's what we were told to do. Now, if the Secretary wants to receive whatever recommendations we agree on and then come back to us and say, great, now chapter 2, we want you guys to tackle the following five

issues and give us some feedback on that, then that becomes the second round. But I think we were simply responding to what Dr. Zerhouni was requesting of us. At least, that's my sense of where we were.

Alan, you're next.

DR. GUTTMACHER: Yes. I just want to quickly associate myself with Hunt and Reed's comments and maybe comfort Jim and help rescue Kevin from his bridge jump.

(Laughter.)

DR. GUTTMACHER: I was not trying to suggest that the committee come to any conclusion that this study should go forward. Again, I agree very much that not necessarily it should be here, but it should be someplace, that the committee has considered this and sees enough potential.

My concern is, I think, what Kevin expressed, that one can look at this now and see whatever you want to see in it. And I don't believe that the committee, having looked at it a lot and thought a lot about it, completely comes out, well, you can see whatever you want to see in it. We can see that there's lots of complexity, but there's enough promise here. That's why I just think someplace in our verbiage we need to make that point.

DR. WILLARD: Okay.

So before moving on from this recommendation, I want to specifically ask for a sense regarding the phrase, "and prior to a decision being made." The fact that it's bolded -- it's not bolded in your original documents -- has nothing to do with anything. But if, as Jim suggested, we could just as easily remove that phrase and not lose anything, then I think the committee should make itself heard on that point so we can decide what the final should be. So maybe even just a straw vote, kind of show of hands, of how many would like that phrase removed.

(Show of hands.)

DR. WILLARD: That looks like slightly more than 50 percent.

Anyone feel strongly that it should be there, must be there?

(No response.)

DR. WILLARD: That's a good sense of the committee. I thank you. So that is the overarching recommendation that sets the tone for all the others that come subsequently.

So under research policy, this is the first of the recommendations. It's essentially unchanged from what it was in the previous draft. "The Secretary should continue to promote and facilitate ongoing consultation with the public, the international community, and the private sector to explore opportunities for collaboration."

That didn't seem contentious last time. Would anyone like to --

DR. WINN-DEEN: So it just seems like you left off the end of the sentence. If people are going to read the recommendations in isolation, it should be opportunities for collaboration on large population studies. It seems like you sort of left the sentence hanging, to me.

DR. WILLARD: Okay. That's wordsmithing. In a sense, you're right. There will be a list of recommendations that will be read by some people absent text and even absent executive summary. So each should stand alone.

What's being pointed out to me is that in your text -- and this is why it may be difficult to view recommendations as standalone text -- the lead-in to all of the recommendations under research policy is if a decision is made to move forward, the following considerations should be addressed. So this is a recommendation that has no bearing whatsoever if a decision is made to not bother to go forward for whatever reason.

Now, we could take that lead-in phrase and have the be a starting phrase for each of these recommendations. The task force sort of got tired of that. It makes it, obviously, repetitive to have that in every single one of them, but that's obviously the intent.

DR. TUCKSON: I think, Hunt, the only thing you've got to be concerned about is, obviously, we all know that what people read is the recommendations. Even though you're a Nobel laureate writer, the people will focus on the recommendations. Having still said that, you'll make everyone numb by doing that.

DR. WILLARD: So that's recommendation 1. I'm seeing no particular objections.

Recommendation 2 we also have seen before in essentially unchanged language. "The Secretary, in consultation with relevant HHS agencies and appropriate Congressional committees, should ensure that there is widespread support for sustaining a long-term and stable investment in a large population" study. So I'm going to change the last word, given we've always called it a large population study, not a project. So that word should be changed. But with that change, Barbara?

DR. McGRATH: I'm loathe to belabor this point, but after the discussion about the neutrality of language, I just wonder about the word "ensure." It jumps out to me. I wonder if we inserted the word "assess" instead of "ensure," whether it has a different feel to it.

DR. WILLARD: "Should assess whether there is"?

DR. McGRATH: Yes.

DR. WILLARD: I think the sense of the committee was there's no point in going forward with large population study unless there is some guarantee, to the extent that there ever is a guarantee, for ongoing funding for government programs, that someone has at least realized that this is not just, you know, sequence the human genome and then the last bill is in and you're done. This actually has ongoing support that is necessary in order to benefit from what might emerge from a large population study. So that was the sense of the task force, and obviously, there may be other ways of phrasing that, but that was the sense.

MS. BERRY: Couldn't we just say to capture what Barbara is saying because I agree with her that the Secretary should do all this to ensure there's wide support prior to moving forward with the project. I realize we just had that lead-in discussion, and so we don't want to be redundant there. But that would just kind of nail the point home that before moving forward or before making a decision, he'll look at everything and make sure that there's the support. So it's not concluding that there definitely will be such a study. How we wordsmith that so we don't have all these repetitive phrases, lead-in's and tail phrases, I'll leave that to others to draft.

DR. WILLARD: I mean, that was the task force's concern, that the value of a large population study is the follow-up clinical work with patients every four years for two decades, or whatever the proposal might end up actually being. Therefore, that means you better have some funding that somebody is thinking of stretching forward for two decades.

Alan?

DR. GUTTMACHER: Yes, I think that's right. I think these are both correct points, but they're two different ones in a way. One is that in the run-up, you don't want to do this if there's not popular support for it. On the other hand, once you have launched into it, it would be a waste of money, in fact, to sort of do it halfway. So if it is really going to be launched, well, after that happens, then it is necessary that leadership, i.e., the Secretary, continue to support this to make sure that it is done in a way that really gives results that are worth doing, rather than just sort of going halfway and say, gee, well, we enrolled people, we can stop now.

DR. WILLARD: Yes. It is a longitudinal study, after all.

So what of this issue of the word "ensure" versus "assess whether"? I'm lip-reading to leave it as it is.

DR. FERREIRA-GONZALEZ: I think we need to leave that as it is. This is a very key point. If the Secretary is going to move forward, there has got to be enough funding because you cannot make

an initial investment of millions and millions of dollars and just get short at the end when we're starting to see some of the benefits of this.

Here and I think through the entire document, we don't want to start continually saying, if you decide to do this. I mean, this has to be an overarching recommendation that whatever you decide. But we cannot in each individual recommendation start putting some language to make sure that we go back to the same thing.

DR. WILLARD: I think we have consensus on that, and it will take a little bit of wordsmithing back at the home office.

The third recommendation, again, one you've seen in a previous iteration. "Given the trans-disciplinary nature," which is the third different way we've expressed that, and elsewhere in the document it's "inter" or "multi." Now it's "trans." That may be something we want to harmonize. "Given the transdisciplinary nature of its scope, the Secretary may wish to establish a highly collaborative model of project leadership and management in multiple HHS and non-HHS agencies and with other stakeholders, including," et cetera.

The essence of this recommendation is the first half. It just simply says, "may wish to consider" and "establish a highly collaborative model," as opposed to a project like the Human Genome Project that was run essentially by the NIH and DOE in a joint partnership or something that was done just strictly by one body.

Any points on this one? Yes, Jim.

DR. EVANS: Yes. I'm not sure where to bring this up. So tell me if this comment belongs more aptly somewhere else.

But this is very broad, and I think that at some point, perhaps in the overt recommendations, perhaps in the text that underlies them, it's worth stressing certain things that have emerged during the deliberations that could really facilitate such a project. What I'm getting to is the collaborative model with, for example, the VA. There are models out there -- and I think the VA is probably the best one -- that offer tremendous advantages to doing much of the work of something like this, you know, the electronic medical record, lack of fragmentation of the health care system, really good representation of minorities, et cetera.

I think that it's worth highlighting in some way in our recommendations -- and I don't know if in these very broad ones, it's the right place -- that there are certain avenues towards getting something like this done that has great promise to overcome some of the difficulties inherent in our health care system that present obstacles. So, again, I'm not sure exactly where that should go, but I wanted to make sure to get that out there so it's somewhere.

DR. WILLARD: Is it your sense that this needs to be in a recommendation as opposed to the text that supports and leads up to a recommendation?

DR. EVANS: Yes. One could even consider going halfway and saying that there are specific models -- you know, refer to text -- that provide the promise of surmounting some of the obstacles. So I don't know how far you have to go in the overall recommendations because I think these are appropriately intended to be rather broad at kind of the 30,000-foot level. But I'd just throw that out there for consideration because as we've deliberated it, it seems to me that there are huge advantages to certain specific collaborations, in my mind, most saliently the VA model.

DR. WILLARD: Other points? Cindy?

MS. BERRY: Very minor, but I was just wondering if we were just trying to be very polite when we use the word "may" wish, and we didn't use it elsewhere. And if we don't need to be that polite, then maybe we should consider just saying --

DR. WILLARD: "Should"?

MS. BERRY: -- "the Secretary should consider establishing." But if there's a reason why we're being polite, I'm all for it, but I just thought I would raise that.

DR. WILLARD: I don't think that language was chosen for any particular reason. So we can certainly -- we're nothing, if not polite. Yes.

Yes.

MR. DANNENFELSER: I'm just wondering whether we should be referring to a highly collaborative model of project involvement as opposed to project management if we'll be seen as trying to micromanage how the Secretary proposes to manage the project, if you will, that there might be something to be said for somebody being in charge, rather than running the risk of it being too diffuse that ultimately somebody is taking the lead on it, but that there are very many agencies involved that we want to collaborate with.

DR. HANS: I think the language of this came from looking at other large population studies around the world and how they have constructed their overall governance of those large population studies. Many of them have both a scientific advisory board or scientific governance board. Most have some kind of public consultation governance board, and a number of them also have an ethics board.

So it sort of speaks to the implications of the governance, not the responsibility. So if you were to think of the scientific advisory board, I think we were trying to say that that board shouldn't just be geneticists, but should have a broader representation in the governance of the project.

MR. DANNENFELSER: No, I'm not objecting to that point. I think that we certainly want to advocate that there's a very broad spectrum of people that need to be involved. But I think, in terms of the Secretary's management style and the administration in general, there's a very strong emphasis on accountability, and that somebody should ultimately be in charge and should be ultimately accountable for the management of the project, even though there will be many partners in the project, that somebody in particular needs to ultimately be responsible.

DR. WILLARD: I don't think the task force would disagree with that, but the intent of this language was not suggest that it would be a committee of five who would sit there without somebody being in charge.

Chira?

MS. CHIN: Just to address that, we actually had talked about this before. We don't know who actually will be in charge of this, and we kind of just wanted to leave it open to find out who actually is going to be doing that.

DR. WILLARD: Yes. That was clearly the intent. Okay, that's recommendation number 3.

Recommendation number 4. "The Secretary, in consultation with relevant HHS agencies, should ensure that there are opportunities available to the general scientific community to be informed about the potential for such a project, to present its views about the scientific validity and feasibility of such a project, and to present its views on the commitment of resources to such an effort, including whether there are benefits to leveraging existing" cohorts, "and to provide input on issues related to fair access by scientists to the project resources and the sharing of data and samples collected within it."

This covers a lot, but the recommendation essentially is make this as open as possible and make sure you pull in all those in the scientific community who might be interested at every step. That's my sort of vernacular description of what's written here as a recommendation.

Comments on this?

(No response.)

DR. WILLARD: And the final recommendation under research policy, recommendation number 5, which we've seen before. "The Secretary should require that there are clear intellectual property policies in place for discoveries made using the data and samples collected to ensure public

benefits."

That was a point of emphasis we had before, and some public comments came in on that as well to make sure that those policies are there.

Any comments on this one?

(No response.)

DR. WILLARD: What a committee. That's research policy.

Then we have four recommendations under research logistics. The first of these, "The Secretary should encourage project leadership and the scientific community to develop clear, consistent definitions and parameters for the stratification and classification of the projected sample population to ensure diversity and appropriate representation in the population to be studied."

I don't think this is controversial for anyone. As I say, we've seen this one before.

(No response.)

DR. WILLARD: Okay, hearing no comments, we'll go on to recommendation 2. "The Secretary should seek input from the public, as well as researchers and clinicians, on the best approaches to identifying subpopulations for recruitment and on approaching, educating, and enrolling various subpopulations. Project organizers should be encouraged to consult with community- based organizations as part of their recruitment and enrollment strategies." Okay, that's number 2.

Yes, Sherrie?

DR. HANS: I did wonder, just to capture some of the sense later on that we get to in the public consultation, whether this should say something like "as part of their recruitment and enrollment assessment and strategies," so that it's not just seen as a strategic approach, but it really is truly an engagement portion as well. So add the word "assessment," "assessment and enrollment strategies."

DR. WILLARD: Okay.

Anything else on this one?

(No response.)

DR. WILLARD: Recommendation number 3 under research logistics. "The Secretary, in consultation with related agencies, should" -- and we should, again, harmonize how we say the same thing in three or four different ways and how we refer to the Secretary and his agencies -- "refine methods for collecting and analyzing environmental (physical, behavioral, and social) factors influencing health and ensure that resources are devoted to developing new tools to validate existing methods and improve assessments of the environment."

Michael.

DR. AMOS: I was looking through the section before, and it talks about other government agencies. In this section here, it talks about related agencies, but it really doesn't spell out which other agencies should be considered. I think EPA would be critical, OSHA, USDA, even NIST from a standpoint of working on standards for data collection and things like that. It's just something to consider. I just think that's lacking in the document.

DR. WILLARD: So not necessarily in the recommendation itself, but in the text, you want us to be more explicit.

DR. AMOS: Well, perhaps even in the recommendation, but certainly in the text.

DR. WILLARD: I think we'd have to be careful that it not appear to be an all-inclusive list, lest we forget one particular group. That would be the danger I think. The question is whether the Secretary needs help in coming up with the list that you just came up with.

DR. AMOS: Probably not.

DR. WILLARD: Our intent was to be as open and expansive as possible, rather than restricting him to say, just do this with the NIH or just do this with one other group or two groups or something of

that sort.

Other comments here? Emily?

DR. WINN-DEEN: Perhaps you just want to be clear that it's not limited to HHS, that he should consult with non-HHS agencies as well like EPA.

DR. WILLARD: Good point. We used that actual parenthetical in one of the other ones referring to both HHS and non-HHS. That's a good point.

Other comments on this?

(No response.)

DR. WILLARD: That was number 3.

Number 4, "The Secretary should encourage project leadership to consult with healthcare providers and organizations to develop uniform and secure approaches for collecting, storing, tracking, and centralizing clinical information to be gathered over the course of the project, including the use of electronic health records."

Reed?

DR. TUCKSON: Yes, I think this is a good one as well and well stated. I think that we may be able to, with a slight tweak, take better advantage of a discussion that happened yesterday, Hunt, where we spent a little bit of energy on the Secretary's initiatives regarding the interoperability and health information technology and the advances.

I do note with interest that the body of the report does speak to it, but one of the things it says is that -- I think the way that we described it was that anybody doing this work ought to connect to the initiative. I think one of the things that we might want to say to the Secretary is that the people designing the system ought to be thinking about uses such as this because, by the time we ever get to that point, so much of the HIT interoperability around collecting this data will have already been basically -- you know, the train would have already gone way down the track.

So just as a matter of subtly I'm sort of suggesting, not in the recommendation, but maybe in the body of the report, but somewhere we sort of urge the Secretary to have his people be thinking about these utilities as they design the health information interoperability.

DR. WILLARD: Other points from anyone else?

(No response.)

DR. WILLARD: That's research logistics.

The third policy area, regulatory and ethical considerations. We have four recommendations. The first, "The Secretary should convene a working group of representatives from the Office of Human Research Protections, the FDA, the Office of Civil Rights, and other relevant HHS agencies, to develop a set of recommended best practices and standard operating procedures, including for the institutional review board(s) that will oversee the study. Public input on the policies and procedures should be sought. This working group would be charged with ensuring that all research sites involved in the project are implementing the regulations established to protect research subjects, medical privacy, and patient safety."

Comments? Robinsue?

DR. FROHBOESE: I apologize for raising these eleventh-hour concerns, but I do have a number of suggested edits and issues that I'd like to raise about this recommendation.

DR. WILLARD: Okay.

DR. FROHBOESE: The first recommendation really does get at the issues raised within this section about ensuring the privacy and confidentiality of the information, as well as protection of individuals participating in the study. Clearly, we want to highlight this. But in looking at this recommendation now in context with the public comments as well, I have two major concerns and will

suggest some edits.

One is that in terms of this working group to develop a set of recommended best practices and standard operating procedures, the groups that are identified for this working group already have very clear laws and regulations that the agencies have promulgated in their respective areas, and to ask them then to develop standard operating procedures and recommended best practices sort of puts them in this quasi-regulatory mode that could be complex in terms of, number one, authority to do this and, number two, crossing over a number of areas.

So what I'd like to suggest there is rather than having this work group of HHS agencies actually developing standard operating procedures, to characterize their role instead as to provide technical assistance on legal requirements regarding protection of research subjects -- I would substitute "health information" for medical privacy" -- and patient safety. So the role is really one of technical assistance rather than actually promulgating a set of guidance or operating procedures that then could become binding and get us into a regulatory framework.

My second major comment is with this last sentence. "This working group would be charged with ensuring that all research sites involved in the project are implementing the regulations established to protect research subjects, medical privacy, and patient safety." I'd like to recommend a more generic statement that just acknowledges that individual HHS and other federal agencies would continue their enforcement and oversight responsibilities to ensure that all research sites involved in the project are implementing, and then the rest of the sentence.

Now, because I know that these are pretty detailed suggested edits, I don't know whether we're at a breaking point and it might be good for me to type these up and people can see them on the screen.

DR. WILLARD: Well, I'm less worried about the specific wordsmithing than the general comments, and I want to make sure the committee has a sense of what you're suggesting and whether there's general agreement.

Sherrie?

DR. HANS: I think actually the task force was very deliberate in suggesting that the Department of Health and Human Services and the appropriate offices that have the regulatory and oversight responsibility for these functions sit down and create policy in a very deliberate way.

The reason that the task force went in that direction is because many, many, many, many of the public comments were around a number of issues of privacy and confidentiality, of protection of human subjects, of ensuring that this data and information would not be made available to other third parties in government or outside of government. It was really in response to the concerns that until there was an assurance of protections and that that was well defined, it would be difficult to get broad public support for such a project.

So it really was deliberate, on the part of the task force, to ask HHS to establish a very deliberative policy to address some of those questions, interpreting existing regs.

DR. WILLARD: There are a couple of red lights down the line. Yes.

DR. CAROME: Just from the perspective of the Office of Human Research Protections, I do share some of the concerns that Robin raised. I agree that best practices, SOPs -- there might be different words for that like guidance and recommendations -- could be developed.

We would be particularly concerned about the last sentence. I don't think the last sentence, in terms of the charge of this work group, is feasible to implement this. The work group is going to be relatively small. It's going to have representatives from these regulatory offices. They're not going to be able to ensure that hundreds of institutions are complying with the various regulations that would apply.

Even more broadly, in the Office of Human Research Protections, we're not capable of ensuring that all the sites are going to comply with human subject protection regulations. We can facilitate it, we

can advise, we can give guidance, but where assurance comes prospectively that people will comply and where it's ensured that that happens, that rests with the institutions, that rests with the sponsors. It's not focused on a regulatory agency. We would have proposed significantly modifying or even removing that last sentence.

DR. WILLARD: That's very helpful. This is why we have a committee, to get this kind of input. I don't think it was the task force's intention to argue any differently than you just did, and so if it's inappropriate, as it sounds like it is, to say the word "ensure," then obviously we need to come up with a different word.

So maybe what I can suggest is that during the break -- and I don't think we're at the break yet -- Sherrie, Robinsue, and Michael get together and sort of craft better language that would meet the intent of the task force in considering the public comments, but then also be agreeable to your agencies and FDA as well if, Elizabeth, you want to listen in on that. That's a good point.

So let's have other comments, but then my intent would be to sort of table this recommendation and come back to it after it the break. So I see Martin down the line.

MR. DANNENFELSER: Just a point on that fourth line there. Do you need to limit this just to HHS, or should it just say "and other relevant agencies"? I think, for instance, perhaps you'd want the Census Bureau to be part of that kind of working group. There may be other agencies.

DR. WILLARD: I'm sure we don't intend to limit the Secretary. So we could use our same language of HHS and non-HHS.

MR. DANNENFELSER: Or even just take out HHS and say other relevant agencies. It doesn't limit it to HHS at least. So either way.

DR. WILLARD: Kevin?

DR. FITZGERALD: Just a quick question for Michael because I think you raised a very good point. So my question is normally the responsibility for something like this is with the sponsors. So who's the sponsor? Who would you see as the sponsor for this sort of large population study? And if it's the government, then -- this is a question. Who would you see then as the responsible group or a potential one?

DR. CAROME: Actually the primary responsibility lies with the institutions engaged in the research. So a secondary responsibility lies with the sponsor. So if it was an NIH institute that's funding some or all of the research, they would have responsibility for ensuring that IRB reviews are in place, certification of IRB reviews happen, that they have assurances. If it's other agencies involved, then they would also have some responsibility for ensuring that.

DR. WILLARD: Thank you for that, Michael.

Anything else on this one? We'll come back to it after the break once we have a few modifications to look at.

(No response.)

DR. WILLARD: Okay, the next recommendation is a new one based on the public comments, which is that "an independent ethics committee should be established to serve in an advisory capacity to the IRB and project management."

This probably does require some discussion and general consensus because it is brand new based on the public comments. Any comments?

DR. TUCKSON: So the question would be, independent of what?

DR. WILLARD: It's actually independent of project management, but advisory to project management. So it wouldn't be simply the project managers who would be doing this. It would have the air of independence as an ethics committee that would oversee.

DR. TUCKSON: So those of you who are familiar with NIH projects now, in terms of how

you get ethics oversight -- I'm not sure I have enough detailed knowledge to know. Isn't there an independent ethics function that advises the conduct of these projects? Not at all? Are there any ethics folks who oversee?

DR. WILLARD: Individual institutes have councils but there's no sort of "uber ethics group."

DR. TUCKSON: And you guys, Alan, in terms of -- what's the ethics thing for genetics?

DR. GUTTMACHER: ELSI?

DR. TUCKSON: ELSI. It's like a cow's name.

(Laughter.)

DR. TUCKSON: Does ELSI do this?

DR. GUTTMACHER: There's a difference between what institutes have in place and what individual projects would have in place I think. So the institute has lots of different kinds of advisors, including advisors, different sets over the years in different ways, to our ELSI portfolio, but that's different from being advisors to a specific research endeavor.

DR. TUCKSON: So this is not calling for -- I guess what I was concerned about -- I should have said it -- in terms of my question was, is this calling for a redundant level of bureaucracy and is it a statement that says that existing ethics activity is not sufficiently independent so this becomes a slap in the face of existing infrastructure?

What I think I'm hearing here is that, no, such a thing does not necessarily exist for a particular project which has not yet been created. So when you create the project, you create an independent ethics activity for it, and that's the normal way you do this.

DR. WILLARD: The intent is also to be independent of the IRB. There is an IRB that's charged with making those kinds of decisions in terms of the actual substance of the project and how that's going to operate. But then this recommendation is that there's a group independent of that one which is looking down on top of the deliberations of the IRB and making recommendations.

DR. TUCKSON: So, again, I think all rational people would be in favor of having great ethical oversight. So the issue here is if you've got an overarching ethics committee looking down on the IRB in an advisory capacity, it sounds like it doesn't have juice because it's advisors. The real action is still in the IRB. So what would this group do other than to nod and look grim?

(Laughter.)

DR. HANS: Well, you might ask that of the ethics boards that sit in each hospital that help clinicians and management make decisions when values are in conflict about individual patient care. This board was really seen, once again, in response to public comments about concerns and particularly about the informed consent process and the ongoing informed consent process.

What I mean by that is there were many, many questions raised about how -- to sort of back and review informed consent. Informed consent is intended to be specific and to have knowledge about what it is you're consenting to, whether it's research or patient care.

However, we know that over time additional research questions may be raised which are very valid, exciting, and which the scientific community will want to pursue. One of the envisioned functions for this ethics board is to be able to, over time, assess those questions and determine whether the initial consent received remains valid for those future projects or whether a reconsent process may be required over time.

It's also envisioned that in the initial informed consent process, that they develop a statement that explains how that is to be handled so that the principle of transparency is embodied in the decisionmaking process for consent.

There were also a lot of other issues outside of informed consent that touch on some of the other issues, privacy and confidentiality, access to research data from non-researchers, how it will be used

both internally within the Department and externally. So there were a number of issues in the design and ongoing oversight of the project. In response to public comments, it was felt that a very practically focused, problem-based ethics board should be in place to deal with those issues.

DR. TUCKSON: And, Sherrie, you obviously don't believe -- and I think from what you've just said, this would not weaken your normal function of the IRB. It doesn't create a competitor to the IRB. It doesn't create a parent of the IRB.

DR. HANS: No. In VHA, you know, we have ethics boards at each of our hospitals. We have IRBs at the majority of our hospitals as well. We also have other ethics functions. What we find is there is often a need, when the issues cannot be resolved within those parties or they feel like additional input needs to be brought to bear, that there needs to be a place for those questions to go. As a national office, we manage those sorts of questions. It's a similar idea.

There's nothing in here that says it has to meet whenever. It may be that such a board would be constructed and would meet very rarely and only be called in to deal with specific questions. It's not intended to be, as you say, an additional layer of bureaucracy. It's an opportunity for deliberative discussion of competing values and issues.

DR. TUCKSON: So, Sherrie, I like that then. So my concern is -- you got half of it which was a sense of not having a redundant layer of bureaucracy that just costs more money and just makes work and takes away resources from doing the science.

And secondly, my concern was that it not in fact or appearance weaken the legitimate, normal infrastructure of ethical scientific review called the IRB. You're saying that this would do neither and it would be in place and be there to serve if needed, and if it wasn't needed, you wouldn't have to -- at least you wouldn't have to create it de novo on the fly. And I think that makes sense.

DR. HANS: I think there were some initial design questions that this board would be helpful in informing the IRB initially and the governance body, but then its ongoing function would be, I think, more on of an on-call basis, as needed.

DR. WILLARD: This recommendation is remarkable for its brevity, but as I'm sure you'll recall when you read the full document, Reed, there's a long list of particular functions that this ethics committee would undertake, and I think they are different from what a standard IRB would do, even a specific IRB designed for this project.

Michael?

DR. AMOS: My question would be, is this scalable? I mean, if this is a 2 million- or 3 million-person study, there might be several IRBs that are involved. The way the project may be set up is that grants would be sent out to various sponsors, as Michael was talking about, to run certain aspects of the research. Each group would have its own IRB. Is this intended to be one ethics group that oversees all of those IRBs or --

DR. WILLARD: I mean, that's a level of detail that one can't address until one knows, A, is the project approved and, B, how is it set up. Some have argued for a central IRB. So regardless of how many millions, there would be a central IRB that would deal with it rather than dispersed IRBs. But we're not even prejudging that particular question.

DR. AMOS: I just want to make sure that it's something that's actually workable in case different scenarios occurred in the way the research is conducted.

DR. WILLARD: If the Secretary, in his wisdom, felt that we needed three independent ethics committees instead of one, that wouldn't be inconsistent with this recommendation, if it needed to be that because of scale or because of added complexities. At least for me, that wouldn't be an issue. That's a decision for him and project management to make.

Barbara?

DR. McGRATH: I'm sorry. Andrea was next.

DR. FERREIRA-GONZALEZ: With this recommendation and the previous recommendations, I have an issue with consistency. Here we talk about IRB without an S at the end, and in the previous one, we have an IRB with an S at the end. Here are we telling them they need to have only one IRB versus in the previous one where we have the S? It's just a multiplicity of IRBs. Just to be consistent throughout the document, where we have it open-ended, it might not be just a central IRB but something that they need to decide.

DR. WILLARD: That's useful. Thank you.

Barbara.

DR. McGRATH: Maybe the word "ethics committee" is a problem, though I don't have a better one in mind. But when I think of this committee, ethics ties into IRBs a lot, and I think the vision is that it's not just an IRB oversight committee, but it covers all of ELSI-kinds of issues. But I don't want to call it an ELSI committee either. That just sounds wrong. I think in the text it describes it more accurately.

One of the tasks that it does that is outside of that purview of IRBs is looking at issues like Dr. Mittman brought to our attention yesterday in her public commentary, sort of less policy type of issues but more social impact kinds of issues. I would see this committee as sort of looking at the big picture of what's happening with the results out of this study. Are recruitment strategies really capturing people? Not just following the IRB kind of requirements but the larger, broader, sort of global issues that the public commentary is sort of raising that this type of study is new issues versus just a large, regular genetic study.

DR. WILLARD: I think there's an opportunity for -- not that there's anything wrong with brevity, but I think probably this is too brief. It could read an independent ethics committee should be established to blah, blah, blah, and serve in an advisory. So actually give it's function in a brief phrase that would take the previous page where it's gone through in some detail and distill that down to a phrase that is meaningful in the context of a recommendation so that it doesn't just sit absent any clarity whatsoever.

Chira?

MS. CHIN: I work with a group that has several institutions that has their own IRB for one particular project, but they also have an overall, larger IRB to make sure everybody follows the same rules. Then from that point on, they have an ethics committee above that to kind of talk over. When we first drafted this, that's what I had envisioned this is what's going to go on because this is going to be a large project, many, many institutions. They will have their own IRBs. They have their own ethics boards, but overall, they need to come together with even ground somewhere so that they could kind of work together and share samples and stuff like that.

DR. WILLARD: Other points on this recommendation?

(No response.)

DR. WILLARD: So I'm hearing support for the general concept of this recommendation and perhaps some of the language can be improved and made consistent with the other recommendations. But I'm not hearing anyone argue against the need for such a committee. Okay.

Recommendation number 3 under regulatory and ethical considerations. "Project leadership should systematically and regularly seek the input of study subjects regarding their experiences, concerns, and recommendations for enhancing protections to ensure that the appropriate protections are in place and are being consistently implemented."

Comments? This is not a new one. This we've seen before in the previous draft.

(No response.)

DR. WILLARD: And the final recommendation under regulatory and ethical considerations. "Project leadership should develop guidance on the use of data and samples to promote the ethical use of clinical and epidemiological data and specimens. This guidance should be made available to subjects."

DR. FROHBOESE: One quick suggestion here, and that is rather than using the word "promote," use the word "ensure," given the critical aspect of ethical use, but also to insert "to ensure the legal and ethical use of clinical and epidemiological data and specimens."

DR. MANSFIELD: I would actually argue against using the word "guidance," which has another meaning in another world in that it's not binding.

DR. WILLARD: Do you have another substitute?

DR. MANSFIELD: Maybe something like rules. I don't know. Something that's a bit more binding. Guidance sounds like suggestions.

DR. FROHBOESE: One thing that we could do is just say, "Project leadership shall ensure the legal and ethical use of data and samples."

DR. WILLARD: Or is "policy" stronger than "guidance"? The home office can figure out a better word than "guidance," but that's a good point. Thank you.

Joseph?

DR. TELFAIR: Just that you may also want to consider "protocol" since that's a pretty straightforward word.

DR. WILLARD: Other points on this recommendation?

(No response.)

DR. WILLARD: Then public health, social, and economic implications. There are two recommendations here.

The first one, which is not brief apparently, "The Secretary and project leadership should systematically and regularly integrate project findings with other emerging data from other types of studies and regularly disseminate the accumulated knowledge base with clear descriptions of the possible clinical implications of the results and the limitations of the data, their generalizability, and their clinical and public health implications." Breath. "This information should be tailored to meet the information needs of the public, healthcare providers, and the public health community to use integrated information for the benefit of the population's health. Project resources should be sufficient for the integration, dissemination, and translation activities necessary to maximize the public health impact."

That is a large, sort of overreaching recommendation that covers a number of things, but it is mostly to make sure that information is disseminated and then used wisely in its broadest possible way for the good of the public. That's the short version of what's here.

Other comments? Jim?

DR. EVANS: Yes. The part about the possible clinical implications gives me some pause. They're going to be incredibly nascent. They're going to be incredibly contentious and conflicting. I have some concerns about kind of, in a way, requiring that aspect of it because of, by necessity, their preliminary nature as they're released on a regular basis. I just have some concerns about that.

DR. WILLARD: Do you have an alternative way of phrasing that?

DR. EVANS: Yes, leaving it out. Seriously. I think that dissemination and release of data is very important. I think that the clinical implications will be something that is picked apart immediately by everyone who's receiving it. I'm just not sure how feasible it is to have that. I'm throwing that out there. I understand the concern and the desire to highlight the clinical implications, but man, they're going to be contentious. Look at how contentious every clinical implication that gets promulgated is.

DR. WILLARD: Emily?

DR. WINN-DEEN: So I just would urge you to think about it in the context of the Women's

Health Study and the interim results, which were published and resulted in quite a substantial change in medical practice regarding hormone replacement therapy and prevention of heart disease. So I think there's an ethical obligation to publish interim results at the point where you have something to say, and I think your issue is do you publish interim results before you really have something to say.

DR. EVANS: Right, and I think you bring up a very important point. I think that that particular example illustrates one end of the spectrum. When results are so clinically compelling, then they need to be highlighted. So maybe saying something like descriptions of the clinical implications when they have reached a level that contributes to our clinical knowledge.

In other words, look at the Human Genome Project. You got a lot of release of a lot of data, and that's a really good thing. That's going to go on, and then every once in a while, there will be things with clinical implications that should be highlighted. So maybe some modifier there that -- clinical implications when the data specifically address such issues, or something like that.

DR. WILLARD: First Linda, and then Kevin.

DR. BRADLEY: Yes. I think that if you read further into the sentence, you get to the point that the clinical implications are going to be discussed. We know they are with everything that's found. The point of this is to look at the limitations of the data, their generalizability, and their clinical and public health implications. So I think the point is exactly that, to be sure and look at the clinical implications in the context of what the data actually can show.

DR. WILLARD: Maybe the word "balanced" can be in there.

Kevin?

DR. FITZGERALD: I just realized this now. We have clinical implications twice there. We have the possible clinical implications of the results -- and I'm presuming -- and the limitations of the data. So maybe we could say instead something about pertinent or relevant clinical public health implications to try to avoid what Jim is raising of the possibility of just dumping something out there which, of course, is just going to add fuel to fire and not necessarily enlighten anyone, but try and throw in some kind of phrase that says pertinent or relevant or something like that. Balanced could be it too.

DR. WILLARD: We'll come back to you, Jim.

Scott, did I see your hand up?

DR. McLEAN: No. I was just going to reiterate that I think the language is in there, the implications of clinical findings. You could simply leave out the second "clinical" and I think have simply the "public health implications," and that would be fine.

DR. WILLARD: Chira?

MS. CHIN: That's what it was initially intended to do, to make sure the clinical implication is strong, so that the report will be given out. One of the reasons why we have that in the document is one of the public commenters addressed that they wanted to have it to disseminate it out to the public when good data is being released and the patient wants to know what's going on.

DR. WILLARD: Elizabeth?

DR. MANSFIELD: Maybe I'm a minimalist, but I don't think we need to tell the Secretary exactly how he needs to release the information. I think you could just go "disseminate the accumulated knowledge base in a manner to benefit the population's health" and leave the rest of it to be decided.

DR. WILLARD: Michael?

DR. AMOS: Yes, I actually agree with that. That's a great way to put it because who's to say who's to make the call that the data is good or not. Without getting into more detail of whether it needs to be peer-reviewed published and reviewed and then repeated 10 times by independent investigators, or at least analyzed on several different fronts, just to keep a general statement like that is much better.

DR. WILLARD: Gurvaneet?

DR. RANDHAWA: Yes. I just want to support what Elizabeth said because I think some of the debate that we're having here will not be resolved by this study. The study will be an observational study. Most of the findings are going to be hypothesis-generating, not hypothesis-testing, unlike the Women's Health Initiative, which is a randomized controlled trial, specially designed to test whether the hypothesis was true or not. So people will always understand the caveats of an observational study and the implications. So instead of being too directive, the minimalist approach is better. I recommend that too.

DR. WILLARD: I'm sensing some of that.

Jim, we're back to you.

DR. TELFAIR: Yes. Gurvaneet makes a great point. I think that we want to avoid the inherent misleading that can result from observational studies. I like the minimalist approach.

DR. WILLARD: That's called consensus-building. Thank you, everyone, on that. That's a good one.

The next recommendation under public health, social, and economic is a new one. "The Secretary, in consultation with project leadership, should establish an independent standing committee for the duration of the project to periodically assess persistent and emerging social and economic implications of this initiative with special attention to health disparities. The committee should consist of individuals with expertise in the relevant sciences, medicine, law, ethics, and patient and community advocacy. The committee would routine seek public input on the implications of the project results and report its findings."

A previous version of this was in the draft report. It's the addition of economic, which is what's really new here, and that's why that's highlighted on the screen.

Comments on this one?

(No response.)

DR. WILLARD: We used it all up on the previous one.

We've got two more to go. So my intent, with your forbearance for being a couple minutes over the allotted break time, is we'll do the last two recommendations under public engagement. That's then a good time for a break. We'll come back from the break, revisit the one recommendation that we said we would revisit, and then move on with further discussion from there.

So under public engagement, there are two recommendations. The first one is this. "The public's willingness to participate in a large population" study "should be assessed before embarking on such an extensive endeavor. Willingness could be assessed through opinion polls, requests for comments posted on agency websites, and other proven methods. Such an assessment should be made in advance of a funding decision."

Comments? Elizabeth?

DR. MANSFIELD: Are the first and last sentences perhaps a bit redundant?

DR. WILLARD: As I was reading it, that did occur to me.

DR. MANSFIELD: Just in the interest of brevity.

DR. WILLARD: So combine those two. I think the sense of the task force was in advance of funding and in advance of starting are perhaps two separable events, but nonetheless, they could be merged into the same sentence to make it read better.

Other comments on this?

(No response.)

DR. WILLARD: And the second recommendation under public engagement. "If a decision is made to proceed with the project, it will be important to ensure that public engagement occurs throughout all aspects and stages of the research process, from conceptualization through design, planning,

implementation, conduct, and data analysis and reporting. Public engagement also will be important in applying the knowledge gained by the research and in addressing its implications. The Secretary should ensure that sufficient project resources are dedicated to public consultation activities before and throughout the duration of the project."

Michael?

DR. AMOS: What about following up after the project is over as far as how the recommendations or the data is actually affecting public health on an ongoing basis afterwards?

DR. WILLARD: As part of public engagement or as sort of a separate question?

DR. WILLARD: No. I mean as part of public engagement from the standpoint of after the study is over and the reports are out and people are starting to follow the recommendations, over the years it's going to be important to find out the actual metrics with some metrics of how -- if this is really having an effect on people's lives, if they were actually using and paying attention to this.

DR. WILLARD: So I'm seeing that as assessment of the value of the project, but I'm less seeing that as part of public engagement. That's actually an assessment on whether the incidence of diabetes has actually decreased somehow or we have better management of diabetes because we've done this project. Unless I'm missing your specific point.

Yes, Joseph?

DR. TELFAIR: I think I have a sense of what's being asked. I'm just not sure whether or not this is sort of in our purview at this point. I think it's the whole idea of when you do collaborative work and the actual engagement of that, that at every stage of collaboration from the actual implementation to the follow-up, which is what's being discussed, you maintain that level of engagement. So everything involved in assessing things like efficacy and outcomes and that sort of thing is there, but also now you're adding the element of those that are involved -- basically the whole principle is those you're experimenting with are also involved in the decisionmaking process. So even in the follow-up, the assessment process, that sort of thing, you also engage them as well. I think that's kind of what -- is that in the ball park of what you're asking?

DR. AMOS: Yes, and also the people in the study. It would be important to find out what impacts it had on their lives moving forward after the study is over. We heard the lady talk about the issues of the Ashkenazi Jewish population yesterday, and it would be important to assess if this had any sort of negative or positive effect on the study participants.

DR. WILLARD: I see the point.

Joseph?

DR. TELFAIR: I understand that, and so I guess my point is that I think we are sort of engaged to the point of where, if this is done, that's where we are. But in terms of the other, as you said, second part, part two, or second phase thing, that's kind of what this falls into, the way I see it. We're at our point in saying that we should have participation, full engagement up to that point, but if the decision is made to move forward with it, then that's another phase. That's another level of consideration about this engagement. That's what I would recommend we consider.

DR. WILLARD: So we just need language that expresses what we mean by follow-up for the two parts of this, which should be easy enough for the home office to add.

Elizabeth?

DR. WILLARD: We're going to have a minimalist alternative from Elizabeth.

DR. MANSFIELD: Yes, I think you just need to make a recommendation, like you have in other ones, and you could probably do that with a little restructuring of the last sentence. I don't think we need a thesis, but a recommendation.

DR. WILLARD: And you will help us with that.

DR. MANSFIELD: Of course.

DR. WILLARD: Thank you. We pay by the word.

Any other comments on this recommendation?

(No response.)

DR. WILLARD: Okay, terrific. So we have consensus on 17, with some suggestions for changing of language, and we have one that we can consider after the break. Mr. Chairman, back to you.

DR. TUCKSON: Well, let's see now. How long a break do you want? Do you want 10 minutes, 15 minutes? 15? All right. So we'll see you at 20 after.

(Recess.)

DR. TUCKSON: I forgot to bring something to your attention. It's the greatest thing since sliced bread. So here's the deal. You may have taken it for granted it was so good, but if you notice in the report, each one of them has something called Tabstract. Did you notice? And if you didn't, you should have noticed them. I was supposed to have told you this from the beginning. You like that? This is like copyright-level stuff. Who came up with this?

(Applause.)

MS. CARR: Let me clarify that. This was in response to a specific request from Jim Evans.

DR. EVANS: But I didn't call them Tabstracts.

MS. CARR: No, you didn't.

DR. EVANS: That was the genius.

MS. CARR: That goes to Yvette.

DR. TUCKSON: So anyway, we're going to keep this format, by the way, because I think it's really terrific. It gives you the key questions to consider. So Yvette did a good job on that. So we want to thank you.

DR. SEGER: And the rest of the staff too.

DR. TUCKSON: And the rest of the staff too, and she's giving out credit to everybody.

Take it away, sir.

DR. WILLARD: Okay, thank you.

So we have two things to deal with quickly. The first of these is our revised recommendation number 1 by this cracker jack legal team of Robinsue, Sherrie, and Michael. So this recommendation now reads: "The Secretary should convene a working group of representatives from the Office of Human Research Protections, Food and Drug Administration, the Office for Civil Rights, and other relevant agencies to address issues and questions raised by the public and to provide technical assistance and guidance to research sites on legal requirements regarding protection of research subjects, health information, privacy, and patient safety."

Comments? So it's the best of both worlds. It creates the working group, allows them to provide input and guidance, but without stepping on the legal issues that were misstated last time. Go ahead, Sarah.

MS. CARR: I was just wondering about whether in the phrase "to address issues and questions raised by the public," you might want to describe the nature of the issues and questions that this group would address versus any other. I don't expect that they would address questions about design of the study or the scientific goals and so forth. The questions that would be put to this working group from the public would be those pertaining to ethics?

DR. WILLARD: With all due respect, these were three lawyers who wrote this. The phrase at the end regarding protection of research subjects, health information, privacy, and patient safety," I read as modifying everything that appeared above, which includes issues and questions. Is that correct?

DR. FROHBOESE: That was certainly the intent, but we'll defer to the wordsmithers to make

that clearer, if need be.

DR. WILLARD: Other comments? Kevin?

DR. FITZGERALD: Just a clarification. So here, the focus seems to be at the end there on legal requirements regarding protection of research subjects. So I presume that's intentional, and we don't want to add ethical and legal requirements because that would be outside the purview of this group?

DR. WILLARD: That's a different group.

DR. FITZGERALD: Okay.

DR. RANDHAWA: Just for clarification, how does the committee envision the mechanism of public input for this working group?

DR. HANS: The initial public input really was this public comment period. A lot of the issues and questions that need to be addressed were raised during the public comment period. So the first task would be to sort through those public comments and determine which of those are legal questions that need to be answered, and then after that, there are a variety of public engagement mechanisms that, if established, could be drawn on to provide additional feedback and input.

I suspect that throughout the process of public engagement, issues will continue to be raised that need to go somewhere for this kind of assessment.

DR. WILLARD: Although you could imagine that the issues and questions could be raised by anyone, not just the public. They could be raised by project management. They could be raised by project participants, as well as the subjects themselves.

Other comments?

(No response.)

DR. WILLARD: Thank you very much to the team of three there. That was terrific.

Another suggestion came up during the break from Scott McLean, and I'll ask you, Scott, to explain it better than I ever could.

DR. McLEAN: Well, I was struck, in reading the public comments and getting the tenor, that there was a lot of concern on the public's behalf of ethical oversight, protection. One of the things that I'm familiar with in some of the military research that we do on protected and vulnerable populations is appointing an ombudsman to speak for that group who may not be able to articulate their concerns or their position adequately. There might be a role for that on some overarching level, dealing with particular vulnerable populations that this study will address.

I just thought that that might be -- I wasn't sure how that would fit into what we've discussed so far. We have an overarching ethics committee that might be independent, and I'm just wondering what the thoughts were on sort of the ombudsman type of element to this.

DR. WILLARD: Comments or reactions? Sherrie?

DR. HANS: It's an interesting question whether an individual needs to be appointed per se or whether one of the two committees that have now been recommended be explicitly given that role because there's the ethics committee and then there's the committee that's been recommended for the social and economic issues, whether in the consideration of the formation of either of those two, to ensure that the functionality of an ombudsperson is explicitly described in there.

DR. McLEAN: I think the ethics committee would have its primary allegiance to the ethics, and an ombudsman would have their primary allegiance -- and it may not be an individual. It may be a group -- to be a spokesperson for those research subjects. I don't think it's a subtle difference. I think it's a real primary differentiation.

DR. WILLARD: Other comments or reaction? Barbara?

DR. McGRATH: I think it's a great idea. But it's not an absolute certainty that it would be a useful role. But maybe one place to put it in, just to plant the seed, would be in the description, the text of

that social, legal, and economic policy advisory group, such as the appointment of an ombudsperson for issues or something like that. Put it as an example of one of the functions of that second group.

DR. WILLARD: Within the text.

DR. McGRATH: In the text.

DR. WILLARD: Is anyone opposed to the inclusion of that as one of the possible roles this committee could play? All we're doing is providing examples of the kinds of functions. We're not trying to prescribe, not that we could anyway, the action the Secretary might take.

(No response.)

DR. WILLARD: Scott, thank you for raising that.

So here endeth the recommendations. At this point, there are a number of questions which are on the slide. I think we have touched on most of these as we've gone through. I think it's really the bottom two bullets on this. Are there additional areas that need to be addressed that somehow we've missed? Now that we've just run the gamut of everything in the report, have we missed something? And then if yes, let's address that now. If no, then we can move on and spend the time about what actually our conclusion is, given all of this, because that is a section of the report that will, I'm sure, receive more attention word for word than many of the other areas of the report.

So, first, are there areas that we have missed either from what people have read about the public comments or just in thinking this through?

(No response.)

DR. WILLARD: I think that is a reflection of the fact that we've been mulling this over for the better part of a couple years now.

So then the question comes to the conclusion. The one issue I think, to come back to the discussion we had at the beginning this morning, speaks to the tone of the report. So I think, as we discussed previously, we do want to appear neutral. We want to actually be neutral and have the tone and the language sound that way.

On the other hand, as Alan articulated, there certainly is an opportunity to phrase that in such a way that says explicitly that we acknowledge that there is a substantial potential benefit from such a study for the improvement of health of the American public and that, therefore, the following issues need to be addressed and tackled prior to deciding whether, in fact, such a project should be undertaken and in what way.

The alternative is to be completely neutral, even in the conclusion, and simply to put our hands up and say we were told to suggest some issues. Here are the issues. Here are some potential mechanisms, and best of luck to you, Mr. Secretary.

So I'm going to open that wide open to the committee. I think this remains the one issue that we have to settle as a committee in order to come to a consensus on what the tone of the conclusions should be so we can be of greatest help to the Secretary and yet also reflect what we've been doing for the better part of two years.

Comments? Joseph.

DR. TELFAIR: I guess I would just comment that I think it's important that the tone itself be consistent with, first, the overarching recommendation that we made which, to me, does set the tone for the rest of the report, and secondly, that it be very succinct.

Well, let me just back up. What I mean by succinct is that the concluding remarks themselves do not have to be extensive. They just should reflect or even summarize briefly what we have there. But I do think importantly the tone should be consistent with the overarching recommendation because that was done after review of everything else. I do not think it's inconsistent with what we've discussed or has come up so far. Just a comment.

DR. WILLARD: Other comments? Kevin?

DR. FITZGERALD: Just to try to climb up on the bridge that Reed pushed me off --

(Laughter.)

DR. FITZGERALD: -- and then said I jumped --

(Laughter.)

DR. FITZGERALD: I think getting back to what we were asked to do and the three things that we identified was identify the issues, outline approaches that could be used, and then recommend mechanisms, I don't think it's inappropriate to say that we see this process in and of itself as being of great benefit, not trying to in any way, shape, or form say how the process will eventually work out, but that the process in and of itself is something, the process of doing, A, what we did, and then the Secretary going forward and doing a rigorous evaluation of these issues that were raised.

So, in other words, if there's a positive to really be emphasized here, it's to say what we're doing is a good thing and what we ask the Secretary to do we think is, obviously, a good thing in and of itself, without conditioning that on any particular conclusion being reached.

Is that better? Can I stay on the bridge now?

DR. WILLARD: Other comments? Sylvia?

MS. AU: I just want to make sure the conclusion shows that we are really supportive of a careful public consideration of the participation and costs of this project in the overall scope of our current healthcare system and maybe failing healthcare system so that it's very supportive of the Secretary needing to do a lot more consultation with the public, economists, health insurers, policy makers, so that it's not a for or against the project. It's for consultation for sure.

DR. WILLARD: Other comments? Alan, do you have a reaction that you wish to share with us?

DR. GUTTMACHER: I don't want to take up the committee's time by saying the same thing I said before, but I would say the same thing I said before.

(Laughter.)

DR. GUTTMACHER: So I do think that we ought to come to some kind of -- I agree with what other people are saying. I absolutely agree, for instance, with Kevin's point that even if there was a decision eventually not to go forward with this process, that the process of looking into that in and of itself is worthwhile. This will say things that would be pertinent not just to a large population base. It will say stuff that's pertinent to a lot of health research, et cetera. It's worthwhile for the Department at the highest levels to be thinking about, et cetera. So I absolutely agree with that.

At the same time, I do think that we should, in the conclusion, have a brief statement that the potential benefits of this to the health of the American people are significant and unique, in fact, I would argue, whether we want to use the word "unique" or not, and that's what makes it worth spending the amount of time and money that it would cost to do this kind of further thought.

So I'm not sure it's up to me as advisor to the committee, but the committee might want to decide up or down whether it wants to have that in there I guess.

DR. WILLARD: Yes, because you're not saying that we are supporting the concept of a large population study. It is simply that we're supporting an extensive and comprehensive analysis of the issues.

DR. GUTTMACHER: And the reason why we do that is because we think that it has potential. I would include the word "potential" in there. You know, there are such potential significant benefits.

DR. WILLARD: Barbara?

DR. McGRATH: I don't disagree with that, but if I were to include that cause, then I would have to attend to the other side of me that's feeling -- a big subtext with this is the lessons we have learned

from the Human Genome Diversity Project and the history of other large databases internationally that have had issues of confidentiality and privacy concerns really rise to the top and put a reason for slowing down and being very, very careful about this.

But then we get into those phrases of there are benefits, but there are risks. So that's why I keep coming down to the idea of neutral because I keep seeing them pretty equal. I don't personally feel that the uniqueness of this is so much bigger than the potential challenges of it. But, luckily, I'm not the Secretary and I don't have to make that decision, but just sitting from where I am --

DR. GUTTMACHER: I guess I would say that I see this as distinctly different from the Human Diversity Project. Some of the issues may be the same, but this whole process that the report is suggesting is that this process in many other countries, for instance, when they have considered this, have lacked and is exactly the reason why they've gotten to some of the, I was going to say, ethical, but let's just say quagmire that they have gotten into. So I think we are being evenhanded by including all of the rest of the report.

DR. WILLARD: Jim?

DR. EVANS: I tend to agree with what Barbara said in the sense that I'm agnostic about whether the benefits will outweigh the risks.

DR. WILLARD: Kevin can help you with that.

(Laughter.)

DR. FITZGERALD: But it will cost you.

(Laughter.)

DR. FITZGERALD: Eternally.

DR. EVANS: I think that, given our charge, maintaining neutrality is highly appropriate. I don't think that prohibits us from saying that it is possible this will reap great benefits, but I think if we say that, we necessarily have to say, on the other hand, it could be a waste of a lot of money. So my tendency then is to avoid those "if on one hand, then the other" things by maintaining the neutrality that I think was very nicely summarized in the overarching statement.

DR. WILLARD: Just to give an alternative view to that, however, if we don't write the sentence that says it has great potential but it also raises a number of issues that require exploration and therefore, someone else is going to write that phrase. Therefore, isn't it in our best interest to write what we really mean? And if what we really mean, in terms of consensus from the committee, is there are both significant, potential benefits and a number of troubling issues that require in-depth analysis, then that's what we believe. It can be written in a way that is "balanced," but if we don't write that, my concern is a whole bunch of other people will be writing that, and you have no idea how that's going to come out. The difficulty with appearing neutral, trying to be completely neutral is that others will then decide how they want to describe what you are being.

I think it can still be written in as balanced a way as possible because I do think there are nuances here, and depending on how analysis of the issues comes out, any one of us might then say, great, fantastic project, let's go do it or say, no way. Notwithstanding the great potential, it's just not worth these other issues. But that's going to take a full in-depth analysis that we hope the Secretary would support. So that's just a different point of view from the --

DR. EVANS: I completely support that. Again, I think Barbara summed it up, like you did, that if we avoid that flat, neutral language, then we have to put in pluses and minuses, and I think that is certainly doable.

DR. WILLARD: Other comments?

(No response.)

DR. WILLARD: I find it remarkable that there are no other comments.

Mr. Chairman, what kind of a conclusion would you like us to articulate? This is a report of the committee. It is a report of the committee after two years of intensive work. Are you wishing a sort of the committee reached five conclusions, here they are, or are you looking for a general statement of the conclusion pointing to the 18 recommendations?

DR. TUCKSON: No. At this point it is whether or not we are prepared for this to go out to the Secretary. So I think the issue is, is the committee satisfied that you have reviewed these issues enough that you understand the consensus in terms of any modifications that we've made, and basically it is now time to put a bow on this and send this to the Secretary?

I would urge you, unless you have any particular major unreadiness, which did not come out at the end of reviewing these, to authorize your subcommittee to present this in final, typed, nice form and it goes out to the Secretary for his review. If you have any unreadiness that you want to be concerned about that causes you not to be able to have that report go to the Secretary, then you need to speak up as to why that is.

DR. WILLARD: Is there anyone who feels they are not ready to essentially vote on approval or non-approval of the final report? If so, why? Joseph.

DR. TELFAIR: I'm sorry. I apologize. This is going to be a little bit out of order. But my question is about the conclusion. Are you envisioning that the conclusion will be written sort of after this particular vote you're asking? Do we need to see that conclusion?

DR. WILLARD: Yes. The conclusion would come to the full committee.

DR. TELFAIR: It's a process question.

DR. WILLARD: Yes. In fact, the whole final report will be, but you're not expecting to see any surprises in the first 60 pages, but the conclusion page or two or half a page, or whatever it turns out to be, will be de novo in that you'll see it for the first time. We'll have to do that as an iterative process of refinement and ultimate approval essentially by email.

DR. TELFAIR: Okay, thank you.

DR. WILLARD: But I think what Reed is calling for or will soon call for is a statement that says, subject to that, we're ready to say this report is done essentially with a few minor tweaks that the task force and the home office will take care of, and then you're prepared to see it as the final report.

DR. TUCKSON: So let's just make sure we're absolutely clear here because Joe is right on the money in terms of this. As far as we are, I think, concerned, you have approved a report that's going to the Secretary. The thing you have not seen is this last little bit of conclusion language which staff is prepared -- "home office" now forever known -- to turn around in the next couple of weeks.

Sarah, I need to be real clear in terms of how you view this. Once that conclusion is done, everybody gets a copy of this. It is not for revote, re-anything. It's to look at it. I assume if somebody sees something overwhelmingly noxious, that's completely different from your understanding of what we agreed to in that conclusion sentence, you have the opportunity to call me or Hunt, and we will jump and get involved. But as far as we're concerned, you're getting the courtesy of taking a look at the final, but you've already approved it at this meeting, if you in fact so do in the next minute, and it goes out the door, so that the Secretary would get this report on or about Christmas. Before. January.

(Laughter.)

DR. TUCKSON: They just told me it turns around in two weeks.

You know, you've got to make sure it's pretty and polished and looks nice and there are no typos and so forth. So the Secretary gets the report on or about January 1, which means you don't get to have another meeting about this, not another giant conference call, not another yamma, yamma, yamma about nothing. So that's where we are on this thing.

So I will turn it back to you, Hunt, to bring this vote to a closure. In fact, I guess I have to do

that.

DR. WILLARD: Yes. That's your job, man.

DR. TUCKSON: Darned, man. You did such a good job.

So let me put a motion on the table for you. The motion for you to vote on -- who gets to vote on this?

MS. CARR: Members.

DR. TUCKSON: Members. We love you, ex officios, but you don't get this one. But you voted a lot yesterday, so you should be in good shape.

(Laughter.)

DR. TUCKSON: The members vote to accept the report and recommendations as described and discussed at this meeting. Let's stop there. I will get to plan 2 in a minute. So you are voting now to accept the report as discussed and revised and consensus reached on each point at this meeting.

All those in favor of that, accepting the report and the recommendations --

DR. WILLARD: And the recommendations.

DR. TUCKSON: And the recommendations. All those say aye.

(Chorus of ayes.)

DR. TUCKSON: Anybody opposed?

(No response.)

DR. TUCKSON: Good. All right.

Second is that we will forward this report to the Secretary to include a conclusion that will be shown to you in the next two weeks, and if there is any major upsetness about something in that conclusion, you will notify Hunt Willard or Reed Tuckson immediately. Otherwise, the vote is that this a concluded report that is being transmitted to the Secretary on or about January 1.

All in favor?

(Show of hands.)

DR. TUCKSON: Anybody against?

(No response.)

DR. TUCKSON: You are terrific.

Hunt Willard, you did a fantabulous job. The committee did a fantabulous job.

(Applause.)

DR. TUCKSON: And the Tabstract is a fabulous job.

DR. FITZGERALD: Just a clarification. So if that were to occur that somebody were to get a hold of you and Hunt, what's the process then at that point?

DR. TUCKSON: We will, first of all, look at it, agonize over it, and decide whether or not it's deserving to go back and let people take a look at it and weigh it, always believing in the respect for the consensus process.

Okay. We are now at the next stage where -- by the way, I'm supposed to remind you all about lunch, wherever it is. We're going to keep working for a minute. What time is it now? It's 12:00 now. Lunch was at 12:30.

Do we have the public people here?

MS. CARR: We have one public comment.

DR. TUCKSON: We have one public comment? Terrific. Where? David, come on up.

I got to say this because it's official and I have to sound sonorous when you do it. One of our critical functions is to serve as a public forum for deliberations on the broad range of health and human societal issues raised by the development and use of genetic technologies. And no playing around. We do greatly value the input we receive from the public. It is very important to us. So we do set aside time

each day to hear from members of the public, and we welcome and appreciate the views they share with us. So we're happy that David Mongillo -- did I do that right?

MR. MONGILLO: Better than most. Mongillo.

DR. TUCKSON: I haven't gotten one right this whole meeting. He's with ACLA, and actually based on the discussions yesterday, I'm sure that you're going to have some very interesting comments to make today.

MR. MONGILLO: I hope so. Thank you very much.

DR. TUCKSON: Five minutes, but you know, I'm pretty tough.

MR. MONGILLO: Thank you very much. I'm David Mongillo with American Clinical Laboratory Association. ACLA represents local, regional, and national hospital and independent clinical laboratories across the United States. All of our members, to some degree, perform genetic testing. Thus, we have a keen interest in these issues that are addressed by the committee.

ACLA certainly shares the goal to bring the full promise of genetic/molecular medicine to the health care system by incorporating the highest quality of diagnostic testing. We applaud the committee on such an ambitious and strategic approach to the multiple complex issues on yesterday's and today's agenda.

We wish to focus on one particular item that was discussed yesterday and that has to do with the regulatory oversight of genetic testing. ACLA is preparing our formal response to FDA on their recently released guidance document. So these comments should be considered preliminary.

There was a key question raised during yesterday's discussion. It was asked, is there a gap in the regulatory oversight of genetic testing? And the committee reached the conclusion that support for clinical validity and utility may be an area that needs further study.

Let me speak to that question from a CLIA perspective. The laboratory director of a high-complexity laboratory, which is the only laboratory that can perform genetic testing, is responsible to ensure that the test systems provide quality laboratory services for all aspects of test performance. That's subsection 493, dah, dah, dah.

Further and more importantly, in the same subsection, CLIA explicitly requires the laboratory director to ensure that -- and I quote -- "the test methodologies selected have the capability of providing the quality of results required for patient care." We believe that implicit in that statement is the requirement of the responsibility of the lab director to select test methodologies that have the capability of providing quality laboratory services for effective patient care. We believe this service is in keeping with the ordering physician interest in patient management and is consistent with clinical validity.

CLIA also explicitly requires in subsection 493.1417 that the laboratory must have a clinical consultant who provides consultation regarding the appropriateness of the testing ordered and interpretation of test results. This is also a CLIA requirement component, in our mind, used to ensure clinical validity.

Our intent is not to dismiss the issue, but to raise this as a point of discussion. We heard from the agencies that there are some very colorful players that are performing direct-to-consumer tests that have questionable clinical validity, as was described in the recent GAO report and the congressional hearings. All laboratories that do human clinical testing must be CLIA-certified. They provide tests that advance patient care and are held responsible for false marketing and advertising claims. All ACLA members are CAP-accredited. Most are licensed in New York and, thus, are subject to the highest level of regulation, inspection, test validation, and accreditation. As was stated yesterday, 75 percent of all genetic testing is performed in labs which are licensed by the State of New York. Let's not let the minority drive regulations for the well-meaning majority.

Continuing that theme, the second point I wish to make has to do with the new FDA guidance

on IVDMIAs, multivariate indexed assays, in vitro diagnostic MIAs. Essentially this guidance defines a new category of laboratory-developed test that will be subject to FDA approval, and essentially it will make laboratories manufacturers. Again, because our comments are underdeveloped and without taking a stance on the need for such regulation, let me touch upon the impact this guidance may have or will have on laboratory-developed tests and innovation.

CLIA regulates labs, as we heard yesterday. FDA regulates tests. There are fundamental differences and redundancies between these regulatory approaches which will make simultaneous compliance with both sets of regulations difficult, impractical, and burdensome.

What are some of the differences? FDA requires quality system regulations to produce essentially identical products from the first kit to the last. This is because it ensures that each approved product will perform in multiple settings as expected.

CLIA, on the other hand, operates as a QA/QC package, as Judy Yost described, so that each individual laboratory on a daily basis can responsibly perform thousands of different laboratory tests with an assurance of quality.

The new FDA guidance will include package insert requirements consistent with the need to perform the test by multiple laboratories. On the other hand, laboratory-developed tests are developed and their standard operating procedures can be quickly modified and validated in a particular laboratory consistent with CLIA quality assurance. There are also major differences to ensure compliance with test modifications. But most importantly CLIA explicitly allows for the timely ability to modify tests to incorporate the latest medical knowledge and enhancements.

FDA has consistently stressed the importance of smart regulation and following the least burdensome approach. The future of genetic testing will include numerous IVDMIA test applications. ACLA is concerned with the ability of FDA resources to keep pace with not only the initial approvals, but with the ongoing approval of valuable test modifications that contribute to medical innovation and improved patient care.

I probably don't have to tell this committee as an example of how this works, but I'll use one. HIV genotyping was used as a laboratory-developed test. Laboratories had the ability to modify that test to include the latest innovations, the latest thinking, the latest information that was provided. It really revolutionized the care of patients with HIV. It really has done wonders for that dreaded disease. As time went on, as the tests matured, manufacturers now have produced kits for HIV genotyping in therapy. That's a sort of natural evolution. But the point is that laboratories early on can be innovative and move nimbly and quick to make these tests available to patients.

We appreciate this committee's thoughtful deliberations on this and all the issues associated with the need for increased genetic testing, but not at the expense of innovation and timely patient access. We thank you for the opportunity to comment and we look forward to working with the committee and the regulatory agencies on this important issue.

DR. TUCKSON: Terrific. So two things come up. First, that is great.

The last paragraph, page 1. It sounds like what you're saying here is there is a rule that says that any CLIA lab must have a smart person who provides consultation on the appropriateness and interpretation of the test. So do you really believe that that sort of "must have" is reasonable enough to say to the public that the evaluation of clinical validity of a test being done by that laboratory is sufficient? Because Dr. Joe Jones with a license says I'm hired by the lab and I'm here, and CLIA says I'm supposed to certify it. Therefore, I do certify that this is a clinically valid test and that the interpretation of this test by a doctor that then leads to a therapeutic intervention on this kid is absolutely A-OK. You all go back home and don't worry. Is that what you're saying?

MR. MONGILLO: You heard yesterday a couple things. One of the things we heard yesterday

was that the College of American Pathologists has actually introduced additional checklist questions into their inspection process that get at these issues of test validation, particularly for genetic and molecular testing. These tests are done in highly sophisticated laboratories, genetic and molecular testing, the highest complexity level of testing. And, yes, there are laboratory directors that have the expertise, the knowledge, and the ability to make sure that these tests that are ordered by physicians and are integrated into patient management have clinical relevance and are effective for patient care. So, yes.

DR. TUCKSON: So the ability to oversight of that process and how well it works -- somebody is going out there and saying, okay, Dr. Consultant Jones, let's review every decision you've made. I was to review the criteria you use for clinical validity for that test and I'm going to make sure that it's squared away because you may be a well-meaning doc, but how do we know, so that somebody is actually on the case reviewing that.

And by the way, somebody in government and CLIA would know whether or not the appropriateness criteria used by Dr. Jones is the same as Drs. Smith, Henry, and Johnson in four different places, and that would all be completely consistent. And we could get that from CLIA.

MR. MONGILLO: I think you're talking about the expertise of the inspection and how --

DR. TUCKSON: And the criteria.

MR. MONGILLO: And the criteria.

The other thing you heard yesterday -- you heard it from Judy Yost at CMS that they are enhancing the individuals who will be inspecting laboratories in this area of molecular and genetic testing. The College of American Pathologists has already moved to have individuals who are highly expert in this area when there are genetic and molecular testing performed as part of the laboratory's routine testing. They bring in experts to do that kind of credible inspection that's necessary.

DR. TUCKSON: The second question for me, and I'll see if others want to ask you some things. I guess I'm a little confused. So you represent folks who must jump through the CAP hoop and the New York State hoop. That's what your people do.

MR. MONGILLO: We have a member pledge that in order to be a member of the American Clinical Laboratory Association, you have to be CAP-certified or equivalent, and New York State, as we heard yesterday, is certainly --

DR. TUCKSON: So why is it if you are taking -- and you sound like you are -- a responsible position on behalf of responsible laboratories who are more than prepared and willing to be subjected to the tough regulations of New York, why would you say it's okay that the other 25 percent not have to go through that? What should be done? What is your remedy for --

MR. MONGILLO: We're not saying it's okay. In fact, what we're saying is let's not regulate for the lower 25. If there need to be changes -- yesterday the recommendation that came out of this group was a multi-agency approach. I think the main message we're sending is that let's make this multi-agency and let's do it in a way that doesn't --

DR. TUCKSON: Well, what do you want us to do about the 25 percent? What should we do about them?

MR. MONGILLO: At a minimum, they all should be CLIA-certified because we heard from the GAO report --

DR. TUCKSON: No, no. You're terrific. Let me just make sure. You're willing to play by super-CLIA because that's New York. Let's just say New York is super-CLIA, CLIA on steroids.

(Laughter.)

DR. TUCKSON: It's probably illegal. But you're willing to play New York-level CLIA. Are you saying that everybody else should play New York-level CLIA?

MR. MONGILLO: Our members abide by the College of American Pathologists accreditation

process and New York State licensure.

It's not for us to make decisions about this 25 percent. I really think that's a government responsibility. You suggested they should get together. What is the issue? What's the concern? If there needs to be some enhancements, the agency should look at that.

DR. TUCKSON: You're a responsible organization representing mature corporations and laboratories and others in this field, and you have the opportunity to advise us as to what we should say. What do you want us to say about the 25 percent? If we make the assumption, as you are asking us to make, that the 75 percent that go through CAP plus New York, that combination, you're saying it's pretty damn good and don't pile on any more than that on our members because it's sufficient for the protection of the health of the public. So you're prepared to say that for you. What do you want us to do about the 25 percent?

MR. MONGILLO: Have them all become members of ACLA.

(Laughter.)

DR. TUCKSON: Others, please help out.

DR. FERREIRA-GONZALEZ: I think that the issue here is that there have been changes in the process of the CLIA inspection through the College of American Pathologists. Most laboratories performing genetic testing today are CLIA-certified through the College of American Pathologists. The CAP checklist has significantly been strengthened to specifically address questions of the clinical validity of this testing. Actually we took the template that the FDA uses for their review and kind of translated it within our capabilities to the checklist. So there are a number of issues. They are still very similar to the FDA review.

Now that there's a multi-agency or the need to add more agencies to this regulatory oversight, currently there is oversight of genetic testing through CLIA. The issue is that also the FDA now has introduced through the multivariate indexed analysis a new category of testing for the laboratory-developed assays that will have to go through FDA clearance. So in here we have the FDA saying we do have statutory authority over laboratory-developed assays, but then CLIA said we have authority over the laboratory-developed tests. So I'm not finding that there's a need to increase oversight.

The idea that I have is maybe we need to strengthen a little bit CLIA in certain specific areas for creation of a specialty, for example, to assure that there is proficiency testing to strengthen the quality of the testing that is being done in this country.

DR. TUCKSON: Does anybody want to ask any other clarifying questions of our guest?

MS. CARR: I just want to ask you about the last sentence in your fourth paragraph. You're talking about the role of the clinical consultant, and you say that "this is a CLIA requirement component used to ensure clinical validity."

Yesterday Judy Yost -- and I think we've always understood that CLIA does not speak to, address clinical validity. She made that, I think, very clear. This sounds a little bit -- it's confusing. Can you clarify that?

MR. MONGILLO: I tried to build the case, using the CLIA language, where we believe that there is specific language in CLIA that addresses the need for effective patient care. The tests have to be effective for patient care. Is that the word "clinical validity"? We think that there's clearly comparable intent associated with effective patient care and clinical validity. So our opinion is that that language leads one to perform in a way that the tests have clinical validity.

MS. CARR: But I just wonder whether CMS would agree that their regs ensure clinical validity that way, through that component.

MR. MONGILLO: I think that's a question for CMS.

DR. TUCKSON: Well, I want to thank you. I do hope, as you heard yesterday, that as we try

to write something and refer this to the Secretary to be thinking about -- and I'm just making an observation here. But one of the things that private sector people often do when there is confusion like this is they will often think that it is in their interest to step up to the plate and actually try to form a public/private partnership that actually gets at the solution to these things.

I sincerely hope that you guys will use the time available in the next weeks to try to get with the people in government and try to see if you all can't just decide to get the right people together across government and the private sector and try to work this thing out without somebody having to like beat you in the head to do it.

This is just a little, old small advisory committee working in the woods trying to do the best we can day by day. All we can do is advise and so forth and so on. But I think a lot of people are going to wind up paying attention to the transcript of this kind of discussion that we've been through in the last couple days, and I've got a feeling that it's going to get some people's attention. If I've got anything to do with it, it will.

MR. MONGILLO: I appreciate it.

DR. TUCKSON: So I just hope that you guys will just jump up to the plate and say, hey, you know what? We're going to take care of this. Whatever this loophole is, whatever this little problem is, we'll work with government and then we're just going to solve it. That way everybody can go home and not worry about it. But anyway, that's on you.

Hey, listen. You're terrific. Thank you.

Now, here's the deal. Do we have in the audience yet --

DR. BOURI: I have a question. Thank you.

I'm not going to question the clinical --

DR. TUCKSON: Name.

DR. BOURI: Sorry. My name is Khaled Bouri. I'm from the George Washington University.

I'm not questioning the validity of the test, but in the clinical setting usually, there is a genetic counselor who delivers the test to the patient. In this case there's a test that is directly between the laboratory and the patient. So there's a specific thing about this test that you're not telling him that your cholesterol level is 200. You're telling him that in 5 or 10 years, you're going to have cancer. So how are you going to deal with this issue?

MR. MONGILLO: That sounds like a direct-to-consumer issue.

DR. BOURI: Yes.

MR. MONGILLO: And we actually use that in some ways as the example of what is now being sort of considered that this 25 percent. So we believe that those are the tests that certainly there should be physician involvement at a minimum. They should be CLIA-certified labs that are performing those tests, meaning that there would be medical oversight. There would be some acknowledgement that the tests have to be effective for patient care, and because of the physician oversight, we think there should be communication as a clinical consultant to communicate the results.

DR. BOURI: Because usually this is done by mail. They send you the results by mail.

MR. MONGILLO: And that was the whole issue of the GAO oversight hearing.

DR. TUCKSON: Thank you for that.

I think one of the things that our questioner reminds us of again is that that's a big part of the complexity here, and always the thing about what's so special about the genetic stuff is that this is the predictive value of these things. It's probabilities. It's prediction. That's what's continuing getting at this underbelly of concern around the clinical validity of these tests. It's not just your hemoglobin was up too low or high. It's something else going on here.

So, Suzanne, I think one of the things that I want to make sure that we at least think about

going forward is do we know anything about the behavior of these certified consultants who are supposed to make sure in a CLIA lab that the clinical validity of these tests is actually intended to address. What do they use? Does anybody know anything about inter-rater reliability? Is there any set of standards in that regard?

DR. FERREIRA-GONZALEZ: CLIA has specific standards for who actually is a clinical consultant.

DR. TUCKSON: So the standard is for who is a consultant. I'm questioning does anybody go back and look at the actual behavior of the consultant. Does anybody know what the consultants say, what they use as a yardstick to determine clinical validity? Is there a standard format?

DR. FERREIRA-GONZALEZ: Well, this will be for the --

DR. TUCKSON: So in other words, could you go back and look at performance assessment criteria for a clinical laboratory consultant who made a decision on clinical validity? How do you know if they're any good?

DR. FERREIRA-GONZALEZ: Well, during the process of inspection, if you're using the CAP with a specific checklist, your inspector will come and look at your clinical validity not only of what you have introduced in the last two years, but they can go back to anything that they have done in the past.

DR. TUCKSON: So the answer, just to make sure we heard that -- and this is a very helpful comment for us to think about in the future -- is that what we are hearing is that the College of American Pathologists guidance may be good enough and specific enough that you could use that as a performance assessment tool for the quality of the consultation from this particular person.

DR. FITZGERALD: Just asking a question of some fact, if you have that. At the end of this first page, you mentioned that in the GAO report, certain labs were called very colorful players, and some of those labs are doing direct-to-consumer tests, as we've heard. How many of those labs -- I don't need specific numbers. Let's put it this way. Are some of those labs in ACLA?

MR. MONGILLO: No.

DR. FITZGERALD: Are any of those labs CLIA-certified? Do we know?

MR. MONGILLO: Some are, some aren't.

DR. FITZGERALD: Thank you.

DR. TUCKSON: All right. So here's the deal. We've got people who have to leave at 3:00. We're going to take our lunch break now, and the actual lunch is available early. We're going to be back in this room ready to rock and roll at 1:10. Our guests that were coming at 3:00 are coming at 1:15. So we don't want Sylvia to miss anything. So you're going to come back at 1:10 and we're going to do five minutes of business. At 1:15, the presentations start, and then we're out of here early.

Thank you all. See you at 1:10. Not 1:15, 1:10, because Sylvia has to go.

(Whereupon, at 12:25 p.m., the meeting was recessed for lunch, to reconvene at 1:10 p.m.)

AFTERNOON SESSION (1:18 p.m.)

DR. TUCKSON: Welcome back, everybody. Right on time as always.

Steve are you here? We are very pleased to be able to welcome Steve Groft, Director of the NIH Office of Rare Diseases, to provide us an update on the Collaboration, Education, and Test Translation Program, or the CETT, which promotes the translation of tests for rare genetic diseases and also works actively to encourage clinical labs and research collaborations.

Steve briefed us about CETT in early 2005, and we're eager to hear how the program is progressing. Steve, I think you've got about 15 minutes of presentation and 5 or so minutes of questions. Thank you very much.

DR. GROFT: Thank you, Reed. This has been a real unusual program in which we've had the opportunity to start something right from the beginning and learn as we go. I have to say we've met with a lot of very, very good comments from many people. This was a program that was an idea that we really needed to do something to facilitate the translation of genetic testing from the research laboratories to the clinic situation. So we developed this program.

Some of the people involved in it are, unfortunately, on the last slide. I did hand out copies of the slides. I won't use all of them. I've tried to reposition. I think maybe 10 or 11 of these I will actually use. There was just a lot of background information that we've used to explain the program to others, and I didn't want to just limit it to the ones that I would talk about here. So I'll try to go forward on this.

You see there the partners that we've been involved with. I've made several presentations to the advisory committee in the past. We really haven't changed partners. Just I think we've solidified partnerships particularly with the CDC folks and HRSA and the CMS people talking about genetic testing. And then in have come these societies, and they're very supportive of what we'd like to do and how we want to move forward in this program of translating research of genetic testing into the clinic.

You see there some of the program objectives where we're really talking about new genetic test development and then the translation of that from research to practice.

We'd like to increase and improve the education about the rare genetic disorders, and we're also thinking about trying to find ways of collecting and storing the clinical and genetic information so that there can be some genotype/phenotype correlations. Of course, there are other programs going on in research and through the NIH that people have been discussing at length. So we think we have a nice jump on this aspect.

We have had several meetings focusing on genetic testing. The first one really was to identify the issues and the needs, and that was focusing primarily on molecular genetic testing. So after we started the CETT program, the biochemical genetic testing is an area that we felt needed to have some emphasis. So we were able to pull together a conference, I guess about six weeks ago, on biochemical genetic testing.

The other two URLs there are for the reports from those meetings, and we are circulating the current report from this meeting. I would say within a couple weeks there should be a website and we'll pass it on to Sarah or Amita for them to distribute out to you. We have a draft that's been reviewed by the steering committee, but we wanted to pass it out to all the participants to give them an opportunity to comment on it before we move forward.

I just want to go over briefly some of the recommendations that came out of the meeting and then some of the programs that have been implemented as a result of this.

The first one was that the CETT program should be expanded and include biochemical genetic testing. The other emphasis that we found was that we really need to start to look at those tests that are only available in non-U.S.A. laboratories really to get a feel for what's going on, why tests are not available here in the United States. If we're going to run into problems -- and there are different groups working on the international collaboration and how to facilitate transfer of samples and quality assurance of the labs outside of the United States. So we are going to be looking at this as well as we move forward.

As we did with the molecular testing, we had a laboratory consortium that volunteered to help get things started. It's been very successful and we've been able to provide some support almost as a pilot project to really begin to initiate these activities of developing the genetic tests. We'd like to see a similar consortium be developed in biochemical genetic testing, and we seem to have a group of individuals who are willing to bring themselves together and form this consortium.

Where we go in the future we're really not sure. So many things depend on the availability of funds, but certainly this is a program that has gained a great deal of acceptance in the outside world with the laboratories and the patient advocacy groups who have a need for having the genetic tests developed and made available. But we also have been gaining acceptance within the NIH structure itself, to gather resources to facilitate the translation of the test and the development of the test. In fact, we just had a co-funded project with the National Institute of Diabetes, Digestive, and Kidney Diseases to help fund the development of some genetic tests that I'll just mention here in a few minutes.

So things have been growing. They've been moving very nicely. Again, as I mentioned to Linda Bradley before the presentation, I just can't believe the amount of support and collaboration that has come about in this whole area. So it's been really rewarding to start a program and have support and have it grow. Now, of course, our big problem is having enough money to sustain the growth and have it grow even further.

There's a great deal of concern about the training of laboratory and clinical personnel in biochemical genetic testing. I think as many of us -- not too many people here who are as gray as I am or maybe thinning hair or losing hair. But in the biochemical genetic testing area, particularly, the issue has been raised that we really do need to find a way to increase the number of individuals who are willing to participate in this activity and become the practitioners and the lab directors in the future. Again, there was a feeling that there's going to be some consolidation of some of the laboratory activities with the refinements in genetic testing and other things in the future. But at the present time, there is a need that we have to start to look at for increased training and sustaining the training sites. I know there are people at NIH who have this concern as well, that we really do need to look at this.

There was mention that guidelines should be developed to ensure the quality of testing, result interpretation, and diagnosis for inherited metabolic disorders and other genetic diseases. This is something we're looking to the American College of Medical Genetics and the Society of Inherited Metabolic Disorders and others to help develop some of the guidelines that will be useful to the clinicians and the laboratory people as well to help them really get a better understanding and appreciation of the test and what is needed.

Quality assurance measures need to be enhanced for the various laboratory tests, and we spent some time talking about that. These are several of the programs that the other individuals will work on outside of the government people. We feel it's society's responsibility and the professionals' to bring these ideas together.

We noticing more and more international collaboration in research efforts. This is going to just move right into this whole idea of quality assurance and transfer of samples across borders. So this cooperation and collaboration is going to become even more important as we move into the future, and

particularly for the rare diseases, we're finding this more and more, that the collaborative research efforts are extending beyond the borders and truly becoming international with the scarcity of patients in any individual countries. We're finding more and more collaborations being formed, and they're working on all aspects of research. So this is another area that needs to be worked on.

Again, as is usually always the case, information resources need to be enhanced to provide easy access to that user-friendly information on biochemical genetic testing. The availability of testing services and testing strategies need to be expanded and exposed to the public and other practitioners more extensively than what we've done in the past.

So the outcomes of the meeting and something that everyone has agreed to do. In our office, we're taking steps now to expand the CETT program to include biochemical genetic testing by adding several advisors and several individuals on the review teams to help review the biochemical genetic tests when they come in for consideration for support for development.

GeneTests, that Bonnie Pagon has primarily responsibility for, will be providing specific information on biochemical genetic testing either by expanding the current capacity or by setting up a companion site through subcontracting. So we're going to have an equal emphasis on biochemical and molecular diagnostic testing.

You can see there the ACMG and SIMD are committed to developing testing guidelines needed by users and providers in collaboration with other professional organizations. So again, this is something that this issue just needs the cooperation of everyone in order to make it work appropriately and really to get the best information out to the public and to practitioners and researchers, laboratory directors and staff. So many, many things are starting to develop.

CDC. The folks there will prepare a report of the meeting and will soon be posting that report on the websites and will be making that available.

The steering committee will review the recommendations to refine the roles and responsibilities and then to begin efforts to see what else is needed in the near future. We usually give ourselves about two or three months after the meeting, and then we start to think about, okay, where do we have to go after this meeting and what needs to be done.

Usually we've been running, about every year or so, a meeting to follow up and review what has happened during the past year. Again, it's a good way to look at responsibilities and see who has taken up the initiative and moved things forward. So we will continue to do so.

Here are some of the tests that have been developed through the network. It's quite a few different ones. You can see there the spread to various laboratories that are developing the tests, a couple of commercial organizations that are helping out, and then a couple different methodologies that are being used to develop the tests.

I would like to add one other thing. What we have done also, since we are involving the patient advocacy groups extensively, we've got a group of about six or eight individuals, leaders of patient advocacy groups, now that have come together and have gone through a little bit of a training program. They are now serving as a resource to other patient advocacy groups to explain the program and what does all of this mean. What is the CETT program and what are the values of having the genetic tests developed and made available. So they've come in with a great deal of enthusiasm, and we have them broken out into the various review groups.

Some of the experiences that we've had up to this point. Again, the need for templates of educational materials so that people can understand what genetic tests really mean, what can they expect both before and after, before the test is administered and then looking at the results, what should they be aware of. So people will be working on these templates. I guess we have to figure out better ways for the test results to be understandable by everyone. That's a major, major issue. I think it's hard breaking down

the information sometimes out of the scientific and medical language that we're so used to using to make it really understandable and useful to patients and their families.

I think I will just end it there. I've got several slides on procedures and activities, but those you can look at. They're highlighted within the website for you to look at at your leisure.

So I will try to answer questions, if you have any.

DR. TUCKSON: First of all, thanks a lot, Steve, again for coming.

Yes, please. The floor is open.

DR. EVANS: I was wondering if your group had thought about the issue of patents, how they affect what you're trying to do. Has that been an issue on your radar screen?

DR. GROFT: That's when we dance quickly. We do more than the two-step.

DR. EVANS: You have 30 seconds.

DR. GROFT: Oh, my goodness. Yes, we've stayed away from the patent issue a little bit by trying to pick up some of the tests that have no patent life on them, just for now. I think we wanted to gain some experience here first in seeing how can this all be done, and then we'd start to address the issue of tests with patents and rights.

DR. EVANS: So is that fair to say, though, that your decision about what tests to develop and all has been informed, to some extent, by whether patents exist?

DR. GROFT: I would say yes. I mean, it's an area we're not really prepared to deal with yet. It's something we'll be getting into, I think, as we gain more experience. Again, you run into problems. We didn't want to run into a lot of logjams here when it comes to developing tests and be held up in the legal circles, as far as developing the tests. We thought let's just go ahead and get started and gain some experience and use an Internet approach and gain the experience and keep growing and keep changing as we go along. Then we will begin to start to address that problem. It is a big issue.

DR. EVANS: Yes. It's really straightforward.

DR. GROFT: And that's been with us for about the past two and a half years. Even at the Clinical Center when we were paying just to have a few tests developed, it was an issue that Bill Gault stayed away from because he said it's going to bog us down, but it is something we have to address.

So if you can give us help later on or any suggestions, we'll be happy to have a forum on this, if you like. I mean, we'd be happy to sponsor a workshop or part of a conference on this issue. So always open.

DR. TUCKSON: By the way, Jim is all over this patent thing.

Andrea?

DR. FERREIRA-GONZALEZ: I really want to commend you in your attention to the biochemical testing now. It's an area of genetic testing that is not receiving enough attention, and we're starting to see that it is not being offered as widely as it used to. So I commend you on taking these issues.

There are two comments I want to make. One of the issues that we have regularly in genetic testing is the availability of controls. What are the efforts? Are you working with CDC with the Genetic Testing Quality Control Materials Program, or do you have any efforts within NIH to deal with these issues?

DR. GROFT: That's one of the nice things, the partners that we have. Everyone brings some different expertise, and certainly we're in close contact with the people from CDC in the quality control area. We had the partners listed, and it really didn't reflect the attendance of the different groups. There were people there from CDC who were really keeping us up to speed on quality control, and we recognize this as a potential problem.

DR. FERREIRA-GONZALEZ: The other issue that we wrestled with is there's a continuous

lack of standardization in the reporting of genetic testing, not just rare disease. It seems you're going through that process, understanding how to report. I will strongly encourage you to work with the professional organizations, in addition to the ones you have, other ones, that are going through some process of trying to standardize, really understand how are we going to post these results so clinicians can fully understand.

DR. GROFT: Again, you're right. That's where all the partnerships have to come in and have input into what's going on because we need the professional societies and organizations. We need the patient groups to really help us get the message correct when we're putting it out to the public. And then the health professionals that have to deal with working with the patients and the families. That's why I think this coordinated and collaborative effort is really so important. It's a nice model to try to develop the information that's so badly needed by so many people.

DR. FERREIRA-GONZALEZ: Yes. The idea is to learn from what we have already gone through. The idea is not to reinvent the wheel. We've gone through this process already. So just gain information from that.

DR. GROFT: It's quite a process to make sure you get the right message and the right timing of information out.

DR. TUCKSON: Any last questions? Oh, good. Emily?

DR. WINN-DEEN: I just was wondering if you could comment a little bit more on how the educational materials that you're developing would get out to the people that need them when they need them.

DR. GROFT: Again, our plans are to put the educational information on the website, but then to interact with the professional societies, the specialties that would see the patients, and the genetic counselors who would be counseling the patients. So it's a multi-system, multi-agent approach to try to get that information out to people. So we're going to be using different resources to contact the professional societies, the genetic counselors, the patient advocacy groups, and then whatever physician groups, nurses group, whoever is most likely to see the patients. That's who we're looking for.

We do have one example, the Cornelia de Lange. That's the first one that has really hit the market with educational materials and information. Again, it's going to be the first model that we have, how is this working, and then we have to go back and assess are we really reaching the audiences that should be reached with this message about the genetic test and all the information that accompanies it.

DR. WINN-DEEN: Have you thought about linking to GeneTests or something?

DR. GROFT: Oh, yes. There will be gene reviews for each of these, as we go along. So they're working on those as we move forward. As we develop the genetic tests, I think a gene review also is going to be made available. That's one of the good things of having Bonnie Pagon working with us as one of the directors. She's making sure that we're tuned into everything that's going on there.

DR. TUCKSON: Kevin, you actually have one more before you.

DR. RANDHAWA: I can yield to Kevin.

DR. TUCKSON: No, no. You were right there.

DR. RANDHAWA: Will you give us a sense of the criteria chosen for prioritizing the tests for translation?

DR. GROFT: They go through a review. Here's a review board, the team of reviewers who participate in looking at the information that is provided. Is the test ready for translation yet? Just what is the current status? We look at little bit at the cost and can we afford that right now where we are. So thus far, we haven't had to turn anyone down because of the cost of developing the test.

But we do look into a lot of the background. Has the laboratory that's involved completed the test in the research laboratory? Has it been useful? So we're looking at the utility and a lot of other

factors that come into play before the decision is made.

What I would suggest, if anyone has a test that they're really thinking about, get in touch with somebody like Andy Faucett, who's really the distributor of information, and have him lead people through what is needed and how we're going to move forward. So we've been very, very open and accessible to people trying to educate them about how to get a test translated.

So it is a decision process that the review team goes through, and then they make a recommendation to the steering committee. Then we try to find funds if we don't have them. This is where we've been turning it over to some of the institutes at NIH, especially if they are in a research protocol at the time, to try to gain some funds from them to develop the test.

DR. TUCKSON: Great. Now, Kevin.

DR. FITZGERALD: Well, I forgot my question. No.

Again, thanks very much for the update. Just a quick question. Is there a procedure that you're employing? Are you collaborating with somebody on how you're setting up to collect and store clinical and genetic information?

DR. GROFT: You know, I can't say that. I know they are looking at collecting that information on a database and storing it, trying to maintain the anonymity that's required. But I couldn't say for sure. I don't know myself, but I certainly can get the answer for you and get back with you. There are people who certainly are more knowledgeable about what's going on. Unfortunately, I haven't been able to spend the time that you'd like to on this issue, but I'll get back with you on that.

DR. TUCKSON: Yes, Scott.

DR. McLEAN: I just wanted to mention that the biochemical aspect of GeneTests has been needed for a long time. But do you think that that availability of information will increase the demand for biochemical genetic services, to the extent that that will become problematic more so than it is already?

DR. GROFT: We've been confronted with a few of the labs shutting down and some other issues because of legal problems arising. It's certainly something we don't want to look at in the future, but I think the reality is we need to have an emphasis on this to make sure that the biochemical genetic tests remain available. I don't want to say until such time as molecular testing becomes available.

But there are certain issues here with biochemical genetic testing that we have to address. There are weaknesses that people have expressed that we need to look at and make sure that it's shored up enough that people have confidence in the results that are coming out. We're looking at a decreasing population of practitioners and laboratory directors in the area, and these are all issues. The biochemical genetic testing is not going away because of molecular testing. So we have to make sure that the services are still available, the best we can. So we are looking for ways to increase the training aspect of this that hopefully will take care of part of the situation.

I hope I answered your question because I'm dancing a little bit there too because it's loaded with problems that we're trying to resolve. Of course, if we had unlimited funds, you could do some of these things and have lots of training programs. The parties are interested. Now it's a matter of putting things down on paper and getting them out and start to work on them.

DR. TUCKSON: Any last ones?

(No response.)

DR. TUCKSON: Terrific. Thank you so much. Thanks for coming back.

DR. GROFT: I'll get back with you.

DR. TUCKSON: On that patent thing.

DR. GROFT: Yes, and the patent issue too.

DR. TUCKSON: Thank you so much.

We're now really pleased to move to our update on NIH proposed policy on genome-wide

association studies, GWAS. Susan Shurin, who is the Deputy Director of the National Heart, Lung, and Blood Institute, is now with us, and we appreciate it.

Let me just remind you that this is an important policy proposal from the NIH on whole genome association research. NIH wants the committee to be aware of the proposal, which is generally referred to as the GWAS proposal. We wanted to hear more about it because it raises some of the same policy issues as the topic that we have spent most of today discussing. NIH has GWAS as a high priority because such research will lead to greater understanding of the common genetic factors that influence health and disease and possibly to better ways of predicting and preventing disease. This type of research is also important for the development of personalized medicine.

God, am I good at filling time.

The GWAS proposal has some important components aimed at facilitating the sharing of genome and clinical information that will be generated by the research, including the creation of a central database at NIH to house the data. We cannot get away from data and databases and all kinds of stuff here.

Such a proposal clearly raises important policy questions, including some that we've identified in our large population studies report. NIH is currently seeking public comments on the proposal, and the agency is working hard to broaden public awareness of it.

Susan is a prime mover in the development of the proposal, and so she's going to sort of chat with us about it.

Susan also, as you get into the presentation, would you sort of, again, help us to understand from early on are you doing this for information for us, or is there something that you want us to listen acutely for?

DR. SHURIN: I'm going to start out with that. First of all, it's information, but the other issue is that we're in the middle of a public commentary period right now, and we are actually very eager to hear people's input and advice and suggestions. I wanted to give you an overview of what it is that we're doing and why it is that we're doing it and how we see these extremely complex issues because we're trying to balance a number of different issues in terms of potential benefits and risks to numerous groups, and there are not easy solutions. So it's going to be a matter of figuring out how to make things really work.

My name is Susan Shurin. I'm the Deputy Director of the National Heart, Lung, and Blood Institute. My background is in pediatric hematology/oncology. I spent 30 years on the faculty at Case Western Reserve. I ran a laboratory. I've been heavily involved in clinical research of multiple types. So my background actually is not from the standpoint of NIH administration, but from having been out in the trenches doing this kind of work and spanning a period of time of tremendous advances in pediatric hematology and oncology. The landscape is radically different now from what it was some 30 years ago when I entered the field.

So I can't promise you that the slides will be readable, but I think I can probably interpret them for you.

First of all, I don't want you to spend a lot of time learning about GWAS. We haven't come up with a better name for it. We think maybe when we're done with the public commentary period, we'll have a contest to name these things.

What we're talking about is a group of studies in which we're looking at scans across the entire genome. We're getting 375,000 to 500,000 single nucleotide polymorphisms, which are then linked to the phenotype which is in the person from whom it came. So we've got both control groups and patient groups. The idea is to help us better understand the etiology and background of diseases which often have a genetic component but may also have environmental components, may have behavioral

components, may have lots of different components, and to try to sort some of these things out and to be able to come up with better ways of predicting risk, of implementing preemptive therapies and preventing the development or progression of disease, and developing new diagnostics and therapeutics.

So one of the big issues that we look at from the standpoint of the NIH is that the NIH really represents the public -- our job is the stewardship of the public investment in the biomedical research arena. We're really trying ultimately to improve the public health. If we're going to steward these resources well, we want to get the maximum benefit as we're making progress.

We have, for a very long time, encouraged the wide sharing of data. We've encouraged people to put papers on the Web in forms which are widely accessible to not only investigators but to the public. The work that we share we're eager to have widely available to people.

One of the things that we're encountering right now is -- and it's always been true that there's been a bit of an information glut. The information glut is now of a different order of magnitude from what it's ever been before. Basically we're doing studies now. I'm sure many of you have seen what these chips look like, and you've got thousands and hundreds of thousands of pieces of information. We are now generating far more data than any investigator or any single group of investigators will ever be able to analyze.

Many of the studies that we're doing that we're supporting are very resource-intensive. First of all, they cost a lot of money. But it really is more than that they cost money. Many of these studies are unique studies that are done on very limited groups of patients. The ability to get really well-defined phenotype data and to link it to the genotypic information, to compare it with people who are not affected with similar sorts of diseases is very limited, and you don't want to be particularly doing this multiple times if we're really going to benefit these subjects who are participating in our research. We want to make sure that that investment is maximized so that rather than having the same study over and over and over again, we'd rather have the data where people could use it and analyze it in a number of different ways to be able to come up with new beneficial interventions, both diagnostics and therapeutics.

It's very important that the participants in our trials have their privacy protected. So that's a huge issue. What we're talking about largely is maximizing the benefit to the public health, the investment that we're making in the support of research, trying to ensure that the privacy and safety of the participants in these studies are protected.

And there's a huge intellectual property issue. I heard a little bit of this discussion before because one of the things that's happened is that if we're going to come up with new therapeutics, if they're going to be developed, people have to be able to protect their intellectual property or they won't actually develop things. On the other hand, if things are patented at too early a stage, they may tie up data which then won't actually be available for publication.

So what happened really at about the beginning of 2006 is that as we're looking at our research grant portfolios, what we're finding is that we are receiving an exponentially increasing number and double exponentially increasing cost of applications to do genome-wide association studies on persons, in our instance, with heart, lung, and blood disorders.

Dr. Nabel, who is the Director of NHLBI, and Dr. Collins at Genome were discussing a number of these things, and we felt that it was going to be important that we develop some policies that would enable us to ensure that investigators share their data very widely, as long as that's consistent with the consent that's provided by the subjects.

So we started a discussion between our two institutes. NHLBI put out a request for information from our investigator community, and they gave us some idea of what they thought. And using that information, we started developing a policy and had a discussion with the other institutes and center directors saying, we're going to be doing this, would you like to opt in. It rapidly progressed to the point

where everybody said it's not a good idea for us to have different policies across the NIH. It's confusing to the investigator community. It's confusing to the participants in studies. We really need to try to develop some kind of coherent policy.

Now, you understand this represents now millions and millions and millions of dollars in research applications.

We are at NHLBI doing genome-wide association studies on a number of the cohorts of patients. We followed some for many decades. The Framingham Study, for instance, we're doing genome-wide association studies on. This started in 1948 and now includes three generations of subjects.

One of the things that I want to be sure that you understand is that wide sharing of these data is already taking place and has been taking place for a very substantial period of time. What we are looking at doing is to try to develop a coherent approach to this, to try to change the culture in the investigator community so that instead of having a totally proprietary sense of their data, they're willing to sort of put it out there and let other people look at it in order to maximize the benefit.

It also becomes clear that if we're really going to be able to provide optimal protection for privacy, for intellectual property issues, to standardize the phenotyping information that we're getting, to standardize the oversight to really protect folks, it's very helpful to have a single portal of entry. Now, we may have different ways in which you get in there. There may be different standards that apply to how you access data depending upon what's in those data. But we'd like to develop something that's reasonably coherent. So that's actually what we've been working on.

It's very easy for you to find a lot of this genome-wide association data available right now. The CGEMS project at the NCI which looks at prostate and breast cancer has just posted a vast amount of genome-wide association data. Among other things, if you go in and try to manipulate that, you'll see that you actually do need to know what you're doing if you're going to make any sense out of it. It's not like it sort of sits there and says, this is me. It really doesn't. On the other hand, we are talking about genetic data, so it is intrinsically potentially identifiable.

So our guiding principle is that the greatest public benefit will be realized if the data are available under policies and procedures that are consistent with the informed consents that are provided by the participants in a timely manner to the largest number of investigators. So this is what we're trying to accomplish.

There was a wonderful cartoon in the New Yorker a couple of months ago which had a couple of cave men sitting in their cave and they're sitting there over their fire, and they're saying, I don't get it. Here we are. We get lots of exercise. We breathe fresh air. We eat this high-roughage, healthy diet. He says, how come we're all dying in our mid-30's?

(Laughter.)

DR. SHURIN: So this is the issue. If we're going to make advances, we better learn to do something with this.

So we've broken it down into a number of elements. The first is data management, how do the data get into something that we're going to be sharing, how does it get out. Publication issues and intellectual property issues.

One of the things that happened, as we were having this conversation, is it became increasingly clear that it would be difficult to have either the kind of coherence that we felt we needed, particularly for such things as the extent to which the genomic data are curated and the extent to which the phenotypic data are defined, unless we had a common repository for all of this. If we're having a common repository for all of this, we need to have it done in such a way that we can ensure that there's a longstanding commitment to it.

So our proposal is that the repository be at the National Library of Medicine, at the National

Center for Bioinformatics, the NCBI. So the idea is that it's going to improve the public health and actually maximize the return on investment really.

So what is this about? The genome-wide association data -- and that's both phenotype and genotype then -- would come in under a peer-review process at the NIH. What we are proposing is that people who do this research with NIH support basically must share the data, again consistent with the consent. If subjects don't consent to having it be shared, it doesn't get shared.

We will, however, as we're creating the repository, be happy to receive data from non-NIH-supported investigators who meet the standards and are interested in sharing. I'm going to come back to this in a minute because this is actually something that's got quite a lot of interest, among other things, from industry who are remarkably interested in sharing.

The submitting investigators and the institutions at which they work are responsible for submitting the data using a random code, no identifiers, note any limitations of the use. Contact with the participants happens here. The code is maintained in the institution. NCBI and the NIH and the government have no way of knowing who anybody is.

So then these coded-linked genotype and phenotype data are put into this repository. It will be possible to get access to data which are aggregated, which won't give you, obviously, access to any kind of information about any sort of individual. You won't see anybody's single nucleotide polymorphism pattern through this repository.

If you want to gain access to anything beyond that, particularly anything which might give you access to the SNP patterns, you go through a controlled access process. There will be precomputed data from these that are posted on the Web.

This is designed, among other things, to make it so that the obvious associations are immediately available. This then becomes obvious and not patentable. The things that would be patented would be things that would be downstream from those because they would have to involve manipulations of the data that are done by the secondary investigators.

As you can imagine, we're putting a tremendous amount of time and energy into discussing the oversight for each one of these steps. So the oversight of the repository itself, the oversight of access. Much of the oversight of the access is likely to happen at the level of the institutes and centers that support the original studies because they will be in a better position to be more accountable and to be able to look at what's proposed.

Anybody who wants to actually use these data then has to submit a request. It doesn't have to be NIH-funded, but it does have to be at an institution because we are going to ask the institutions to take responsibility for some oversight of who's actually getting access and what they're going to do with this. So they will have to tell us what they're planning to do. They have to agree not to identify any individuals, and this won't be easy anyway. But it is absolutely true that even now, some of this is potentially identifiable, and as some of these technologies advance, a lot of this is anticipated to change. And for protecting the data confidentiality. This thing goes through the Data Access Committee. They will have data set-specific access rights to these data.

There are, obviously, infinite numbers of implications here. There are privacy implications. There are patent implications, intellectual property implications, and the implications of what's actually done with this. This does create some burdens for the institutions which, first of all, have to tell us that the data that's coming is compatible with the informed consent that's provided by the participants and for the institutions where the secondary users are, again, which will be asked to vet the folks who have access to this.

There are a number of industry inquiries so far of people wanting to participate. What we've learned already is that most of the industry that's very actively involved in using genomic data are

interested not only in using but in depositing. Amgen, for instance, has done this. One of the things that set off this discussion is a group of studies called GAIN, the Genetic -- I can't even remember.

DR. FROSST: Association Information Network.

DR. SHURIN: Okay. Which is funded not by NIH, but by the Foundation for NIH. The money comes largely from Pfizer. It is a public/private partnership. There is NIH money that's in it.

In the GAIN studies, the investigators tell us what phenotype data they have, and if they're approved investigators, then they send their samples. Pfizer actually does the genotyping. They then have access to all of that data. But the condition for the free genotype data is that they have to be willing to share with everybody else. So that is actually recently funded. We're just getting going on that, and it does require the wide sharing.

So the investigators who submit these data will have to provide a lot of information about what they're doing, the quality of what they're submitting, issues related to the subjects, assurance of compliance with applicable laws.

And the investigators who request the data are going to have to present a whole bunch of stuff as well, including telling us not only what they plan to do, but also we're going to ask them to tell us what they have done, among other things, to try to enhance the extent to which we can share the results of these studies with the participants. Now, we're not going to know individually who they are, but we can put it out so that people actually have access to it.

So we met with OHRP to discuss what it is that we're planning to do to ask them the question of whether this secondary use of the data actually constitutes human subjects research. It's removed from the original participants. The secondary users have no contact with and no ability to have contact with the participants. It's stripped of identifiers. Under the discussion that we had with OHRP, they feel that this does not constitute human subjects research.

There may be pieces, however, for which it does constitute human subjects research. There are some studies, such as the gene/environment interaction studies which are currently underway, in which we may actually need to have some of the data which constitute identifiers under HIPAA or it won't be meaningful. I mean, you're not allowed to have anything that tells you anything smaller than the State that somebody lives in. Well, you may actually need to know what the ZIP code is in order to be able to make anything out of it.

Their suggestion was that we customize the oversight, whether it's an institutional review board or some other form of oversight, to the situation. So what we're trying to do now is to develop something. We're not expecting this to be one-size-fits-all. We're expecting to have to be able to do a certain amount of customization.

So the issues for participants I already sort of pretty much mentioned. There are a couple of things that are a very significant concern to us. One is the issue of genetic discrimination. We still don't have laws that prohibit genetic discrimination. This is a concern. And the information on any individual has implications for the family and sometimes a community from which people derive.

This is something we've been addressing quite intensely not only in the Framingham share project because we have a longtime relationship with the participants in Framingham. We're on to the third generation now. The participants in the Framingham study are actually part of the oversight here. We are embarking on genotyping of a number of the other cohorts of longstanding NHLBI studies, and again, we're going to be involving participants in those studies in the oversight process to address a lot of these issues.

We are involved in extensive conversations about all of the issues of the protection of the data, how we're going to do access. Again, I can't give you a simple answer because it's a complex question. So at the end of August, we put an announcement in the NIH Guide and in the Federal Register with our

draft policy. We worked very, very, very hard to keep it short. Because it's short and it's really focusing on policy rather than on the implementation, of course, in many instances here, the devil is in the details, and so the implementation makes a lot of difference. But we tried to do it so that people wouldn't get lost. It's hard enough as it is. It's difficult to understand all of these implications.

As you can see, what happens is we have the experience that one usually has which is sort of the caboose effect, which is you go along with a low rate of responses and then as the deadline comes near, you get a little blast of responses. So we actually extended the deadline, and at the end of this month, we'll be closing out the public commentary period on the Web. That will be followed by a town hall, which will be on December 14th, to which you're invited, that will be webcast -- you're invited to participate on the webcast as well -- asking really primarily these questions: risks and benefits, additional protections, the proposals that we have for how we're putting this together, and any specific resources that investigators and institutions may need to meet the goals of the proposed policy. We're eager not to have totally unfunded mandates on our already overwhelmed institutions.

If you go to the main NIH website, go down on the left side to "research," the first one under that is "genetic repository." Or, as Dr. Collins discovered, if you go into Google, and you put in GWAS, you come up with our GWAS policy, and that will take you to it as well. And this gives you, more or less, the same thing, which obviously isn't very helpful under the current circumstances.

So that's what we're doing. We're eager to have commentary. We expect that there will not be unanimity. Obviously, people come at things from different -- people will weigh the relative benefits and risks in different ways. So we're planning a process in which we'll be able to take these things into account and try to put in as many controls as we can. We cannot make any of this totally risk-free. On the other hand, the down side of not sharing the data is that we don't get the potential benefits of this incredibly valuable resource at a point at which we think we're just poised to be able to benefit.

I will be happy to take questions and comments.

DR. TUCKSON: Well, thanks a lot Susan. I think just the overarching thing -- you weren't able to be with us yesterday and today earlier, but we've put a lot of energy into this idea of, again, the databases and how those things connect. So one of the things that we hope that I would share, at least from my seat at the chairmanship here, is that you would -- just to make sure that the America's Health Information Community efforts, of which your boss, the Secretary, is so involved -- is that you are connected to that activity.

Can I just ask you? Is there an explicit conversation going on between this kind of data collection and what's going on in AHIC? Is that familiar to you?

DR. SHURIN: I'm aware of what's going on. We're looking at it purely from a research standpoint.

DR. TUCKSON: I understand.

DR. SHURIN: We're looking at a slightly different aspect of the same picture, but I think we have a sense of the overall picture.

DR. TUCKSON: Okay, good.

Emily?

DR. WINN-DEEN: Do you anticipate, once you create a database of a certain size, that you'll also entertain what I would call sort of purely bioinformatic proposals from investigators?

DR. SHURIN: Well, actually the bioinformatics is a huge piece of this because one of the things that's a limiting factor in our ability to use these data is that we're not yet skilled enough in analyzing them. So actually one of the major things that we'd like to do as a part of this -- and this comes into the oversight piece that's over the repository -- is asking the secondary users to share their methods.

DR. WINN-DEEN: Okay. So there will be secondary users who can come in, never did a

thing in the lab, never touched a patient, but who can just go in and analyze the data with new questions.

DR. SHURIN: I think many of the folks who will be using these data are primarily statistical folks, bioinformatics folks, and very likely not to be people who have ever actually seen patients.

DR. WINN-DEEN: And you'll have a gatekeeper mechanism where you entertain specific proposals?

DR. SHURIN: Well, that's what that was all about, yes.

DR. WINN-DEEN: So part of it is just anybody who is getting funding to do the wet part of genome-wide is going to have to deposit their data.

DR. SHURIN: Correct.

DR. WINN-DEEN: And the other part is that then becomes a repository for the future.

DR. SHURIN: Right. Because the point at which people are getting the data that can be deposited, they are in contact with participants, and that's clearly human subjects research. The secondary users will not have such contact. So it's really totally separate oversight, yes.

DR. TUCKSON: Now I get the joy of flipping the order. So Kevin gets to go.

DR. FITZGERALD: Thank you very much for the presentation. I guess I'm fascinated, on the one hand, because I think this is an excellent example of some of the tension that we are going to be facing because the very power of this database in one sense for the research and all also raises the issues that are on the other side, say, ethical, privacy requirements.

I mean, I understand you're going to try and anonymize everything, but one of the things I'm thinking about is considering what's going to be in that database, both genotypic and phenotypic information, if something goes to a researcher who's involved with a particularly small patient pool, that the possibilities of identification just increase exponentially because there may be certain characteristics that allow for relatively easy identification, inadvertent identification, needless to say.

DR. SHURIN: Well, that was exactly my point not only about Framingham, but it's also the case for our other cohort studies.

DR. FITZGERALD: Right. So you mentioned you have participants in the oversight and all that.

That brings me, I guess, to the focus of my question. When you get to your informed consent procedure -- and as you mentioned, this is not a totally risk-free endeavor -- how is that risk captured in your informed consent? I mean, who decides what the risk is and how it's framed and how that's explained? And then how do you look ahead and describe the risk to future sorts of developments from this database? I'm fascinated to see how you capture that.

DR. SHURIN: It's a very touchy question because, in fact, one of the big issues that we have right now is that we have a lot of data and specimens, and is that original consent that was obtained 15 or 20 years ago compatible with data sharing? And regardless of what it says on paper, did the folks who signed it have a clue that this was going to happen? The answer is obviously not.

So one of the big issues that we're dealing with is we think we're going to have to be dealing with retrospective studies somewhat differently from prospective studies. And we're going to do the best we can in terms of assessing the potential risks. We are not arrogant enough to think that we are going to be able to predict all of those risks. We think this is rapidly changing.

DR. FITZGERALD: Right. And when you say you're going to do the best you can, do you have a sense of what that procedure will be?

DR. SHURIN: Well, a huge amount of it is going to be the issue of how the repository is handled, whether or not folks can download the data, where it goes, and a lot of that kind of thing. The other piece, of course, is what it takes to be able to identify somebody, which right now really requires a comparison specimen or a first-degree relative to be able to do that.

But increasingly, as we're able to analyze these data, we're going to be able to sort of make predictors about phenotype from the data itself, and I think we're anticipating that that's likely to happen. I think we're going to have to just sort of say -- we all make these kinds of risk assessments every time we cross the street, every time we use an ATM, every time we buy from Amazon.com. So basically what happens is the people who really aren't willing to assume any of that risk probably will not permit the data to be shared.

Again, there's going to be a tradeoff. We're going to try to be very honest with folks. We need them to trust that we will do the best we can, but we also recognize that we're not all-powerful in this. These data, whether we hold it at the NCBI or whether we contract with somebody else, will be subject to FOIA because even if it's held by a contractor, it's basically on our behalf.

We're in a situation now. We're in territory in which the science is way ahead of the law. So we think a waiver needs to come out for that. And we think there are approaches to a number of these things. But certainly laws against genetic discrimination -- because we're sort of saying, okay, it's completely deidentified. Therefore, you have this set of privacy issues, and then you turn around and you say, oh, but this is the ultimate identifier. Well, which is it? And the answer is, of course, it's both.

DR. FITZGERALD: Just one last one. You keep saying, we, we, we. Ultimately, I guess my question is, who is going to decide if what you have done is adequate? Is this an in-house decision, or is there some --

DR. SHURIN: Well, we feel that we need to assume responsibility for it because I think the biggest way we'll get into trouble is if we don't have accountability. So at a final level, we're going to have to. We think this is going to be an iterative process, and it's going to be one in which not only we take the current level of public commentary, but we also take ongoing public commentary as this goes forward. So we are listening hard. I really mean it when I'm inviting you to comment, and we are, indeed, listening hard. But I think the big issue is that if we get to a point where the responsibility is too diffused, then it becomes too easy to sort of say, well, it wasn't my fault when there's a problem, and we do want accountability.

DR. TUCKSON: Good.

Robinsue?

DR. FROHBOESE: Hi. I'm Robinsue Frohboese from the Office for Civil Rights. And as always, we offer our technical assistance with the privacy rule issues.

But on another point, you've mentioned ongoing public input and comments, and I know that when the press release came out at the end of August, you talked about a public forum in early December.

DR. SHURIN: I just said that. It's the December 14th town hall meeting.

DR. FROHBOESE: Okay, all right. Thank you. And where is it?

DR. SHURIN: It's out in Bethesda. We were hoping to gather the commentary that's come in to us to sort of frame a big piece of that discussion.

DR. RANDHAWA: Can I ask a question?

DR. TUCKSON: See, that was the payback for the earlier.

DR. RANDHAWA: I have two questions. One is the data that I understand will be deidentified. Will it be available as individual-level data or as aggregate-level data?

DR. SHURIN: For the people who are using it to reanalyze it, it will be individual data because it has to be linked to the phenotypic data.

DR. RANDHAWA: So that gets to the second question about phenotypic data. How phenotype gets defined is fairly challenging, you know, how one defines diabetes or hypertension or early stage or late-stage breast cancer. Is there going to be some sort of a guidance or a glossary from NIH as to what would be the definition --

DR. SHURIN: I think I mentioned at the beginning that one of the things that we're involved in now is establishing what the standards will be for the phenotypic information. We actually won't accept data that aren't in accord with the phenotypic standards. We anticipate that that's going to take a significant amount of time. In the GAIN initiative, for instance, a huge piece of whether or not a given project was funded had to do with the quality of the phenotypic data, that if the phenotypic data isn't tight enough -- it's actually much more difficult. The phenotype piece of it is more challenging than the genotype piece.

DR. FERREIRA-GONZALEZ: I strongly agree with you that the phenotype is a lot more difficult than the genotype. So I would strongly encourage to develop very clear standards.

My question actually is about intellectual property. As these specimens are deposited into this database in which there is access and already analyzed data, one can start identifying patterns with the association of different phenotypes. How is the policy going to deal with development of intellectual property?

DR. SHURIN: Well, we would like people to develop patents. We would like people to protect intellectual property as they move along and start to find targets which may be useful for diagnostics and therapeutics because they won't get developed unless people do that. So I think it's important to understand we're not discouraging patents overall. We're trying to ensure that what is patented is not at such an early stage -- sort of like not patenting a gene. If things get patented at a point at which you actually can't do anything with it and then it locks up a whole lot of other things, it doesn't achieve the goal.

DR. FERREIRA-GONZALEZ: How are you going to do that? How are you going to achieve that people don't patent things very early --

DR. SHURIN: When we post the data, we will post the first line through on the biostatistics. The linkage disequilibrium and the number of the simple associations that we've identified, those will be out there. And because they will be out there --

DR. FERREIRA-GONZALEZ: Then it will be publicly available.

DR. SHURIN: Yes.

DR. FERREIRA-GONZALEZ: That will not be patentable.

DR. SHURIN: Yes. That is what makes it obvious because we will put it out there. So it then is in the public domain and it's obvious and therefore not patentable, we hope. That's the idea.

DR. FERREIRA-GONZALEZ: I'm not following this. The data or the association is going to be --

DR. SHURIN: The association.

DR. FERREIRA-GONZALEZ: You're going to do the associations and you're going to put publicly available data.

DR. SHURIN: Yes. That will be posted -- the first pass through, that will be posted with the data. And the secondary users, as they come up with new things, then presumably, hopefully, will be developing targets for diagnostics and therapeutics. And we'd like them to patent that because that will encourage them to develop the products. But those will be what would be called nonobvious.

DR. FERREIRA-GONZALEZ: Is there anything within the NIH policy to look at restricted patents or --

DR. SHURIN: We can't do that.

DR. TUCKSON: Well, thank you.

By the way, one last quick one as we get ready. Linda, you might want to start. Do you have slides?

DR. BRADLEY: Yes.

DR. TUCKSON: We'll give you a chance to fiddle.

The ethics consultation that you spent a lot of energy on in the first part of your presentation. Where do you get that resource from? The ethics infrastructure. Did I miss something? You talked about some of the ethical --

DR. SHURIN: We see the ethics as totally integrated into --

DR. TUCKSON: But where does the expertise come from? Do you own that? Are the employees who do the ethics consultation part of your institute, or do you have to go outside someplace in NIH to get it?

DR. SHURIN: We haven't gone outside.

DR. TUCKSON: It's all inside?

DR. SHURIN: We've looked at this as so inherent and intrinsic to the entire process that it's not something that's a separate process.

DR. TUCKSON: Kevin?

DR. FITZGERALD: Just on that note -- and I thank you again for explaining this in some detail -- I certainly commend the desire to take accountability and responsibility for what you are doing. I think that's absolutely imperative. But in that process, it may actually require you to go outside to have some sort of oversight or ethics response from a group because you might need that perspective in order to be able to go to the public and say, we have been accountable. We're not just relying on ourselves.

DR. SHURIN: This is actually part of the public consultation. We would like people to comment, and there will be ethics people involved in the oversight of various components of this.

DR. FITZGERALD: Oh, they will. Okay.

DR. SHURIN: Well, they are in most of our advisory bodies.

DR. FITZGERALD: But, again, are they in-house or are they outside ethicists?

DR. SHURIN: It depends on where they are in this. It depends on which component.

DR. TUCKSON: We had been having some earlier discussions about this idea of sort of where do you go and how is it integrated. You looked at me like I was completely nuts. It's terrific. It's so integrated in what you do you don't even think about it.

DR. SHURIN: (Inaudible.) My goal, as we set up that, is that we would have everything that we did so integrated in the conduct of research that it would not be identifiable as a separate activity.

DR. TUCKSON: I'm sort of noodling over the large pop activity where we sort of thought about this issue of do you have this activity sort of above it that provides advice. But that's fine. We'll keep at it.

Well, Linda, we're happy that you're going to tell us something about -- can I say EGAPP?

DR. BRADLEY: You can.

DR. TUCKSON: As opposed to EGAPP.

(Laughter.)

DR. TUCKSON: You've got to have a rule that says that you say either the first letter and then the whole thing or the whole thing, but you can't have combinations.

The Evaluation of Genomic Applications in Practice and Prevention efforts. Now, your goal is to develop a coordinated process for evaluating genetic tests and other genetic applications that are in transition from research to clinical and public health practice.

Our first report on this was from Muin Khoury back in '05 when the program was about a year old, back in January of '05.

We're very pleased that you, with Muin, are deeply involved in supporting the work of EGAPP and have agreed to provide an update on this important program. Thank you very much.

DR. BRADLEY: Well, thank you, and I want to thank the committee for inviting us to come

and provide an update on what's been going on because a great deal has gone on since the last time we spoke with you.

I feel like I should take off my ex officio hat and put on my EGAPP hat, but I'm not as prepared as Deb Leonard.

Just to give you a little bit of basics on EGAPP, for those of you who aren't as familiar. It's the CDC-funded pilot project that began in October of 2004. It is non-regulatory in its approach, and it's focused around an independent, non-federal, multidisciplinary -- I've heard that word before today -- working group.

The goal is to integrate existing processes for evaluation and appraisal. In other words, we didn't want to start over. We wanted to take all the knowledge that had been collected through the Task Force for Genetic Testing and SACGT and SACGHS and all the other processes like the U.S. Preventive Services Task Force and the Community Guide and see if we could come up with a methodology.

Another important objective was to minimize conflicts of interest and essentially to develop and implement an evidence-based, transparent, and ultimately publicly accountable process.

This is the more updated version of the goal. That was our original planning goal that you just read, and it hasn't changed much. But to establish and evaluate a systematic evidence-based process for assessing genetic tests and other applications of genomic technology in transition from research to practice.

It's important to throw the caution sign out, I think, particularly at this point in where we are here in that EGAPP's methods are still under review. We're still in the process of development. We're starting to move into the product phase, but most of our products are not yet final. So what I'm doing here is presenting from CDC's perspective a description of a work in progress with a great deal of work, including an important stakeholder evaluation, to come.

The working group, as many of you know, was established in May of 2005. The 13 original members are still there. I did put a list of the working group members and the steering group members on the back of the handout and was kind of horrified last night to notice that in the process of doing that, I lost two of the working group members, and we don't like to lose them. So just to point out that James Van Allen and Carolyn Sue Richards are also very active members of this group.

The group has met six times. They meet for a day and a half in a forum very much like the one you're sitting in. As I'm sure all of you can relate to, they have had countless subcommittee teleconferences. They have three standing subcommittees: topics, methods, and products. In addition to that, each of the members sits on topic-specific groups that are working on specific evidence reviews, and some of them now are actually also working on writing teams. So they're very busy, as I'm sure you can relate. The next meeting will be at the end of January in 2007.

In terms of support, we've relied very much in the first two years on an interagency agreement with AHRQ so that their evidence-based practice centers could conduct five of the reviews that are part of this pilot project.

In terms of staff and consultants, in the CDC National Office of Public Health Genomics, where I'm located, we have a support staff there that works quite closely with the working group. We also have a number of technical consultants and contractors who work with us.

And our centers for genomics and public health that are funded through CDC have also been very helpful in thinking about some of the stakeholder issues and talking with us about dissemination and translation of products. In fact, the University of Michigan center has set up a stakeholder advisory group on EGAPP that started meeting a couple months ago.

The steering committee which is an interagency, mainly federal steering committee, although we've added some new members now, was a group that was incredibly critical in the early development of

EGAPP, was involved in many of the early planning discussions, and certainly was totally important and involved in the selection of the working group members. We are now moving into sort of a next phase. We went into sort of a phase where we were beginning a lot of reviews, but we didn't have any products and we were just sort of working forward. I think now that we're moving into the product phase, we're sort of rejuvenating that group. We've added some new members, replaced some wonderful members who have rolled off the committee. Alan Guttmacher was just a tremendous help in the beginning, and Suzanne Feetham, who's since retired from HRSA.

But we're going to start meeting again quite intensively with this group to look at the review of where we are now, the processes and the products. We want a lot of input from them on the evaluation phase which starts this spring, and really now that we're starting to produce some products and starting to get a feel for this process, begin to consider again how this becomes a sustainable process, which any of you who know Muin Khoury know that this is a very important part of this process.

In terms of the scope of topics for the pilot phase, we decided not to try and take on the whole world of genetic testing, but rather to try and focus a little bit and to begin with applications recognized as important or more common -- there are some examples there: tests used in a clinical scenario, screening tests -- but tests with a potential for a broader population application and, therefore, a broader public health impact. Also, when they choose tests, they're also looking to maintain a portfolio of tests that can challenge the methodologies that they're trying to develop. So they have sort of two main reasons for prioritizing topics.

The approach they're taking is really to start with the lessons from the ACCE process. I use that acronym to mean a couple of things. Certainly from the Task Force on Genetic Testing and the SACGT, who really laid out the analytic validity, clinical validity, clinical utility, and ethical, legal, and social implications as components of review -- and we are carrying on from the ACCE project which also did a formal assessment of analytic validity and relevant ethical, legal, and social implications, which at least the analytic validity part has not really been a component of most evidence reviews up until this point.

We're also still using questions to organize collection of information with a focus on attempting to synthesize the information and find out where the gaps are.

We're also integrating from existing evaluation processes a number of, I would say, gold standard methods. We started with reviews from evidence-based practice centers because of their credibility and their experience. We're using formal analytic frameworks with key questions and explicit search strategies. We're assessing the quality of individual studies and the strength of evidence, providing recommendations with a clear linkage to the evidence. I think that's really important for others to follow behind and see how they drew the conclusions that they did. And obviously, to identify the research agenda.

I think EGAPP has tried to do some newer things and that is, because there's such pressure of these products and tests moving into clinical practice so quickly, to attempt shorter time frame reviews that are targeted and practical, to focus on hard medical outcomes, morbidity and mortality, but also to consider specific family or societal outcomes when appropriate. They've begun to look at the usefulness of modeling and have commissioned some modeling in a couple of the evidence reviews, and it's become clearer and clearer as we move forward, that really it's going to be necessary to address cost effectiveness in a formal way as well.

The products of the group are, obviously, evidence reports that come from AHRQ or from other contractors in some situations. There is a peer review of these drafts as part of the process. When they're released by AHRQ, they're posted on the Web, and then under usual situations, a summary of the evidence is then published.

The recommendations, based on the evidence developed, are being written by the working group. There will be peer review of these drafts as well. We are planning publication and posting. What we're hoping for, in situations whenever it's possible, is concurrent publication of the evidence summary along with the recommendations. We have been talking with our friends at Genetics and Medicine who are very interested in working with us on this.

The publication of methods and evaluation, obviously, needs to follow very quickly, and that will include the results of the stakeholder surveys.

Just to give you an idea of the topics that are in the pipeline right now and where the different topics are, there was an EPC evidence report released by AHRQ a few weeks ago now. This particular topic was actually funded by CDC's Division of Cancer Prevention and Control who asked for a partnership with EGAPP to look at the results. It was more of a horizon scan on genetic testing for detection and management of ovarian cancer. The working group is currently working on a draft recommendation that's focused on proteomic tests, and that draft is in internal review.

There's also an EPC evidence report that's complete and pending release on testing for cytochrome p450 polymorphisms in adults with depression treated with SSRI drugs. And there's also a draft recommendation that's in internal review with the working group right now.

Draft reports. Testing for hereditary nonpolyposis colorectal cancer in newly diagnosed colorectal cancer patients and family members. This is a final EPC report in development. The draft review has been reviewed and has gone out for peer review, and they're now working on the final report.

And UGT1A1 mutation analysis in colorectal cancer patients treated with irinotecan. This is a non-EPC review that is quickly moving toward peer review as well.

Topics recently selected. The impact of gene expression profiling tests on breast cancer outcomes was awarded to an EPC in late October, and that's underway.

Screening for CYP450 polymorphisms to predict response to pain management with codeine. This request for proposals is in development. That will also be an EPC review.

And the use of genomic profiling to assess risks for cardiovascular disease and identify individualized prevention strategies is a review that's in planning currently.

I think it's important to point out that EGAPP is not alone in this, for sure. It's one of a spectrum, I think, of non-regulatory initiatives for translation and evaluation of genetic tests, and I think it's important to remember that all of these groups are learning from these processes and that all of this information really needs to be collected and considered. Certainly the U.S. Preventive Services Task Force has done two reviews on genetic topics, BRCA testing and hereditary hemochromatosis.

There are a number of technology assessment groups working in the country. This is not a comprehensive list. This is just to give examples. The American College of Medical Genetics Foundation recently funded a rapid ACCE review on warfarin and CYP2C9 and VCOR.

The Blue Cross/Blue Shield Association Technical Evaluation Center has done a couple of very nice reviews.

Intermountain Healthcare is working on internal reviews using the rapid ACCE format.

You heard from the CETT program, which is more of a translation program, but certainly looks at some of the issues of translating and the quality of testing for these rare diseases.

HRSA had a very interesting meeting a few weeks ago on evidence-based evaluation and decision processes for the Advisory Committee on Hereditable Disorders and Genetic Diseases in Newborns and Children.

And I think there are a number of funded projects, and I mentioned one that I know about because it's CDC-funded, and that's the Genetic Alliance project on access to credible genetics resources network.

For EGAPP, I think the next steps are very much about maintaining momentum. It takes a lot of work to get a process like this started and to continue to use what we're learning from each review and roll that into what we do for the next review. The working group is, obviously, spending a lot of time thinking about these issues.

Publication of methods and what's been learned, obviously, is going to be very important for the group to publish what their experience has been.

Publication and dissemination of products. Obviously, we need to make sure that these evidence reports and recommendations are widely disseminated to professional organizations and health plans and a number of other groups.

Initiating a project evaluation. We really need to know what is the value and the impact of these kinds of products and how they're being used and are they reaching the folks that we're trying to reach. So we're going into an evaluation phase that will take a year and that will involve a lot of stakeholder surveying.

Then there's a step that we feel is very important that I think is going to be very challenging, and that's the translation of the knowledge gained from the evidence reports and the recommendations into informational messages that are for different target audiences and finding ways to appropriately get that information out.

This is sort of a happy announcement. The EGAPP Working Group is very comfortable with their relationship with CDC, but has also made it very clear that they want to emphasize their autonomy in terms of the decisions that they're making for the recommendations. So one of the requests that they made of CDC was an independent website. This turned out to be something more of a high hurdle than we anticipated, but we actually got formal notification of a waiver approval yesterday, and so we should be able to get this interactive website up by the end of the year. And we're very excited about that because I think it's going allow us to enhance interaction with stakeholders, which has been more limited than we had hoped. We'll allow the working to post topics lists, their methods and process, evidence reports or links to those reports as they come out, obviously, to post the recommendations, and to post informational materials as they're developed. It will also allow the group to solicit feedback and to get input from stakeholders on suggested topics for review. So egappreviews.org coming soon.

I think that the real challenge that both the working group and the steering committee and CDC as well will be thinking about going into the next year is really how to build a sustainable process. Where do you go with a process like this? Obviously, we're going to learn a lot about methods and what works and what doesn't and the quality of information that exists and all of those things.

But I think there are other questions that need to be addressed, and I think one of them certainly is the future composition of the working group. We have a very committed group that's committed for the pilot study, and they've all stayed with us. This group was put together very much with a science focus. The first year was spent almost entirely thinking about methodology and approaches and looking at a very dispassionate process that avoided pretty much any stated position either from the advocacy or the criticism point of view.

But now, as we move into a policy phase, I think there's a need to think about what's the role of consumers and industry and other folks in a group like this.

Do we expand the scope of topics? Certainly the methods that are being developed could be used to look at any kind of emerging technology. Right now, we've been very focused on sort of the population-based applications, but should that change?

Should we go on and evaluate with a broader range of stakeholders? We're really focusing on health care providers and pairs, policymakers, and consumers on this first round, but should we move out from that?

And how do you support such a sustainable process? What's the role of the different Health and Human Services agencies and what's the role of public-private partnerships?

And then I think something that we think is very important is the need for a postmarket data collection process of some kind because we've really got to understand how these tests actually work out in the real world. So we figure we have enough to do for a while to keep us very busy scratching our heads.

I can't tell you how many people it takes to do something like this. So I really want to give a lot of appreciation to the EGAPP Working Group. What a hard working group they are. Our wonderful partners, the people on the steering committee, our interagency partners have really been great supporters, and Gurvaneet, who we just bug to death, and our Centers for Genomics and Public Health who really have also become very invested in this process. My wonderful staff. We have a tremendous group of technical consultants you can see there, including Deb Leonard, who have done a tremendous amount of work for us, and our technical contractors who we could not live without.

DR. TUCKSON: So remember all the stuff we went through painfully about clinical validity?

DR. BRADLEY: Yes.

DR. TUCKSON: Show us how what you're doing relates to that activity. And also, are people like CAP the end users, do you envision, of the kind of stuff that you're going to be producing? Because to me, what you just presented is extremely optimistic-making in my heart.

DR. BRADLEY: Mine too, but I hope we're right.

I would like to point out that we have a working group member in the audience. So, Joan, feel free to jump in here.

I think there are a couple of points that come to my mind, relative to your question, from what I've listened to for the last two days. I think one of them is that all of these groups, CAP and ACMG and all the professional organizations, and CLIA and FDA -- I think everyone benefits from the information that's developed by a process like this. I think how they use it is going to be the interesting thing that we need to learn about. And how useful is the information? Are we getting the right information? Is it presented in ways that are useful? We're really trying to take that practical approach. I know the working group spent a great deal of time talking about that.

This is me talking now, Linda Bradley, clinical geneticist. But analytic validity I think is something that really seems to keep cropping up as this problem, and I think it is part of what every laboratory does, to do the basic validation of a test. But if you think about the numbers that most of those labs are able to generate and how wide the confidence intervals are and what they know about these tests, there is a need also for aggregate data, for someone to take a dispassionate look at studies from different groups and say, okay, overall, how well do these tests perform in practice?

And I think then you get to clinical validity, which is really the crux of the matter. Are we getting to what we think we're getting to when we run these tests, and then how useful is that information? How is it going to impact management and the outcomes for the patients and potentially, in some cases, their families, as with HNPCC.

So I hope that they will be able to show where the gaps are with these different examples that we've chosen to test the methods, what does the data look like, what's the quality of the data, how much data was out there. Where are the gaps? How big are they? Can they be easily resolved? Are they really problematic? Those are the types of issues that we're trying to get to.

DR. TUCKSON: Your other challenge is going to be scale. So let's just say this is wildly successful. I mean, at the end of the day, how many of these things can you do and what are the economics? Is that the legitimate role of government, or are you proving a process that then gets reproduced?

I think it's extremely important for you all to be wildly successful. My God, if you are successful, think about all the hassle you take out of stuff, moving from bench to bedside on these kinds of things and speeding that up and giving an analysis that everybody can use, and you don't have to reproduce the wheel. This is terrific except you could probably do like one a year.

DR. BRADLEY: Well, we've done four in one year. No, it is very challenging.

Joan, I'd love it if you'd comment on this. I think one of the things that surprised me is that there aren't as many topics or tests or new applications out there that are ready for review as you might think. I think that what we've got to do is to figure out how do we prioritize that. And then do they all need the same level of review? Do you need a comprehensive review on everything, or can you do targeted reviews on certain types of things that are going to be less expensive and a little faster? These are questions that we're looking at but we don't know the answers to.

DR. TUCKSON: Well, maybe AHRQ will get a whole lot more money in their budget.

DR. BRADLEY: That would work.

(Laughter.)

DR. TUCKSON: Emily?

DR. WINN-DEEN: So, Linda, looking at the list of topics that you're reviewing, I imagine that the review process for some of these might say ready for prime time and some of them might say either not ever going to be ready, that your review basically concluded it was not suitable, or that your review concluded that there's not enough data yet to support it.

For that last category, what do you envision as a rereview kind of thing? You say it's not ready for prime time. You identify certain gaps, but at some point, you presumably would like to look at it again when some of those gaps have been filled.

DR. BRADLEY: I think that's one of the most challenging things that we've talked about is how do we do that update process because this group I think -- again, jump on me if I get off base here -- is trying to be very practical in not just saying, insufficient evidence, and throwing up their hands, but saying, here's what we know right now and here's how that might be appropriately applied. Here are the gaps and here's potentially what could be done to resolve those gaps.

She's the chair of the Topics Committee.

MS. SCOTT: Yes. I mean, a lot of this has been a learning experience and trying to decide what are the priorities of tests to address. We had a certain set of priorities for this demonstration project to try different methodologies and different types of tests. But going forward, what are we going to recommend for an ongoing process as to how to prioritize tests and what to do about looking at things again as more information comes up? We're also trying to look at tests within very specific clinical scenarios. So we're really addressing a particular test in a particular indication as opposed to a wide spread. We do think that perhaps the biggest thing we can contribute is to help identify just where the gaps are and help set the research agenda around those issues.

DR. WINN-DEEN: I guess my concern is, in the spirit of what Reed was asking, if you come up with not ready for prime time, but it just needs more data -- we really can't make a firm decision. It needs more data -- at what point when there is, hopefully, more data, do you then turn around and rereview that and say to FDA or CAP inspectors, whoever, now this analyte used in this way is ready for prime time? It has a clinical validity that's established. So anyone who wants to make a test for that only has to be concerned about sort of the analytical side of it rather than the clinical utility side.

MS. SCOTT: I think part of the process will have to include some mechanism either for continued review or some process by which a group can say, well, now there have been some additional studies. Can you relook at it? I don't think there's going to be one process. And the interval is going to vary from test to test, depending on the information that's needed and how --

DR. WINN-DEEN: So I'm just really encouraging you, when you put your website up, to try and think about how to give people guidance on that kind of a process as well. You know, we're going to list five gaps, and when at least three of them have been filled through studies, we would look at it again to see if we're now -- or some kind of something for the things that are in the intermediate phase.

DR. TUCKSON: Let me just do a quick process check. We're going to take one more question from Andrea. Then I want to make a natural segue in two minutes to easily allow some of our members to exit and have Sharon start to come up and talk about the discrimination stuff. So those that are worried about having to slip out, don't worry. The chairman is on the ball. I got it. We're cool.

One more question. Andrea.

DR. FERREIRA-GONZALEZ: I have a couple.

DR. TUCKSON: So much for being in control.

(Laughter.)

DR. FERREIRA-GONZALEZ: I was just wondering how these topics are selected. I mean, you have a committee. How did it come up with the different areas that you think the test must be ready for prime time?

DR. BRADLEY: Again, the first set of topics that were selected were selected rather deliberately to test different methodologies in different clinical scenarios. So it's not necessarily the method that would be going forward. CDC tried to do initially a broad scan from stakeholders as to what groups and individuals thought would be appropriate tests that are ready for prime time that would be useful to look at. We tried to mix and match, given a number of different criteria, including clinical scenarios, how well developed the test was, how complicated the clinical scenario was going to be, whether or not we thought there was going to be a lot of information versus what do you do when you have just a little bit of information. Are they different kind of reviews? So we really tried to be thoughtful for these first topics to test different methodologies, different types of tests.

Going forward, I think that's a different issue as to how new tests will need to be brought into the pipeline because, as Reed says, it is somewhat of a narrow pipeline.

DR. FERREIRA-GONZALEZ: Well, I would strongly encourage you to seek public advice from stakeholders and professional organizations because they, as they're at the forefront, might be more aware of these.

DR. BRADLEY: We have solicited from a number of groups, but I think it's been difficult for people to get to us without this interactive website. So we're hoping this will --

DR. FERREIRA-GONZALEZ: Well, that's what I was getting at, how to more widely communicate you're seeking topics, and then the question that Emily had, that maybe you can seek input with a specific metric maybe when there's more data available for some of these things.

DR. TUCKSON: All right. Thank you all very much. I've got three minutes before the hour.

By the way, that was terrific. Thank you for coming up and thank you so much, Linda. I appreciate it. That was a terrific way to do it.

Three minutes. I just wanted to review, if we can get it on the screen. By the way, what you'll miss, those who are leaving -- but it's going to be terrific, but we can get it to you -- is the update on the genetic discrimination because that's so important.

So with two minutes left, if you look on the board. What did we get done? I want to just review this real quickly.

So pharmacogenomics. Revise the report and recommendations based on the input received during yesterday's session. Send revised recommendations to SACGHS for review prior to seeking public comment. Lewin to seek input of 15 federal and non-federal experts and stakeholders on various issues. Seeking public comment on draft report and recommendations. Good. Does this, so far, look like reality?

PARTICIPANT: Right.

DR. TUCKSON: Gene patenting and licensing practices. We're going to revise the study questions, scope, and time table based on input received during yesterday's session, and initiate literature review and public consultation process.

Does that seem like reality? Jim? Jim, your reality is on the board there. You need to look real quick and make sure that you don't disagree with those summaries, the take-homes on gene patents and licensing. Revise the study questions, scope, and time table based on input received yesterday. Initiate literature review and public consultation process. Do you feel good?

DR. EVANS: Yes.

DR. TUCKSON: What is he going to say at this point?

(Laughter.)

DR. TUCKSON: Oversight of gene tests and testing laboratories in consultation with new work group. Prepare a letter to the Secretary expressing concerns about the adequacy of oversight, noting the forthcoming November meeting of CLIAC, but it will feature a case study illustrating the risks to the public's health due to current gaps in oversight. Oversight work group, which we have appointed, will do that proposal. The work group will also organize further fact-finding session for March meeting.

So notice that that assumes that even though you're sending the letter, you're going to put this on your March agenda, which I want to make sure everybody is comfortable with. You're going to get a report from the CLIAC, consultations with private sector organizations in New York State. We'll work with them in the interim. More in-depth discussion on FDA guidance. And folks may have some other things that will be fleshing that out as we get to that meeting.

Everybody, does it seem like it comports with reality? All right.

Large pop. Revise the report and recommendations based on input received during the morning session. Develop conclusion and executive summary. Circulate final report to SACGHS. Seek confirmation that the wording of the conclusion faithfully reflects today's sense of the committee from today's discussion.

But the real deal that you voted for was to transmit the report to the Secretary. So we're going to get it out the door. No fooling around anymore.

And lastly, these are some of the ideas that are being sort of proposed for the March meeting. Large pop update. Pharmacogenomics update. Gene patents and licensing practices session. Personalized health care initiative, AHIC. We talked a lot about all that integrated electronic data stuff, and we're going to have something more formal at the next meeting. Oversight informational session, question mark. To be determined. Possible presentations. Again, as we talked about, CLIAC. Also, I think CAP needs to be involved in this discussion.

So is the committee, in the last 10 seconds, comfortable? Are you all right? Do you feel like we got done what we needed to get done, and are you squared away for the interim?

(No response.)

DR. TUCKSON: Terrific.

For the three people only that are excused -- the rest of you are not. Just so everybody understands what's going on, we're gong to be able to have four -- Joe, you snuck in on this thing. So thank you all very much.

Last but not least, we do want to hear from Sharon Terry on the status. I'm sure you're going to have all kind of new insights because of the new Congress, and your predictions for all kind of new stuff. After that, we are done. So this is a good way to end up I think, and it really is a way to make sense.

So, Sharon, take it away.

MS. TERRY: Okay. This will take about two minutes. So you don't have to worry I'm

between you and leaving.

Of course, as you all know, things changed with the November election. We were working toward getting the bill on the docket and on the floor before the November election, and we failed to do that largely because of the chairman not putting the bill forth, despite the fact that I think we're up to about 246 cosponsors right now. So we've done a great job, even though in other years we've had 260. That was mostly Democrats. This is almost evenly split, Republicans and Democrats.

With the change in the Congress comes a lot of changes overall, leadership of the committees, et cetera. We do have right now what's called a lame duck session. If I had to predict, I would say we have about a 10 percent chance of passing this bill during this session. So it's not completely dead. It is possible that the Republicans would decide that they did want to put this forward now. It's also very possible they'll decide not to. They have a lot of things they need to do, things like funding the budget and other things that are important in terms of resolutions.

Then our work begins with the 110th Congress in January, new chairs, new committee structures. I just heard today that Senator Obama is on the HELP Committee, which will be helpful to us in the Senate. We have to reevaluate the House and look at who should be the chief cosponsors again, et cetera, have the bill dropped again in both houses, and work again.

This is Genetic Alliance's 11th year trying to lead this cause. We're hopeful. And I say that every single time, but I have seen politics at its best with this bill, and that's basically all that's keeping it from being passed, is a lot of politics.

DR. TUCKSON: What is the bill, by the way, that's in play now?

MS. TERRY: The bill is H.R. 1227.

DR. TUCKSON: And the sponsor as of today is?

MS. TERRY: Is Mrs. Biggerts, Mrs. Eshoo, and Mrs. Slaughter. Mr. Ney was a sponsor, but he's not a sponsor anymore.

DR. TUCKSON: By the way, Sharon, 11 years you've been at this, and thank God for you in what you're doing. It's extremely appreciated.

Do any of the members have questions? Yes.

DR. EVANS: What committee is responsible for it?

MS. TERRY: Three committees. That's part of the problem. Ways and Means, but a very, very small piece and they signed off long ago, and then Workforce and Energy and Commerce are the other two committees.

So there's an insurance piece pretty much signed off on and an employment piece that you all have been trying to help us with with your production of the phone book a year or so ago and some other pieces. Those two committees we've spent a lot of time talking with. We've spent a lot of time talking with the business community. I think we moved the ball far this year. So I don't think it was all for naught. I think we have gotten a lot of consensus around what needs to be done.

DR. TUCKSON: Cindy?

MS. BERRY: Sharon already knows this, but just for everyone else's benefit too, the Democratic committee staff of the committees that have jurisdiction over this have indicated that genetic nondiscrimination is one of their top priorities. It's important because, while this olive branch and outreach and touchy-feely, good stuff is going on, it probably won't last. But while it lasts, they're going to be affirmatively looking for bills and issues that have strong bipartisan support, and this is one of those areas that the Republicans and Democrats can hold hands and sing "Kumbaya" and actually pass in this honeymoon period, however long it lasts. So I'm encouraged by that statement from some of the key staff where they indicated this was one of the ones that they wanted to kind of extend the olive branch on and hope to get some action moving in the next Congress.

DR. TUCKSON: Terrific.

Peter?

MR. GRAY: Sharon, just a question. When you were here last time, you were here with the Chamber. My question is do you have a sense as to whether it would be the Senate bill that was passed by the Senate unanimously that will sort of be the template for the bill that does get sort of reintroduced? And where do things stand now with sort of the changes to the bill that you and the Chamber had discussed?

MS. TERRY: So we did discuss some changes that we never made. So H.R. 1227 is still on the table, which is Senate bill 306. My expectation would be that Senate bill 306 would be introduced.

It will be interesting -- and this is a completely academic exercise at this point -- to see if it will pass the Senate 98 to 0 when the Senate knows that the House is controlled by Democrats. The other thing we've heard is that the House is more conservative, despite the fact that it has more Democrats. The moderate Republicans are not there anymore that were there, and many conservative Democrats got elected. And something called the Blue Dog Democrats are alive and well and very interested in being fairly conservative, fairly aligned with business, with insurance, et cetera.

The future is not easy. So where I think some people may have naively thought that if the House switched leadership, we would sail through, I think we're still going to have a lot of work to do.

DR. TUCKSON: Other questions? This is terrific.

(No response.)

DR. TUCKSON: Well, Sharon, keep at it. My goodness, don't get tired.

(Laughter.)

MS. TERRY: I'll be back next year.

DR. TUCKSON: I don't know whether to feel good, bad, nervous, or anything. We'll just play it out.

All right. The floor is open for any last comments from the committee. Yes, please, Emily.

DR. WINN-DEEN: I just want to say, as the member emeritus here in an ad hoc status, it's once again a pleasure to be here. And I encourage the Secretary's staff to send all of the new Congresspeople coming to Washington a "welcome to Congress" packet of the genetic discrimination pack that went to everyone else that was in Congress in the last session.

DR. TUCKSON: Wow. So we have to ask the Secretary to do that. Right? We can't do it. Okay. Well, actually that's pretty cool. So there are people here who can hear that.

Now, one of the things I do want to end up on -- let me ask, is there anything else that the committee has?

(No response.)

DR. TUCKSON: I do want to end up where we started. Anand, I wish you would take back again to HHS Central and to your colleagues at the Secretary's office that we have duly noted, on more than one occasion during the course of this meeting, the interest on the part of HHS at the Secretary's office that we have not had before, and we really do hope that you all will continue to be attentive, taking leadership, bringing our things back, given that so many of our interests are aligned. Well, I mean, they are always, but really aligned right now.

I think the comment from Emily was actually a pretty good one. It's really a nice thing to do. So it would be a nice gesture to do that. So thank you.

Thank you all for a terrific two days. I appreciate it. See you next time.

Thanks to the staff.

(Applause.)

(Whereupon, at 3:11 p.m., the meeting was adjourned.)