DEPARTMENT OF HEALTH AND HUMAN SERVICES

SECRETARY'S ADVISORY COMMITTEE
ON
GENETICS, HEALTH, AND SOCIETY
(SACGHS)

— Fifteenth Meeting —

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P R O C E E D I N G S

[8:36 a.m.]

Opening Remarks

Reed V. Tuckson, M.D.

DR. TUCKSON: Good morning. Good morning to everyone. Welcome to the fifteenth, amazingly, fifteenth meeting of the Secretary's Advisory Committee on Genetics, Health, and Society.

A couple of quick housekeeping notes so that you all are aware. Your Blackberries, when they get information, the electrical pulse at 18.7 megahertz -- I made that part up -- goes right into the speakers and we get that [static] sound. So move your doggone Blackberries way the heck away from the thing or turn them off. The same, by the way, for your cell phones. So the first person that [causes static], we are going to make you feel badly.

The other thing is to turn the mics on, you push the button. You will see a light. That way you will be heard.

The other thing is, right now the webcast video is not on yet, through some technical issues unrelated to

our crack team of dedicated folk in the back there, who are wonderful by the way and whose work we really appreciate. So the audio is on through the Internet but not the video, so you have that.

The public was made aware of this meeting through notices in the Federal Register as well as announcements on our SACGHS website and listserv. I want to welcome members of the public who are in attendance as well as the many listeners tuning in via the webcast. Thank you all for your interest in our work.

Before I get into the substance of my opening remarks, I do want to point out, to the Committee's great joy and happiness, that my term on the Committee is ending with this meeting.

[Laughter.]

DR. TUCKSON: The Secretary has made a very wise choice, and that is that Steve Teutsch will now be your new chair. We decided that it would be fitting to make the transition on day two of the meeting, and so as of tomorrow morning the gavel will pass to Steve. I am absolutely pleased that the Secretary has made a tremendous choice, and good luck to you.

At the beginning of each meeting I take a moment to review our strategic plan and the status of our progress in fulfilling each of our study priorities. This gives us an overview of what we have accomplished to date. Today I need to really ask for your forgiveness because I'm going to go through this in some great detail today.

I think it is very important that this Committee, especially [because of] the fact that we have so many wonderful new members to the Committee, that you have a real sense of what we have done and where we are in our process because we are going to, at the end of the day tomorrow, have a priority-setting review process in which will have a much more in-depth discussion of where you are headed for the future. So tomorrow we will kick off a process of brainstorming about the issues that may warrant the Committee's attention.

With that, if you will look at the slides that are available, let me just start with the vision statement.

[PowerPoint presentation.]

DR. TUCKSON: That vision statement, which

described our priority issues and how we reach them, was developed in 2004 and has consistently guided our work as a Committee since then. So one of the things that you may wind doing at the end of the day is to revisit that vision statement.

But ultimately, as you see the timeline, we began in October 2003. In March of '04 we did the priority-setting, the discussion, and then in December '04 the report.

Public concern about the misuse of genetic information and genetic discrimination has always been our highest priority issue. We have written three letters to the Secretary championing the enactment of federal legislation to prohibit discrimination based on genetic information by both health insurers and employers.

In early 2005, we provided the Secretary with a legal analysis of the adequacy of current law regarding genetic discrimination. We provided him with a compendium of public comments documenting public fears about genetic discrimination and a compelling 10-minute DVD of compelling testimonies we received from the public

in the fall of 2004.

We strongly support genetic information non-discrimination and the Genetic Non-Discrimination Act of 2007, commonly referred to as GINA, which would protect individuals from discrimination based on their genetic information, including their family history information, by employers and insurers.

GINA has dedicated supporters on both sides of the political aisle, and in April of '07 it passed the House by a vote of 420 to three. Secretary Leavitt voiced support of legislation, and the President is also on record as supporting such legislation.

However, last July, Senator Tom Coburn placed a hold on the bill. In the last few days of '07, Senate leaders attempted to attach GINA to the Fiscal '08 Omnibus Spending bill but were unsuccessful. An article from the January 14 issue of Congressional Quarterly, which is in your table folders, provides more background on the current situation.

Proponents of the bill who are in dialogue with congressional leadership are hopeful that the procedural hold will be dropped and that GINA will be brought to the

Senate for a vote early this legislative session.

In June of '04, we developed a resolution about the importance of educating and training health professionals in genetics and how these efforts could be enhanced. At our last meeting, we convened a roundtable on this topic, during which it became apparent to us that there still are critical needs in education and training.

As such, we created the Genetics Education and Training Taskforce, which is chaired by Barbara Burns McGrath. Tomorrow Barbara will present the charge of that taskforce and we will discuss and finalize that charge so that this important taskforce can then proceed with its work.

In '06, we transmitted a report and recommendations to the Secretary on coverage and reimbursement of genetic tests and services. The report highlights limitations of the healthcare system that are affecting patient access to genetic tests and services and identifies nine steps that can be taken to overcome these limitations.

The recommendations cover a range of topics, including evidence-based coverage decision-making,

Medicare coverage of preventive services, the adequacy of billing codes for genetic tests and services, billing by non-physician genetic counseling providers, and genetics education of health professionals.

In July of '07, CMS sent feedback to us on our recommendations. A small group of our committee led by the terrific Marc Williams reviewed CMS's comments and found several areas that required follow-up with CMS.

In December, we had a very encouraging call with CMS leadership, and Dr. Barry Straube in particular and his staff. A summary of that call can be found also in your table folders.

There are two important messages that we want to emphasize that we took away from that call. Number one, the eagerness on the part of CMS to learn more about and be more actively involved in various genetics-focused initiatives within HHS and its agencies, particularly in the area of family history initiatives and CDC's EGAPP program.

Second, we were impressed by CMS's eagerness in taking and in continuing to move forward in how personalized medicine, genetics, and genomics are

transforming the modern healthcare delivery system. Their eagerness was clear in wanting to explore how the Medicare program can take advantage of the opportunities and benefits that genetics has to offer while also, of course, being fiscally responsible.

We provided Dr. Straube and his team with information that will help them pursue these goals, and we identified for them some areas that we think they should take a closer look at as they proceed with their self-examination.

Two years have passed since we transmitted our recommendations to the Secretary, and while we are excited by the leadership of the CMS team in taking action on our recommendations, we have also been clearly impressed that some of our recommendations, in the opinion of CMS, will require legislative authority that they currently do not have if they are to act on at least one of our key recommendations, particularly the one that is involved with urging Medicare to cover services indicated by a family history of disease.

This is so important to us that I recommend that we write the Secretary calling for legislation or

asking the administration to push for legislation to give them the authority to act.

Also, since the coverage report was written, there have been some developments related to billing for genetic counseling services. These developments are technical in nature, and I won't review them here, but they essentially affect genetic counselors' options when billing Medicare for their services.

In light of these developments, I think we should also ask the Secretary to clarify genetic counselors' billing options. Some legislative action may be needed to remedy the situation depending on the nature of the response.

Although it was not part of our '06 coverage report, I believe this new recommendation is consistent with the spirit of the report. A draft letter addressing these two issues will be distributed to you later today.

I want the Committee to take a look at the letter and let Suzanne Goodwin know if you have any changes to suggest.

They will be distributed later. You will get them today. If you have any questions about it, let

Suzanne know that you have issues off to the side. Then we will take a sense of it and, if necessary, we will have a discussion about it. If it is straightforward, then we want to get it into the hands of the Secretary as quickly as possible.

I think the Committee all know and understand that we cannot ourselves push for legislation. It has to go through the Secretary. That is why we are taking this step.

In '05 and '07, we wrote two letters to the Secretary on the issue of direct-to-consumer marketing of genetic tests. Our efforts in this area led to enhanced collaboration among FDA, CDC, CMS, NIH, and FTC. In '06, a consumer alert was issued by the FTC to warn consumers about using at-home genetic tests that have not been evaluated and to be wary of the claims made by companies marketing these tests.

As part of the Personalized Healthcare Initiative, the Secretary's Office is organizing an informal workgroup that includes various HHS agencies and FTC to explore direct-to-consumer genetic testing services.

This Personalized Healthcare Initiative Workgroup will be discussing the roles and responsibilities of federal agencies in direct-to-consumer marketing and performance of genetic tests, challenges associated with communication of complex genetic information to the public, and assessment of the services offered by various companies engaged in direct-to-consumer marketing, including the quality of information provided and confidentiality provisions. We are actually very pleased by the push that we have done and the response that is occurring.

Regarding the issue of large population studies, the Committee's final report, Policy Issues Associated with Undertaking a New Large U.S. Population Cohort Study of Genes, Environment, and Disease, which we need an acronym for because no human being can say that again in one breath, was completed in March 2007 and transmitted to Secretary Leavitt. A downloadable PDF version is available on the SACGHS website. We will be looking further into the status of the Secretary's response to the report and recommendations.

In November I mentioned that there was an

article in the journal Social Science and Medicine about the report. We drafted a letter to the editor of the journal that clarifies the scope and goals of the report, which you had an opportunity to review and comment on in the November meeting. That letter is now going, we understand, through the journal's review process. A copy of the final letter is provided at your table folders.

For more than two years we have been developing a report on the opportunities and challenges associated with pharmacogenomics research, development of pharmacogenomics products, and their incorporation into clinical practice and public health.

In March, the draft report was released for public comment. These comments were carefully considered over the summer and the fall. In November we finalized the recommendations. The final report and recommendations will be delivered to the Secretary in March, after copy-editing and printing are completed. The report will be made available to the public 30 days after we give it to the Secretary, which is provided, of course, as a courtesy to the Secretary to give him and his staff time to review it.

Although the report has not yet been formally transmitted to the Secretary, we do note that the America's Health Information Community, AHIC's, Personalized Healthcare Workgroup, is actually already reviewing our pharmacogenomics recommendations in the areas of electronic health records, clinical decision support tools, data sharing, and database interoperability as they begin to explore how pharmacogenomics test information can be used for disease management.

There is additional information about the Personalized Healthcare Workgroup's activities on pharmacogenomics, family history, genetic tests, and newborn screening in your table folders.

We have been monitoring the work of this group closely through our liaisons, Steve, Andrea, and Marc.

Marc, let me just ask you, is there anything specific that you would like to mention about the work underway by AHIC or its PHC workgroup?

DR. WILLIAMS: Just to mention that it is moving very quickly. Again, there is a lot of energy behind this and the recommendations that have come

through relating to the use case.

The use cases are the things that the AHIC workgroup has developed to basically lay out the landscape and allow the Office of the National Coordinator of Health IT to be able to say what do we have in terms of available standards and what gaps are there that need to be filled with additional coding standards.

That is moving very quickly. Our use case is out for public comment I think for another two days. Then we will go into final form, which will allow it then to move, by the end of the year, through the standards analysis.

So this is an exciting time. Those of you who have read the entire report on oversight will also recognize that there are references to the AHIC there. I think it will be incumbent on this group to work very closely with the AHIC and particularly the Personalized Healthcare Workgroup because a lot of the problems and gaps we are identifying are ones where potential solutions reside within that group.

DR. TUCKSON: Of course, everyone has read that

report cover to cover.

DR. WILLIAMS: I have read it about five times, so those that are slacking off --

[Laughter.]

DR. TUCKSON: You bring the curve up.

The work with AHIC is absolutely transformative for the future of American medicine. So I think that everybody really needs to continue to focus in on this as the Committee moves forward in the months and years to come.

In June of '06 we decided to move forward with the study on the impact of gene patents and licensing practices on patient access to genetic technologies. Since then, the taskforce hosted a progress session on this issue and a roundtable focusing on international perspectives.

You will recall that we have been working with Dr. Bob Cook Degan and his group at Duke on case studies that evaluate the impact of gene patents and licenses on patient access to genetic tests for hemochromatosis, breast and colon cancer, cystic fibrosis, congenital hearing loss, Alzheimer's disease, and Tay-Sachs disease.

These case studies will illustrate lessons learned in diagnostic development, commercialization, and adoption of patented versus unpatented genetic tests.

We expect these case studies to be completed within the next few weeks. Once we receive them from Duke, they will be used in the development of a draft report and recommendations on gene patents and licensing. Report development will occur during the spring and summer of '08. The taskforce anticipates releasing a draft report for public comment by the early fall, with a final report targeted for mid to late 2009.

Jim Evans, chair of our Patents Taskforce, recently presented an overview of our work on gene patents to another HHS advisory committee, that being called the Advisory Committee on Heritable Disorders and Genetic Diseases in Newborn and Children. That committee is interested in this because many newborn screening tests are administered as panels and patchy intellectual property protections may limit access to these tests.

Jim's presentation, as always, was well received, and audience members offered advice on additional areas to explore as the Patents Taskforce

moves forward with its work.

Some issues of mutual interest to our Committee and the Advisory Committee on Heritable Disorders include informed consent, mechanisms to assess clinical utility evidence, and education of healthcare workers and families.

In March of '07, we were asked to respond to a series of questions posed by the Office of the Secretary on the adequacy of the oversight system for genetic testing. An extraordinary 33-member taskforce, chaired by Andrea, was formed to develop a report in response to the Secretary's charge.

Through the dedicated efforts of the Oversight Taskforce, the draft report was released for public comment November 5th through December 21. In response, we received 64 sets of public comments that have been carefully reviewed and considered by members of the taskforce and staff. A summary of these comments is included under Tab 3 in your briefing booklet.

Most of our agenda today and part of tomorrow will focus on a review of the draft recommendations that have been revised in response to the comments received.

Our first goal for this session, and let me be very clear, is to finalize the recommendations for submission to the Secretary by the end of February. Our second goal is to receive approval on the spirit of the final report so that it can go through final editing and be transmitted to the Secretary in April.

Our commitment to the Secretary based on the charge to us, his Advisory Committee, is that we have to get this to him by April.

I want to be real clear again. We have been asked by the Secretary to do this work. We have responded as urgently as we can. We have been extremely diligent about the process, but we have to bring it in by April.

I also want to just make sure that everybody also appreciates the amount of public comment that we have received and, I will tell you, the diligence with which we have gone to every stakeholder organization that we can find out there in the country to give us their comments. We have just beaten the bushes on this thing. So I just wanted you all to understand how seriously we have taken this process.

Finally, you will notice that when we start this discussion in today's meeting, the public comment will be first. That is to make sure again that we get as much public comment before we start our deliberations. I am extremely focused on the meticulousness of the process here as we go forward.

You may recall that in March of '07 we decided to take up a new priority based on two proposals that we heard: one, the economic consequences of genomic innovations, and second, the evaluation of the impact of gene-based applications on real-world outcomes. We integrated these two together into one topic that would explore what we call the translational analysis for public health and clinical care and a viable economic model that could sustain the work. The taskforce appointed to lead this effort was given the shorthand title of the Evaluation Taskforce.

Because of potential overlap with the Oversight Report, work on this new issue was put on hold. So during the priority session in July you will have the opportunity to revisit this topic, along with any other new issues that you have identified or will identify.

Finally, the cross-cutting issues of access, public awareness, and genetic exceptionalism have been integrated into all of the work that we have been doing. So those have served as a foundational commonality of everything else that we have done.

Well, that took a while. Quite frankly, I'm kind of proud that it took a while. This is one heck of a Committee.

[Applause.]

DR. TUCKSON: I think you all understand that you all are not lazy. The staff is definitely not lazy.

We have a legacy of work here. I'm also thinking, though, that it is absolutely time and appropriate to revisit where we are now with this template. As we, I think, are at a nice transition point by tomorrow, not only do we have a new leader but also so many wonderful new voices on the Committee, it is a real nice time to take stock of everything that we have done, where we are in the middle, and then figure out where do we need to be to continue to be relevant for the future. So I'm excited.

Now we are going to turn to Sarah about a

reminder about ethics rules.

Let me say that I sometimes, in addition to being light-hearted about mangling names -- "Guvernot" --

[Laughter.]

DR. TUCKSON: I actually can do it when I want to.

I also sometimes sort of joke about the theologic tone of what we want Sarah to do when it comes to the conflict thing. Today I'm going to be, actually, very serious and somber about it because I'm emphasizing two things in today's meeting. Number one is, again, the absolute sacrosanctness of the public comment process and getting that input. Secondly is a meticulousness that we always have had and will continue to have around conflict of interest.

I think this is very important, so this time I'm not going to actually tease Sarah about this because I really do want to bring a certain gravitasse to her comments. Sarah.

MS. CARR: Thank you, Reed. As you all know, you are special government employees when you serve on this Committee. As such, you have to follow the rules

that apply to regular government employees. I'm going to highlight two of those rules today, the rule about conflicts of interest, and because we are so close to the Capitol, the rule about lobbying.

Conflicts of interest. Before every meeting you provide us with information about your personal, professional, and financial interests. This is information that we use to determine whether you have any real, potential, or apparent conflicts of interest that could compromise your ability to be objective in giving advice during Committee meetings.

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

In addition, we have provided each of you with a list of your financial interests and covered relationships that would pose a conflict for you if they became a focal point of Committee deliberations. If this

happens, we ask you to recuse yourself from the discussion and leave the room.

Government employees are also prohibited from lobbying, and thus we may not lobby, not as individuals or as a Committee. If you lobby in your professional capacity or as a private citizen, it is important that you keep that activity separate from activities associated with this Committee. Just keep in mind that we are advisory to the Secretary of Health and Human Services. We don't advise the Congress.

As always, I thank you for being so attentive to the rules of conduct. Thank you.

DR. TUCKSON: Thank you very much, Sarah. Again, I think the hallmark word of everything that this Committee has been about and will continue to be about is transparency. This is all extremely transparent, and we actually will keep to that.

All right. Now, ahead of schedule. I'm warning our public comment people that if you know anybody that thought they were on at 9:15, they are on now. So if somebody ran out of the room, come back.

One of our critical functions is to serve as a

public forum for the deliberations on the broad range of human health and societal issues raised by the development and use of genetic technologies, so we greatly value the input we receive from the public. We set aside time each day of our meeting to hear from members of the public, and we welcome and appreciate the views they share with us.

In the interest, of course, of our full schedule, we ask the commenters to, as always, please keep remarks to five minutes. We have copies of your full statements, which will be made a part of the meeting record.

In a few moments, as I indicated, we will be addressing the oversight recommendations in depth. Prior to this meeting, we requested that those who have comments on oversight speak to the Committee today so that we can keep these comments in mind during our discussion.

Some of our commentators, unfortunately, were unavailable today and they will be speaking to us tomorrow, but we are really pleased that we have several folk who have made it their business to travel here today

to give us their input. So we are very pleased.

Let me invite to the microphone Paul Radensky from the Coalition for 21st Century Medicine. As Paul comes up, just so we don't have a loss in terms of travel time, if Jeff Kant from the College of American Pathologists is here, Jeff, why don't you come on up as well. Then we will just start to shuttle people in. Thank you very much.

Paul, we appreciate your being here. Please give us your comments.

PUBLIC COMMENTS

Comments by Dr. Paul Radensky

Coalition for 21st Century Medicine

DR. RADENSKY: Good morning. Thank you all. Can you all hear me okay? My name is Paul Radensky. I am with McDermott, Will & Emory, and McDermott, Will & Emory serves as counsel to the Coalition for 21st Century Medicine as well as counsel to a number of the laboratories that are members of the Coalition for 21st Century Medicine.

The Coalition was formed a little over a year ago in response to two draft guidances issued by the FDA,

one related to the in vitro diagnostic multivariate index assay and the other for analyte-specific reagents as an FAQ document.

The Coalition formed including both laboratories that develop laboratory-developed tests in that area as well as manufacturers of analyte-specific reagents to address concerns that both groups had with the content of those two draft guidances.

But the purpose of the Coalition was not to say "This doesn't work" or "Nothing works. You have to stop these." The purpose was to develop workable solutions that would support public health concerns about appropriate oversight for these technologies as well as provide incentives to continue developing in this area.

We submitted fairly substantial, detailed comments to the record in response to the draft oversight report that came out in November, and those comments were submitted in late December. I'm not going to repeat the 15 pages. We tried to be constructive and to respond specifically to every recommendation, particularly in the chapters dealing with clinical validity, clinical utility, and decision support systems.

What I want to focus on today is something that we appended to our comments, which was a proposal in response to the IVDMIA draft guidance that we submitted to the docket that the FDA has on that draft guidance. I want to explain a little bit about that proposal, how it came about, and very high level, what our objectives were in putting that together and why we believe that it is useful for the Committee to consider that in the recommendations for the final report to the Secretary.

We identified in the draft guidances, both the September 2006 and the July 2007, a number of concerns that stakeholders had, both that we had and submitted to the record as well as those that were submitted by others in the March deadline and then the August through October deadline for the second draft. We also were very aware and had a number of discussions with folks at FDA about their concerns.

The concerns that we identified were, one, transparency, a concern about advanced diagnostics having inherent in them algorithms, equations, and interpretation functions that were different from past diagnostics that folks wanted to understand better and

viewed at some level as a black box. So we wanted to address that transparency concern.

There was also the concern of the fox guarding the henhouse. If you have the laboratories saying this is what our tests do, is there some independent reviewer. Is CLIA sufficient; is FDA the right way to address that.

Third was a risk-based regulation looking at a framework that is not technology-based but more risk-based.

Also, looking for clear definitions. There were lots of concerns about the definition in both the first and second draft guidances and a concern that essentially the definitions of IVDMIA in both draft guidances were inherently subjective, looking at what physicians could interpret, what are standard functions, things that would lead to a lot of confusion by the regulated community.

Looking for clear and predictable pathways. What will be required. What does the science need to look like in order to get various types of claims for these assays.

A transition timeline, because we are talking about laboratories that have been regulated by CLIA, not medical device manufacturers. If they assume those new roles, it will take time for them to adapt to those new roles.

Lastly, needing to have continued incentives toward innovation. The diagnostic life cycle is a short life cycle. If you require substantial amounts of data and substantial timelines for follow-up, by the time you finish the studies you will have new diagnostics already in place and the ones you study will no longer be relevant.

So with those principles in mind, we came up with a proposal. We were encouraged to start with first principles by representatives from PCAST and representatives from the Department, saying rather than simply respond to what you saw, come up with a proposal about what you think would be the right approach.

So we came up with a two-phased approach, saying at the beginning we don't know the number of tests we are talking about. We have heard some say that it is just a few. We have seen others where we have been able

to identify a couple of hundred. We don't know. We don't know what the intended use claims are of these types of tests. We don't know the risks related to those. We don't know what the current state of the art is in terms of the science to look at these.

So our view is that in phase one, very much as the draft report proposed, as others like the Genetic and Public Policy Center, Senator Kennedy's bill, ACLA, have all proposed, a registry to try and get information about what are we talking about, how many tasks, what do they look like, what type of data do we have.

Based on that, our proposal is that that registry would be publicly available to provide transparency and would have a role for FDA to review and comment on those claims. So we would have the truthfulness and we would have an independent review of the validity of the data to support the claims.

DR. TUCKSON: Great.

DR. RADENSKY: We propose three to five years because it takes at least a three-year period to get a year's worth of data. If you want three years' worth of data, it is going to take about five years. From that,

an experience-based and an evidence-based framework for regulation could evolve.

DR. TUCKSON: Thank you.

DR. RADENSKY: That would be one that over time would have an appropriate risk-based framework. We would encourage the Advisory Committee to look carefully at the proposal and to consider that in your final recommendation. We believe it is the best way to gain evidence for what appropriate oversight should be rather than simply to guess about what appropriate oversight should be.

DR. TUCKSON: Thank you, Paul. You have made that point very well, and we appreciate it.

DR. RADENSKY: Thank you.

DR. TUCKSON: Message heard. Just to make sure, is there any need for clarification? He has been pretty articulate about it.

[No response.]

DR. TUCKSON: We have a very good sense of what your recommendation is. Thank you very much.

As Jeff Kant from the American College of Pathologists comes up, can I ask David Mongillo from the

American Clinical Lab Association to come forward as well?

Jeffrey, thank you for joining us.

Comments by Dr. Jeffrey Kant

American College of Pathologists

DR. KANT: Good morning. My name is Dr. Jeffrey Kant. I am professor of pathology and human genetics and director of the Division of Molecular Diagnostics at the University of Pittsburgh Medical Center. I am here today on behalf of the College of American Pathologists, also known as CAP, where I chair a resource committee that oversees proficiency testing programs in genetics. We are following up on written testimony the College has provided to SACGHS on its report, U.S. System of Oversight of Genetic Testing, A Response to the Charge of the Secretary of HHS.

I have modified my remarks slightly and omitted the summary statement in your written to keep to the time limits.

CAP is a national medical specialty society representing more than 17,000 pathologists who practice anatomic pathology and laboratory medicine in

laboratories worldwide. The College's Commission on Laboratory Accreditation accredits more than 6,000 laboratories here and abroad. Our members have extensive expertise providing and directing laboratory services and participate as peer inspectors in the laboratory accreditation program.

The College has been a leader in developing quality improvement programs for laboratories, including programs in genetic testing.

Laboratorians have some of the strongest measures of quality in medical practice. The College's experience from its proficiency testing and laboratory accreditation program is that the overwhelming majority of mainstream genetic tests performed in the U.S. are safe and effective.

As noted in the report, performance on multiple CAP molecular genetic surveys for analytic and interpretive accuracy has been excellent over a wide range of methodologies.

Of note, the performance of laboratory tests on our proficiency services is equivalent to assays that are FDA-approved for the same analyte. This is due in part

to the robust nature of the analytes, along with rigorous attention to CLIA quality standards and practices, as well as medical oversight of every clinical laboratory by a physician.

The College's laboratory accreditation program stresses both analytic and clinical validation prior to introducing any test into practice, recognizing that tests will continue to be periodically improved after introduction, with each improvement revalidated by the laboratory before you send patient samples.

As medical specialists in the diagnosis of disease, the development and oversight of genetic tests constitutes an important and expanding aspect of medical practice to pathologists. We therefore have a keen interest in ensuring that our ability to provide high quality diagnostic services to patients and other physicians is not comprised by overly burdensome regulation. We recommend that changes to federal oversight of laboratory tests be made within the context of CLIA.

CAP supports further enhancement of laboratory testing through educational efforts, improvement in the

quality of CLIA inspections, and additional federal resources for access to controls and standards.

The College agrees that appropriate resources be directed to CMS for required oversight of CLIA and supports SACGHS recommendations for expansion of proficiency testing.

Please consider that CLIA already requires assessment of analytic validity for all assays offered by a laboratory regardless of whether these tests are regulated analyte. We are aware of no evidence that alternative assessment leads to poor quality testing.

Moreover, CLIA requires knowledge of the clinical utility of tests for use in routine clinical practice and stipulates qualifications and responsibilities of the laboratory to patients.

CAP believes that requiring FDA approval for every laboratory-developed test would result in numerous unintended consequences that would not benefit patients, to include delayed implementation of new tests, reduced innovation, increased cost, and greater limitations of access to beneficial assays. Given that high quality genetic testing is already in place, different regulatory

requirements for this group of assays do not seem necessary and, since not all laboratory-developed tests are not genetic tests, difficult to implement.

Finally, the College supports the emphasis in the draft report on public-private partnerships for assessment of laboratory-developed genetic tests. We feel that registration of genetic tests through such partnerships could have positive impacts, but that such a system should be voluntary and devised with broad stakeholder input.

CLIA already requires submission of test lists by laboratories as a condition of inspection. Thus, additional information submitted should remain within the context of CLIA and CMS. New mechanisms for the collection of information should be tested before implementation to assure that the most useful information has been captured and that submission is not overly burdensome for laboratories.

This information could then be made publicly available, assuring clinicians and patients of the analytic and clinical validity of tests they are ordering while not impeding the medical practice of the College.

Thank you.

DR. TUCKSON: Thank you very much, Jeffrey. Any inquiry of Jeffrey's comments? Yes, Muin.

DR. KHOURY: Did I hear you say that CLIA requires evidence of clinical utility? Or maybe I wasn't paying too much attention.

DR. KANT: We interpret the requirement for the medical director oversight of the laboratory in well-run laboratories to incorporate that. Certainly that is part of our accreditation inspection process.

DR. TUCKSON: Thank you very much, Jeffrey. Yes, one more question.

DR. FERREIRA-GONZALEZ: Yes, Jeff. Thank you so much for that comment. You have mentioned in your letter that FDA review of all the laboratories tests in CAP have a significant impact. I was wondering if you could further elaborate, as the director of a laboratory, what is, for example, the impact of having to follow quality regulation systems or additional inspections by the FDA on top of what currently you have to go through.

DR. KANT: I think it would be primarily in the additional time required to generate the supporting

documentation and to host the inspections. Many laboratories, as you well know, a great deal of that work is done by the laboratory director him- or herself, and that is clearly less time you have to focus on developing tests and interpreting tests.

DR. TUCKSON: Great. Thank you again. As David Mongillo comes forward from the American Clinical Laboratory Association, Suzanne Feetham from the American Academy of Nursing, you can come forward. Thanks. David.

Comments by David Mongillo

American Clinical Laboratory Association

MR. MONGILLO: Thank you, Dr. Tuckson. I have had the pleasure of presenting comments to the Committee more than once, and I have always felt welcome. I know that the ACLA members have always felt that the comments have been well received and given full consideration. We recognize to a large degree that is because of the leadership of Dr. Tuckson. So we really thank you for your tenure and appreciate the fact that you have made us feel welcome and the full consideration.

Now the comments. As the Committee discusses

the final report recommendations to the Secretary, we want you to focus your attention on one particularly important recommendation that, if not carefully communicated to the Secretary, could have unintended consequences. Namely, the recommendation in Chapter 4, Recommendation No. 4, which references the debate about the FDA's role in regulating laboratory-developed tests.

That recommendation as currently written states that SACGHS supports FDA regulation of LDTs and the flexible, risk-based approach the Agency is taking to prioritize laboratory-developed tests, an approach that should be robust enough to accommodate new genetic testing technologies and methodology.

ACLA applauds SACGHS in recognizing the need for a flexible, risk-based approach to genetic test oversight and the important role of laboratory-developed tests to keep pace with the rapid developments in this area. However, if the above recommendation is interpreted to mean that FDA's Food, Drug, and Cosmetic Act requirement should be applied to laboratory-developed tests without interagency coordination, needless redundancies and duplications will result.

Let me be more specific. Although there are many similarities between FDA's and CLIA's quality validation procedures, there are clear redundancies and duplications that, if not coordinated, harmonized, and streamlined, will stifle innovation in this area. These include separate inspections, separate quality system requirements, separate reporting and labeling requirements, and additional requirements for design control, corrective action, and prevention.

That is not to say that FDA does not have an extremely important role in this oversight or that any of these requirements are not important, but it is premature for SACGHS to definitively support FDA regulation of LDTs without recognizing the important first step of interagency coordination and requirement harmonization.

Further, the recommendation as written is inconsistent with the rest of the report's clear and overarching guidance to HHS to, and quoting from the draft report, "to enhance interagency coordination so that the agencies with regulatory roles, CMS and FDA, are working synergistically with one another, with other regulatory agencies, and with knowledge generation

agencies."

ACLA firmly agrees that interagency coordination is fundamental to ensure that oversight is least burdensome and does not place unnecessary or duplicative regulation on clinical laboratories providing genetic test services.

ACLA and others have proposed regulatory models that build on this interagency coordination, are consistent with principles of least burdensome regulation, fill the regulatory gaps, avoid overlapping and potentially conflicting regulatory oversight, and allow for a participatory approach that draws on the expertise of industry stakeholders, CMS, and FDA. By invoking public-private partnerships, these models avoid significant new costs for the agencies.

I have provided in the copy of my comments a graphic representation of ACLA's models. We do believe it fills the gaps, it does it in the least burdensome way, it is mindful of limited agency resources, it allows for full public transparency, and really does build on its interagency coordination.

What we are asking is that you take another

look at that recommendation and revise it. We have given specifics, and I will read the change that we would like you to consider. The recommendation would read, "SACGHS supports," adding the words, "an interagency role for FDA," and adding the words, "CMS's regulation of LDTs." The rest of the recommendation would stand.

Very much appreciate the opportunity. Thank you.

DR. TUCKSON: Thank you very much. Let me just take any questions there. I really like the specificity of the comment. He is not playing around.

[Laughter.]

[No response.]

DR. TUCKSON: That's fine. Thank you so much, David. As Suzanne comes forward, let me ask Peter Lurie from the Public Citizens Health Research Group if he might come forward. And, Suzanne from the American Academy of Nursing.

DR. FEETHAM: Thank you.

DR. TUCKSON: Thank you, and welcome back.

Comments by Suzanne Feetham

American Academy of Nursing

DR. FEETHAM: Thank you. Delighted to be here. Thank you for the opportunity to speak with you. You have a written statement that will provide more information than I will present at this time.

The American Academy of Nursing and the Genetic Healthcare Expert Panel of the Academy appreciate this opportunity to comment on the SACGHS draft report. We commend you comprehensive work and recognize that this is still a work in progress.

The American Academy of Nursing comprises more than 1,500 top nursing leaders and is constituted to anticipate national and international trends in health care and address resulting issues of health care knowledge and policy.

The genetics and genomics is obviously one of the most significant trends impacting health care, the public, and all health professionals. The integration of genetic and genomic technologies in the clinical arenas is unprecedented in its implications for health care.

The Academy commends the Committee on its

efforts to assess the systems of oversight and regulation of genetic tests and for recognizing that the benefit of this burgeoning technology is dependent on establishing the analytical and clinical validity of every test. We provide the following considerations.

The Academy is concerned about the decision of CMS not to create a genetic testing specialty and associated proficiency testing, a reversal in the previous position. We strongly support establishing a genetic testing specialty and associated proficiency testing for all laboratories performing genetic tests.

We encourage that you strongly recommend that CMS take action to establish a minimum degree of quality required of any laboratory performing genetic tests and that further study on the issue of performance assessment should be executed while instituting genetic-specific proficiency testing.

The Academy commends the Committee for recognizing the need for interagency coordination in the oversight and regulation of laboratory-developed tests and strongly supports the need to convene the relevant agencies to make recommendations on further regulation of

genetic tests, an effort that should not delay instituting the genetic-specific proficiency testing.

We concur with your recognition that there are deficiencies in the genetic and genomic knowledge of all healthcare professionals. We are concerned that the Committee has not recommended that the HHS allocate resources to address these knowledge deficiencies. In today's fiscal climate, education efforts will be extremely hampered by the lack of funding to develop and implement innovative education strategies. We will propose a different strategy.

The Academy recommends an adjustment in the education strategies for all healthcare providers to one that focuses on system and practice change. There needs to be a shift from the traditional education approaches in schools and CE to one supporting the embedding of genetic and genomic knowledge into practice. Evidence of this knowledge being embedded into practice should be a component of every patient record for hospital and institution accreditation.

For example, education could include that the family history and patient family education materials

address genetics. A successful model of this recommendation is the interdisciplinary program for integration of genomics into practice at the Mayo Clinic in Rochester.

When there is evidence of the application of genetics and genomics in practice, regulators will be influenced to include the expectation of this knowledge for all healthcare providers in licensing and accreditation.

To facilitate the shift of the education focus to practice, SACGHS may want to invite the representatives of accrediting bodies such as the Joint Commission and Health Facilities Accreditation Program to a meeting of the Committee to demonstrate the significance of the application of this knowledge to practice.

The Committee's recommendations on communication and clinical support will not be realized without the key foundation of an adequate healthcare practitioner knowledge base. We know that the Committee has noted that the number of healthcare providers with genetic expertise is not sufficient or adequately

prepared to support best genetic test practices in the absence of clinically competent practitioners.

Many clinically available tests are supported by practitioners other than genetic experts, and an example is Oncotype DX, a multiple-gene assay performed on early stage breast cancer tumors where standards of practice for utilization support lie in the domain of the oncology specialist. This genetics test is just one of a number of tests that illustrate these implications and applications of practice beyond the genetic expert. This further supports the need for the education of all health professionals.

In summary, to reach the potential benefits to the public health, all genetic tests must be adequately regulated to assure minimum quality, and healthcare providers must be prepared to incorporate these tests into their practice.

The Academy is poised to engage our fellows and other key stakeholders to develop an interdisciplinary initiative to increase the competency of healthcare professionals in genetics and genomics as well as develop the standards and practices that assure the highest

levels of health care to all.

I will be happy to respond to any questions.

DR. TUCKSON: Good. Thank you so much. By the way, I just want to make note [of] not only the relevance of your comments for this report we are about to chat about but also on the Taskforce for Training and Education.

Barbara is not here with us today because of a pressing emergency, but I think, Joe, you are on that committee as well. If you will make sure, also, that those comments are delivered into that other process, I would much appreciate it. [They have] another mechanism for dealing with it and you have been pretty explicit, so we will make sure that this gets in to that committee.

Marc.

DR. WILLIAMS: I just wanted to speak specifically to that point, also being on that Education Taskforce. I will certainly take your comments to heart there.

Recognizing that we are focusing on the Oversight Report here, I just wanted to get your sign-off, if you will, that if your sense is that our devoting

an entire taskforce to this educational issue is sufficient that we could leave the education recommendation alone here. Otherwise I think we are just trying to make this report all things to all people, and I just don't see that that ultimately will serve our best interests.

So I would just like to get your perspective if that is an appropriate way to proceed rather than trying to modify the recommendation as it currently stands.

DR. FEETHAM: We recognize that, and part of it is, obviously, the interdependence of all of these recommendations and that the knowledge is inherent in the issues on genetic testing and the validity and reliability of those tests.

DR. WILLIAMS: In our revised recommendation for the report, we specifically articulate the fact that there is a taskforce of SACGHS that is devoted to education. So we are attempting to do that.

DR. TUCKSON: Great. Thank you so much. Very well done.

As Peter Lurie comes forward from Public Citizens Health Research Group, let me invite Mark Sobel

from the Association of Pathology Chairs to also come forward. Peter, thanks.

Comments by Dr. Peter Lurie

Public Citizens Health Research Group

DR. LURIE: Good morning. I'm Peter Lurie, a physician with the Health Research Group of Public Citizens. We are an advocacy group here in Washington. My conflict of interest statement is that we take no money from either government or industry.

I want to talk from the patient perspective and make clear that from the patient perspective there is no distinction whatsoever between a genetic test or any other kind of laboratory test that they might undergo. They don't understand the regulatory framework behind a genetic test or a laboratory-developed test. They just get a blood test or a cheek swab. They assume that the amount of regulatory oversight that is associated with both of those tests is equal.

The fact is that we have a form, to use your phrase, of genetic exceptionalism taking place whereby the vast majority of genetic tests are indeed barely regulated, whereas the vast majority of other tests fall

under the FDA. So indeed there is genetic exceptionalism, and I think very few patients, if any, will understand that. I think that we owe patients that amount of equality and of comprehensiveness in oversight.

Indeed the report itself seems to reach a similar conclusion. "Genetic tests and the laboratories performing them should be expected to meet the same high standards of accuracy, validity, and utility to which other medical information is subject, and that is decidedly not the case here. I don't think that the taskforce's current recommendations will do much to rectify the situation.

Part of the problem is that the voices of consumers have not really come before this Committee or the taskforce to a significant degree, despite what Dr. Tuckson describes as assiduous efforts to reach them, except for a consultant pathologist whom I don't know much about. All 33 members of the taskforce come from government, academia, or industry, and the vast majority of comments that have been submitted to the record, of the 64, only two of those are coming from consumer or advocacy groups.

Despite that, however, it is notable that these primarily professional groups and even groups with a financial interest in the outcome of this report primarily disagreed with the thrust of the taskforce's recommendations. Let me go through three of those recommendations in turn.

The first of those is with respect to CLIA. As throughout this report, the taskforce does an excellent job of diagnosing what ails the system. It concludes that assuring the analytical validity of genetic testing is paramount, and it goes on to identify a litany of problems with the current situation. However, despite the rigorous documentation of the centrality of PT and the limits of current CMS oversight, the draft report provides no rationale whatsoever for failing to endorse a genetic testing specialty. Moreover, as the report itself acknowledges, this is contrary to congressional intent, which is to generally require PT for all laboratories for all clinical tests, no exceptions for genetics.

So we would like to see a much stronger endorsement of PT. If it takes a genetic specialty in

order to make that happen, this taskforce should be endorsing just that.

With respect to FDA regulation, the problem is similar. Again, a ringing endorsement of the importance of clinical validity of genetic testing, described again as paramount, but yet despite the well-documented reasons for expanding FDA regulations and again the problems with current FDA oversight, the draft report simply endorses status quo. It seems to endorse the FDA's efforts with regard to the IVDMIA, and as important an effort as that is, it really is a baby step in terms of reaching the literally 1,200 or more genetic tests that are currently available.

As in its justification for its failure to endorse a genetic testing specialty, the draft report provides only the most meager of explanations for its failure to recommend vigorous FDA oversight.

It talks about the backlog, which you do come to have after ignoring two prior reports from committees rather similar to this one dating back a decade. If you don't implement those recommendations, which recommended more FDA oversight as well as more CMS oversight, you do

develop a backlog over time.

In fact, even at FDA there is a good example of the ability to clear a backlog. It is called the DESI process, in which drugs on the market prior to 1962 but after 1938 were reviewed. Thousands of drugs. Those that were ineffective were taken off the market. So FDA has an ability to do such a thing.

If there is a problem of lack of resources, well, then this Committee is better placed than anybody to be able to recommend an increase in resources rather than to just sort of surrender to that problem. You should be advocating for that if you think it is important enough.

Finally, a concern that new technologies would be delayed. We often hear those kinds of concerns, but no one really provides any data to back that up exactly. What about the dangers, though, of allowing unregulated products in the market? What about people who have abortions that they shouldn't be having? What about people who don't undergo a particular course of therapy that they should, or do when they shouldn't? That must be considered as part of the calculus as well.

The third main element I think in the report has to do with the registry. As the report acknowledges clearly, no one knows the number and identity of currently available genetic tests. This is an unacceptable situation in this country after these tests have been available as long as they have.

But, what is recommended? The creation of a voluntary registry for a trial five-year period. We already have a voluntary system. We have had it for 14 years. It is called gene tests, and the very deficiencies that we currently have in understanding what tests are available are deficiencies in the voluntary system. So, how can it be logical that the recommendation be more of the same?

Indeed that is the overall problem with the taskforce's report. It does an excellent job of identifying the problems. It lays them out clearly. But when it comes to following its own recommendations to their logical conclusion, it falls short and simply endorses the status quo. Thank you.

DR. TUCKSON: All right. Thank you very much. I appreciate your comments, and you can be sure that we

will be wrestling with each of those as we go forward in a very meticulous way.

Does anybody have any questions to ask at this point? Yes.

DR. TELFAIR: Yes. Thank you very much for your comments. I just have a question in regard to something that is always a challenge, particularly with this type of effort. One of the clear challenges that you had, and I will make it as a challenge, was the point about the actual diversity of the comments themselves and where they actually came from.

The challenge is always getting consumer input and consumer involvement with this. I know that every effort is made to do that. Maybe as a parting comment from you, what would you have suggested have been done to get more of the type of consumer that you think should have had comment into this? Knowing that a lot of effort was put into that.

DR. LURIE: Let me just briefly point out, of course our comments are part of the record. Whereas you point out that there is a diversity of comments, there is some, but as I think Dr. Fomous will agree in her summary

of these, the majority of people take a position certainly in favor of a genetic testing specialty, and most as well take a position in favor of some FDA regulation.

I did hear about this report and that it was available for comment via somebody else who sat on the taskforce. Nobody approached me or suggested to me that we might testify before this Committee despite the fact that we had filed the petition with CMS asking for the creation of a genetic testing specialty. I mean, if any consumer group was in play to be invited, it was us, and I only heard about it indirectly.

There are a number of consumer groups in this town who may be interested enough to testify. I can't be certain. I could have led you to them. Somebody might be able to contradict me, but whatever efforts were made to reach consumer groups, they didn't reach me.

DR. TELFAIR: Actually, sir, that was not my question.

DR. LURIE: Oh, I'm sorry.

DR. TELFAIR: My question about the diversity was as to a recommendation to the Committee. This is

only one of many reports that we are going to be working on. If this continues to be a challenge, because I have heard it from a lot of people, what is your recommendation how the Committee in its future efforts can begin to engage a broad base of consumer groups and organizations that, you point out, were not engaged, including yourself. That is what my question was.

DR. LURIE: I see. In a way I feel I have answered it in the sense that I have pointed to the deficiencies, or what I see as them, with regard to this. But it is difficult, and I do appreciate that.

I think the best way to do it is to identify key informants, perhaps a group like ours or other groups like the Genetic Alliance, which has members in a large number of different organizations, and to ask them to put the word out further. Certainly there are Federal Register notices and the like, but nobody reads that. So I think you start with a key informant and you hope that you can get the word out that way.

DR. TUCKSON: Thank you. I want to move us forward, but let me be very clear. First of all, I really appreciate the specificity of your comments. They

are very helpful to our process.

I will say that the Genetic Alliance and every other major consumer organization in genetics is well aware and has been here testifying for years. It would, I think, be a matter of debate. I really don't have time to go through it all, but there is an extraordinary legacy of involvement by this Committee, and it is extremely well known throughout the genetic consumer and professional community. This Committee is no secret. Its work is well known.

We have solicited extraordinary efforts to make sure that we got [that.] You were told about it. You are here. So I would say to you that I think that what we want to take from your comment, and I really think that Joe did a terrific job in making sure, we can always do it better. I think that we will endeavor to make sure with this spur that we continue to try to do better.

But I must suggest for the record that this Committee's involvement with the genetic consumer community is extensive, long, and broad, and that I would not want to have the record not have that comment written into it.

However, I think that your comments are very helpful and we benefit from them and your presence here. We thank you.

DR. LURIE: Thank you.

DR. TUCKSON: Next comment, please, from Mark Sobel. Then I'm hoping Linda is on the phone, Linda Avey from 23 and Me. Do we have the ability to know if Linda is on the phone?

MS. AVEY: Can you hear me?

DR. TUCKSON: Oh, you are there.

MS. AVEY: Hi.

DR. TUCKSON: You are next.

MS. AVEY: Great.

DR. TUCKSON: Well, you are sometime soon.

MS. AVEY: Good. Thank you.

DR. TUCKSON: I have a wonderful list. I'm the chairman, and I'm saying you are next.

MS. AVEY: Cool. Great.

DR. TUCKSON: So, just be right there. With that, Mark Sobel is now here from the Association of Pathology Chairs.

Comments by Dr. Mark Sobel

Association of Pathology Chairs

DR. SOBEL: Good morning. I'm Dr. Mark Sobel. I'm the managing officer of the Association of Pathology Chairs. APC represents the Departments of Pathology and Laboratory Medicine in all of the accredited medical schools in the United States and Canada. We submitted a comprehensive statement in December, and we appreciate the opportunity to highlight the three most significant points in public testimony today.

Those three points are the definition of genetic testing, determining under whose authority quality assurance is best managed, and identifying the best system for test registries.

As to the definition of a genetic test, we see that SACGHS is using a very broad definition of a genetic test, going beyond heritable changes to include somatic variations, and going beyond DNA and RNA to include proteins and other analytes. Under this definition, the tests would more accurately be called molecular tests rather than genetic tests.

We believe that the document needs to define

which intended uses are included in the intended oversight of genetic testing and the Committee also needs to define the difference between genetic and genomic applications.

SACGHS seems to conclude that genetic tests, given the anticipated breadth of their use in the future, should not be considered as significantly different from other clinical tests, and the APC agrees with this perspective, which is also consistent with the approach recently taken by CMS to not establish the genetic subspecialty.

But if this is so and the Committee is opting against genetic exceptionalism, then it is unclear why genetic tests are proposed to require greater oversight than non-genetic tests that are similarly molecular, laboratory-developed, complex, and potentially high risk.

We recognize, of course, that tests for heritable diseases are unique in several respects, including the risk for misinterpretation by practitioners who are unfamiliar with the limitations of genetic risk assessment.

Nonetheless, at the technical level the

diagnosis of genetic disease by molecular methods does not differ significantly from the same techniques that are used to diagnose infectious diseases and neoplastic diseases. Therefore, it is not logical to establish more stringent technical and personnel standards for molecular genetic testing that already exists, including molecular oncology and molecular microbiology testing.

While, unfortunately, harms may occur in genetic testing, these risks are also, unfortunately, present in all areas of health care. We of course must work to minimize all of those, but we are not aware of data that demonstrates that harms from genetic testing are greater or less than from the other medical procedures that are performed or tests.

As to quality assurance and CLIA versus FDA regulations, I think, in the interest of time, my colleague Jeffrey Kant of the College of American Pathologists very adequately expressed the opinion of the APC that further regulation by the FDA in this matter would be inappropriate given the oversight that CLIA has, could be duplicative, and could indirectly have unforeseen consequences such as delaying innovation and

the appropriate amount of time used to develop new tests.

Finally, on the system for test registration, the APC heartily endorses the Committee's recommendation to develop a public-private partnership of voluntary registration of tests. CLIA already requires registration of the name and methodology of each test that is performed, but it cannot necessarily retrieve that information and the public does not necessarily have access to it. By making the information that laboratories voluntarily register with CLIA more publicly available, we feel that the public will benefit and there will be no need to establish a new registry system. Thank you.

DR. TUCKSON: Thank you very much. Boy, this is going to be fun, isn't it?

[Laughter.]

DR. TUCKSON: No matter what we do, everybody is going to be upset with us. We will not have a friend in the world when this is over.

That was extremely clear, though, and you were very clear, just as the people before you have been very clear. I just wish you all could all find someplace

where everybody could agree so we wouldn't have such a hard time. Boy, we are going to get yelled at everywhere.

Questions?

DR. KHOURY: I have a question. Do you think consumers and providers today have information on their fingertips that is available as to the analytic validity, clinical validity, and clinical utility of existing genetic tests on the market, and where would they get that from?

DR. SOBEL: No, I do not believe they have that readily available. There are various public sources of that information. There are two websites that come to mind first to me. One, in the relationship to heritable diseases and tests for those, would be the website called Gene Tests, which is run out of the University of Washington which provides information not only about the tests and its background but also has links to which laboratories provide those tests. But I think understanding the unique areas of analytic utility and clinical utility are difficult to access for most people.

The other website that I would tell you about

is the Association for Molecular Pathology's Molecular Test Directory, which is called AMPTestDirectory.org, which is a listing of tests but does not provide background information on those tests.

I think herein lies the distinction because the AMP website of tests is not heritable disease tests. They are what I would call the somatic tests. They are infectious disease tests. They are tests for disorders of the hematologic system such as leukemia and lymphomas. They are tests related to neoplasia.

So those have listings of tests and do not provide the information. Here again, it is really the purview of the practice of the laboratician. These are practicing physicians.

I think there is a lack of understanding of the testing. There is certification of the laboratory directors for all laboratory tests that require an understanding and an expertise, and that is what we are trained in, to actually understand quality control, quality assurance, as well as the test validity, the analytical validity, and the clinical utility of the tests that are ordered.

DR. TUCKSON: So, how do you respond to Peter Lurie's comments? He basically is saying that we are being exceptional by [being] inattentive to being more rigorous in our oversight. You are saying we are being exceptional by being overly oversightful.

DR. SOBEL: I guess my major point would be that, in my opinion, every single test that is performed, whether it is a glucose test, whether it is my protide for whether I am getting the right level of Coumadine on a daily basis, or whether it is for a cancer test such as is done by the onco system that was previously mentioned, or for a test for an inheritable disease condition, all require absolute, 100 percent accuracy in order for the public to be safe.

My colleagues in pathology once noted, in the days of the multi-million dollar contracts that started for baseball players, that you get a batting average of 0.333 and you get $15 million. If a pathologist misses one out of 1 million tests right, they are sued and their careers are over. People are hurt.

DR. TUCKSON: You are doing wonderful. But other than the legal system for suing them or

professionals yelling at them, I think what the question comes down to is how does the public know that that is happening? Other than the tort system, doesn't the public deserve greater? That is the point that I think people have.

DR. SOBEL: I think the public does deserve better knowledge. They need to be better educated. They need to have access to more information such as in the registry that is suggested by the SACGHS report. I think that is all part of consumerism and better knowledge.

But this really does require expertise. Somebody finally needs to have the expertise to say this is clinically valid, and that is what peer review systems are about, that is what test validation is about. This is the daily practice of the pathologist. So it is just like your internist examining you. It is exactly the same level.

DR. TUCKSON: I've got it. You are really helpful here, and I know we have to get on to the next one. I think you have made your point. Because of everything you just said, and this is a criticism that the Committee has to deal with because --

[Interruption.]

DR. TUCKSON: The dilemma you just presented us with is you just gave a compelling reason why people want us to take greater action. You have said this is complicated, the whole thing is complicated, it is a real problem. People can't possibly in their daily lives figure out or want to figure out before they do a test, let me go research 18 things. People are just trying to live their lives and assume that the tests are fine. You have just given a compelling reason why, other than this phenomenal trust. That is all you are saying we should do, is trust.

DR. SOBEL: That's true. I think systems really are in place to justify that trust. We have proficiency tests. We have quality control tests. We have inspections. The inspections very often go beyond what the regulations require.

For example, there was the question about whether CLIA required clinical utility, but actually, the CAP inspections, for example, that inspect all the laboratories, or most of the laboratories at least in the United States, require that as their criteria for passing

that inspection.

You think you are in trouble. You should hear the complaints that we on the inspection committees get for how rigid we are and how unreasonable we are about what qualifications we are requiring. We are all getting that. That is why I have trust in the system.

DR. TUCKSON: Mark, thank you so much. By the way, one reason why I have been querying you is because you are very articulate. It is a sign of respect for you.

DR. SOBEL: I appreciate it.

DR. TUCKSON: I wasn't being personally confrontational with you.

DR. SOBEL: I didn't feel that way at all.

DR. TUCKSON: Thank you. You are terrific. Thank you very much.

Linda? Did they allow you to stay?

[No response.]

DR. TUCKSON: Linda?

MS. AVEY: Hello?

DR. TUCKSON: Oh, good. Linda, you are there.

MS. AVEY: I'm sorry. I thought I just got cut

off the call.

DR. TUCKSON: No, we won't let them. We are beating them up. Linda, if you didn't know it, you are with 23 and Me.

MS. AVEY: That is correct, yes.

DR. TUCKSON: You have five minutes, and we are eager to hear you.

Comments by Linda Avey

23 and Me

MS. AVEY: Great. Thank you so much for the opportunity to address the Counsel. I will just go through our notes that hopefully people also have a copy of.

23 and Me was founded on the premise that individuals have the right to access their genetic information and learn about themselves in a new way. We believe that individuals have the right to know what their bodies are made of and that they should not have to pay for those services of a healthcare professional to find out those facts about themselves.

Consumers understand and cope with risk-based information every day, and history shows that fears about

how consumers will respond to information are usually overblown and inaccurate. People were able to handle being told that they had cancer in the '60s, that they were pregnant in the '70s, that they had HIV in the '80s, and that they may have had an increased probability of Alzheimer's in this decade, as the REVEAL studies have shown.

We think that federal and state governments as well as physicians should not impede information development and dissemination based on an old-fashioned and, frankly, paternalistic view of what ordinary people can and cannot understand or handle.

We don't plan to stop at providing information to individuals just about themselves. We are developing a way for them to engage actively with a new research effort, something we call consumer-enabled research.

We think that progress in genetic research will be greatly enhanced by the development of a large database of genetic and phenotypic information contributed voluntarily by individuals interested in getting directly involved.

I'm sorry. Can you hear me? I'm cutting out.

DR. TUCKSON: We hear you very well. Be confident. Just continue.

MS. AVEY: Great. I think instead of reading through this what I would rather do, because hopefully everybody has a copy of this?

DR. TUCKSON: Yes, we do.

MS. AVEY: What I think I would rather do is just comment on the conversation that was going on prior to this because I only have five minutes. What 23 and Me is about is really giving people access to information that will hopefully enable us to understand more about the human genome. So rather than talking about diagnostic tests, which we really don't believe we are, we are more about bringing information together about a lot of people so that we can learn more about our genomes and then transfer that information back to people.

This really isn't about genetic testing, and maybe it is not the appropriate time for us to be debating whether or not people should have access to this information because it really is not about performing a test. It is more about having this information flow back and forth. Then, as people are able to give more

information about themselves, we really hope to gather that together, share that back to the research community, and hopefully make it a benefit for everyone.

We are really not talking here about whether CLIA is applicable or FDA is applicable. We are here to say that we don't know enough information yet. This is really more about a research effort. That is really what 23 and Me is going to be focusing on.

I would be happy to take any questions that anyone might have.

DR. TUCKSON: Great. By the way, would you remind me of what 23 and Me is? I should know it, but I don't.

MS. AVEY: 23 and Me is a private-based company here in California, and we are enabling people to get access to their genetic information through the use of the research tools that are being used by laboratories across the country, and actually across the world. We use large-scale genotyping microarrays to give people this information, and then we wrap context around it to give people an idea of what is coming out of the research community so that they have a better understanding of

what these large-scale studies are turning up.

A lot of times you will see publications or stories written in the New York Times and the Wall Street Journal of these reports. Our mission is really to give people the opportunity to learn more about what this means in context of their own genomes.

We don't put it to people that this is a diagnostic test. It is more of a way to give them information that is reflective of what is coming out of the research community.

DR. TUCKSON: We have a couple real, real quick hands, and we will have to have real quick questions and answers. Paul Billings.

DR. BILLINGS: Linda, this is Paul Billings.

MS. AVEY: Hey, Paul.

DR. BILLINGS: We have been hearing this morning about how consumers can judge the quality of the testing that they are provided. Does 23 and Me have a position on that issue?

MS. AVEY: It is a really good question. What we are grappling with right now is finding the right way to provide that QC of the data back to the consumer

community because we really don't feel like CLIA is the appropriate vehicle to do that. In fact, if anything, we feel like putting a wrapper of CLIA testing around what we are doing might be disingenuous to our customers, giving them some impression that the information is clinically validated, which we really don't feel it is.

Because it is coming out of the research community, we are providing this as an educational effort, and therefore to say that this has CLIA wrapping on it really, I think, sends the wrong message.

That said, we are doing everything we can to comply with CMS and we feel like this is an opportunity to have a discussion with them beyond CLIA. Again, we don't argue with CLIA, but it is just that it sends the wrong message, we think.

DR. TUCKSON: Good. Real quick, we have Joe, Jim, and Muin, and then we will stop there. Joe, Jim, and Muin.

DR. TELFAIR: I will pass on my question because it is a little bit longer to answer. I will get it another time.

DR. TUCKSON: We are coming back to that.

Good. Jim.

DR. EVANS: This is Jim Evans. For those individuals in the room who are not familiar with the offering and haven't, for example, toured the website, I was wondering if you could just give any kind of general position on what types of SNP associations that you are providing.

For example, there is going to be an offering soon of a company that is specifically designed to look at medically oriented SNP associations. A) Do you have a particular overarching philosophy, and B) do you want to give any specific examples of the types of SNP associations that you report to the audience here?

MS. AVEY: Yes, absolutely. One of the components of our website is something called Gene Journal. We have a white paper on our website that explains the process our scientists go through before we are willing to report on any particular finding. They are mostly focusing on the common diseases that are multigenic. We are not really focusing on Mendelian disorders because those are well documented and a lot of those have already been identified and studied and there

are genetic tests that exist for those.

For example, with type II diabetes, currently there are about seven genes that have been solidly established as being associated with that disorder. So we report on those and explain to people what the different versions of the genes are and give them references back to those papers if they are interested to read. But we also break it down into everyday terms of what does this mean for an individual who doesn't have a genetic background.

DR. TUCKSON: This is fascinating. Muin, you have a quick question here?

DR. KHOURY: Yes. Linda, this is Muin Khoury. I'm from the Centers for Disease Control and Prevention. I have co-authored a piece in the New England Journal of Medicine in January about the premature readiness of these kinds of research tools being offered to the general public, but I do appreciate your comments and the fact that you are trying to educate consumers rather than selling them "a genetic test."

But, if these were genetic tests to be offered for prevention of disease or health promotion, they would

not pass the test of either analytic validity, clinical validity, and clinical utility. So as long as you appreciate that point, but it seems like you are making a distinction between an educational tool versus a tool that could be offered for health purposes. So I wanted to hear a little bit more of your perspective on this given that these are research tools and they are research in progress. What do you expect consumers to do with the information that is probably incomplete and changing as we speak?

MS. AVEY: That is a really good point. When we read the article in January, we were actually very much in agreement with it. We do feel like a lot of this information is so premature. What our mission is, really, as a company is to continue to collect information back from our customers. So we explained to them that this is only research. We point out very clearly that it has only been done in certain populations.

So if, for instance, someone is of South Asian ancestry, there might be a publication that came out but it only applies to Caucasians and maybe Asians. So the

research is very limited. What we hope to do is empower people to come back to us and tell us about themselves.

So if someone sees the markers for type II diabetes but it is only applicable to Caucasians and Africans, we can say, well, if you are South Asian, you report back to us whether or not you have type II diabetes and we will continue this research together in a very prospective way.

So we really look at the Framingham Study as a great model. What we want to do is move that concept of prospective long-term study to the Internet and into a social networking capability where people can share that information very directly and very dynamically.

DR. TUCKSON: Thank you so much. Let me, by the way, remind everybody again, if your cell phone or if your Blackberry is on, it is receiving messages and that is what that noise is.

By the way, folks, in July we have the benefit of having a special session where we will learn about companies like this. So we will have a chance to revisit it.

I am very cognizant of being the moderator and

the time, but I want to make sure that all the issues are really clearly in front of us. So let me just ask you one thing to make sure I'm hearing what you are saying.

Are you only providing information, not feedback on any aspect of a person's genetic profile? Is it just articles or information? What I think I'm hearing you say is that because you make no pretense about whether something has received any scrutiny of analytical validity, et cetera, et cetera, et cetera, that you are just providing it with information, therefore it, by definition, does not require any oversight.

So it is like a sense that, well, listen, I make no pretense as to what this information is. Here, have at it. How you choose to deal with it is up to your own intelligence as an individual, thereby avoiding any oversight whatsoever. Is that what I'm hearing you say?

MS. AVEY: No. I would say that we welcome oversight and that we are very eager to hear back from both the medical and research communities about what it is we are doing because we do want to educate people about how their genetics are impacted by the studies that

are coming out. With the caveat that it is all subject to change.

We don't even know if cholesterols now are as valid as we thought. I think the lay public is pretty used to getting information and understanding it at a certain level. As long as we present it to them properly that this is a work in progress, that this information is going to be changing in dynamics, but it is more about them feeling like they are part of the research process. Right now when you talk to most people, they don't feel like they get to have a voice in where the research is headed. I think the autism community is a good example of that.

We want people to feel like they are more a part of the process. I was in Framingham when NHLBI was there celebrating the anniversary earlier this year. It was so clear that the people that are in Framingham have a lot of sense of ownership of that process. We want to move that to the Web in a social networking way so that people have that same feeling.

But we welcome opportunities to talk to committees like you guys.

DR. TUCKSON: Let me just say there are a couple other hands here. I think that you have actually opened up an incredibly important issue here. I'm going to take a little liberty as the moderator and get two more questions in because I think that you have put something on the table that, quite frankly, has gotten my full attention.

DR. FERREIRA-GONZALEZ: Linda, I was just curious. You say that the main goal of the testing is for research purposes. I was wondering, when you provide the report back to the individual that requested the test on themselves, are you stating that these results are for research use only, clearly?

MS. AVEY: We do couch it in a way to say that this is initial information. We cite the publications. We have a vetting process where we explain how our scientists have read these papers that come out. If they don't meet the criteria that we have established, and again, those are up on our website, we explain that there are other studies that are out there.

Because our initial response back from our customers is that they actually want more information and

that they are just hungry to know more, we are going to have a way to stack up the research that is coming out and report things to people that we say, look, you have to take this with many grains of salt. We will have more of a gradation of the information.

But people just seem really eager in wanting to get this data in front of them.

DR. TUCKSON: As a last point, Joe, and we will have to close off on this and move to the next commentary. Joe.

DR. TELFAIR: Ms. Avey, it is Joseph Telfair. Thank you for your comments. I think that Dr. Tuckson indicated that groups like yourself have a chance to speak again. To me, it would be very helpful and very instructive if, when you get a chance to present again, you actually map out a case to show how you actually carry out what you do with the information.

Right now, I'm not sure. I just think for myself -- I can't speak for the rest of the group -- there is a number of integrations. You talk about the case. You talk about the process. You talk about also how you think it should go. All of that is integrated in

the responses that you are giving. It is hard to follow since we are not as familiar with your program.

So if I can make a recommendation that the next time you do have a chance that you present a case and just walk us through how you use it, what kind of questions you get, how the information itself you pull together, how you then redisseminate that information, and then what was the intent of that session.

I think that that would be really helpful to us because what it sounds like you do is a good thing. It is just that it is hard to decipher because there is a lot there that you are speaking about.

MS. AVEY: Absolutely. We would be happy to come and give a demo. I think that is the most powerful thing we can do, is show you exactly what it is our customers see and the information that they are receiving.

DR. TUCKSON: Thank you, Linda. Any information you have, send it to the Committee about what you all are doing and examples. I think we would benefit from that. Thank you for taking the time to be by phone and answering our questions. Take care.

MS. AVEY: Thank you so much. I appreciate it.

DR. TUCKSON: Great. Mike Watson, who is well known to this Committee from the American College of Medical Genetics, will come up, and then Emma Kurnat-Thoma? Come on up. Michael will take the floor.

Comments by Michael Watson, Ph.D.

American College of Medical Genetics

DR. WATSON: Thank you very much for allowing me to make some brief comments here today. I represent the American College of Medical Genetics, an organization, unlike many of the laboratory organizations, that bridges both laboratory testing and clinicians who deliver genetic tests to the population. For the most part, I'm going to focus on the heritable disease side of genetic testing today.

I co-chaired the Taskforce on Genetic Testing back in 1995. I'm not certain we have made tremendous amounts of progress since then. Realizing that this is Reed's last meeting, I'm hoping he doesn't get that same funny feeling in 10 years.

DR. TUCKSON: Well, it was the firm foundation you established, sir, that got us here.

DR. WATSON: Well, I didn't do it to spawn advisory committees. I was hoping we would make a lot more progress over the years than we have. But there are some concrete things I think we can do, and I think we need to look very carefully at why the progress that we have hoped for hasn't been made. I think there are some fundamental aspects of genetic testing that get at why we really haven't been able to make some of the progress we had hoped to have made.

Genetic testing is actually highly complex. It is enormously diverse, so not any one group is really well placed to deal with all of genetic testing. And, there are a huge number of tests. We have recently had the entire gene test library transferred to us in the interest of a project we are working on to develop an analysis to see what it would take to lay down the clinical validity of every genetic test currently in gene tests.

People often talk about there being 1,000 or so genetic tests available. That is so far off the mark it is stunning. There are maybe 1,000 genes that we do tests in, and that is very much the way gene tests are

designed, is around the genes on which we focus. From an analytical perspective, I think you can say maybe that we do 1,000 genes' worth of testing.

But from a clinical validity perspective, the problem is one of why we do tests, the intended use of the test. Every single one of our tests can be broken down into a much larger number. When we do diagnostics, we may do directed mutation testing. We may do sequencing that gives us a very much different kind of information and has very different calculations around how one demonstrates clinical validity.

I think that is one of the fundamental problems. The other is that, of the 4- to 5,000 tests that we, roughly, have calculated being present among those in gene tests, the vast majority are for rare diseases. That is another problem that has been very difficult for us to get a handle on.

Manufacturers have not come into the marketplace and done the kinds of studies that are often done when devices are developed because there is no financial incentive in the marketplace to invest in the development of those rare disease tests. It left it to

the laboratories to develop them themselves if they wanted them to be accessible to their patient population.

That has made it very difficult because laboratories in general aren't in a strong position nor well enough resourced to lay out the guidelines and the clinical validity at a general level for the population. They do it specific to the test they offer in their laboratory, and there is tremendous diversity around those tests that are offered, both analytically and clinically.

There is also a lot of variation between different populations -- we have heard it alluded to already -- that makes it much more complex than many areas of genetic testing, like infectious disease. It doesn't suffer from huge variations among one population of Asians versus Caucasians. That does lead to us being very often in a clinical practice of medicine position of interpreting what these sequence variations actually mean.

That is very, very difficult from a regulatory perspective. Lots and lots of rare and private variation that is unique to a family or an individual in the world

that is not easy to regulate. Therefore, we have become convinced that probably the best way to get at this is the public-private partnership.

The registry is a nice idea, but I think it needs to be a bit more deep than a listing of what people are selling in their laboratories around the country.

As we look at the three primary parameters, the first one, analytical validity, CLIA should be able to manage that. It is very difficult to get at otherwise because most of the variation in the analytical performance of a genetic test is at the local level, in the laboratory.

Inspection is the thing that gets it. Proficiency testing is the thing that gets it. I don't think an FDA rule on the analytical side of laboratory-developed tests will help much. It has a very powerful benefit on the manufacturer test side, but I don't think it translates directly to the clinical laboratory environment.

When you think about what people want, the public wants accessible tests that are accurate and have value to them for whatever clinical situation they are

applying that test in. To think about the value side of this, there is certainly lots more information available to the public than there was 10 years ago when we did the Taskforce on Genetic Testing work.

I think people don't really understand what they get with different regulatory models. I think one of the things that is clear from an FDA evaluation of a genetic test is they do clinical plausibility. They are not in the position really to say that a payer should pay for this test. They say yes, that test can detect this analyte and that analyte has a relationship to a disease. But they don't always say that it is X percentage of the time that this will be informative in this particular clinical situation.

So I don't know that FDA is the answer to the question. It certainly needs to be a part of the process of working through the issues of clinical validity, but I think the fact that they focus on plausibility is not what the public is really looking for. They are looking for better discriminants of what is accurate and useful for their own clinical situations.

Clinical utility is certainly valuable, but

genetic tests often don't come with the same level of statistical power that one wants in a clinical utility analysis. Clinical utility is something we all want for things that are done in large populations, significant volumes of testing. But in the rare disease world, it is difficult to get beyond the utility of an etiological diagnosis in the test itself. If you don't accept that utility, it is going to be very hard to accept that any of the tests we do for rare diseases are useful at all.

What we have been doing at the American College of Medical Genetics, as I said earlier, we requested the gene tests send us their entire library. We have built it in now to a complete Access file of every test and gene that is available in gene tests, with the first goal being to see what it takes to lay down the clinical validity for the various intended uses of those tests.

It is hard to do it at a regulatory level because even in a diagnostic setting in heritable disease genetics, you end up in a situation where the variability in a genetic disease is such that you may have a 90 percent chance when somebody has all the features of a disease that you will detect that analyte and it has

clinical value to the patient. But as you move down through what may be a very long differential diagnosis in a particular clinical situation, you arrive at less and less likely scenarios that may still be important for that particular patient.

That is what we talk about in clinical validity, and it is not something easily constrained by a regulatory perspective because certainly the regulatory perspective has lots and lots of exemptions for the practice of medicine, which is how we deal with those decreasing sort of values that might be available as one needs to go down that differential diagnostic list.

So our interest really is in forming that public-private partnership. Unlike the people at this table here, I do get to advise legislators, and I'm going to spend the rest of the day doing that. The fundamental problem, I think, in moving towards developing a registry that is not just a listing of all the tests but also information about why they are clinically valid in particular clinical situations, is [it is] going to be an expensive venture. It is going to require the participation of all interest groups to be able to

accomplish this.

So we want to figure out how to resource it. We are going to spend a fair amount of our time today trying to do that. Then, who are the participants and how do we organize it. We would be happy to work with this Committee in trying to flesh that out and bring some sensibility to it.

DR. TUCKSON: Mike, thank you very much. You have been very, very clear. I'm not going to take any questions because I think you have been so specific I think everybody on this Committee understands exactly what you are saying. Thank you. Don't leave, though, to go away from us today. You should stay around for a while.

Emma Kurnat-Thoma, who is from the International Society of Nurses in Genetics, and the last person is Michelle Schoonmaker from the Association of Molecular Pathology. I want to respect these last ones. I know we are well on the break, and so hopefully you guys will be able to hold off for just a second as we bring this to closure. But we are very pleased to give our full attention to you, Emma.

Comments by Emma Kurnat-Thoma

International Society of Nurses in Genetics

MS. KURNAT-THOMA: Thank you very much. My name is Emma Kurnat-Thoma, and I'm a registered nurse here to represent ISONG, which is the International Society of Nurses in Genetics. It is a global organization dedicated to fostering scientific and professional growth of nurses in genetics and genomics.

We congratulate the Committee's systematic efforts to examine oversight and regulation of genetic tests and test results. In that the Committee found significant gaps in oversight, we share overarching concern that system gaps could lead to public harm.

Furthermore, ISONG is hopeful that the HHS Personalized Healthcare Initiative will advance integration of genomic technologies capable of tailoring treatment and prevention strategies to individuals' genetic characteristics and needs.

Overall, ISONG supports and offers to help implement the Committee's recommendation to enhance interagency coordination of genetic testing oversight. In particular, ISONG supports development of steps to

foster resources, education, and knowledge.

In examining analytic validity, proficiency testing on clinical validity, we highlight four considerations today. Number one, we take exception with the Committee's conclusion that gaps can be identified and addressed without creation of a genetic testing oversight specialty. The absolute value on comprehensive reactions of consumers and patients to genetic tests are still largely unknown, secondary to the highly complex and unique nature of genetic tests.

Number two, ISONG is aware of gaps in the extent to which clinical validity can be generated and evaluated for genetic tests. We support the recommendation to create public resources and recognize that the American public will be best served if diverse ethnic, racial, and geographic subgroups are represented.

Number three, in reducing system gaps and improving oversight, ISONG takes exception with recommendations to establish voluntary genetic testing registration. It will not be sufficient given gaps in enforcement of existing regulations, and we support strengthened federal monitoring and enforcement.

Number four, ISONG applauds the Committee's concern regarding certain types of health-related genetic tests marketed directly to consumers and agree there is insufficient oversight of laboratories currently developing them. Given potential for misinformation and exploitation which may taint public perception of genetic testing value, ISONG supports expansion of CLIA's statutory authority.

With respect to communication decision support, nurses in genetics are acutely aware of deficiencies in stakeholder groups' genetic knowledge and agree that current strategies are inadequate to address them. We have further recommendations in the testimony for today.

We fully support HHS collaboration with relevant agencies and private parties. We support genetic expertise as essential when providing and interpreting appropriate genetic tests. As the largest body of healthcare provider, nurses have continual and close contact with patients and can intercede to prevent and/or reduce public harm that may come from direct-to-consumer genetic tests.

ISONG repeats the need for greater visible

nursing organization representation during the proposal and development of outreach, oversight, and educational efforts.

In summary, ISONG congratulates the Committee for the considerable work done to safeguard the public, and we deeply appreciate the opportunities to comment on this important document. Thank you.

DR. TUCKSON: Thank you. I think that is pretty straightforward. Thank you, and well done. Thank you.

Michelle, who is with the Association of Molecular Pathology.

I do need to let you know that, again, I am well aware of the break time, but the principle of trying to get as much public testimony in before we start grappling I think has been well served by the comments that we have been hearing just now and all of the other ones. So Sharon Terry from the Genetic Alliance it turns out is here. We are going to ask Sharon to come forward and present after Michelle, and then I think that will be our last one. But I do not want to miss the opportunity for Sharon to get her comments in.

Comments by Michelle Schoonmaker

Association of Molecular Pathology

DR. SCHOONMAKER: Good morning. Dr. Tuckson, Dr. Teutsch, and members of the Committee, I'm Michelle Schoonmaker, and I'm speaking to you as a member of the Association for Molecular Pathology. I will forego the explanation of the mission and membership of AMP since we have provided comments to the Committee on numerous occasions in the past.

Our purpose today is to summarize our previously submitted written comments on eight key points.

One, the definition of genetic tests. Under SACGHS's definition, the test would more accurately be called "molecular tests" rather than "genetic tests." We would encourage the Committee to define which intended uses are included in the intended oversight of genetic testing.

Second, are genetic tests different from other clinical laboratory tests. We recognize that tests for heritable diseases are unique in several respects. We are concerned that certain types of genetic testing

marketed directly to consumers fall outside of the current regulatory oversight of CLIA. We encourage the Committee to further explore this issue of potential harm of health-related direct-to-consumer marketed genetic testing on the public health and to state the distinction between clinical genetic testing and health-related direct-to-consumer marketed genetic testing.

Third, requirements for laboratory personnel. CLIA regulations already stipulate the responsibilities of the laboratory director and the clinical consultant. We recommend that these roles be reemphasized with regard to genetic testing. We would like to encourage the Committee to modify Recommendation No. 1B to include the recommendation that CMS work with professional organizations such as AMP to develop interpretive guidelines for their inspectors regarding the levels of expertise that are required for different kinds of genetic testing.

Fourth, the role of CMS, CLIA, and the FDA for quality assurance. AMP offers our expertise to define the molecular targets that would be regulated analytes to promote expansion of proficiency testing programs for

better oversight of direct-to-consumer marketing of clinically dubious genetic tests and to assist in the reassurance of the public and members of Congress of the quality of genetic tests.

Voluntary consensus organizations such as the CLSI created detailed practice guidelines which effectively fill many holes that some individuals believe exist in the FDA and CLIA regulatory framework. The team approach in which government, industry, and practicing clinicians work together is a viable and desirable alternative to regulation for many genetic tests and genomic tests.

Five, voluntary registration. AMP is concerned that registration of genetic tests would duplicate the information already submitted to CMS as required under CLIA. AMP strongly supports that CMS enhance the mandatory CLIA registration of non-waived laboratories by enhancing CMS's infrastructure to achieve this goal.

Six, proficiency testing. AMP supports the proficiency survey programs currently available with additional analytes as necessary. We intend to begin publishing best practices, laboratory and clinical

practice guidelines, and look forward to working with other organizations such as the CAP and ACMG to develop these guidelines.

Seven, clinical validity. We strongly favor reliance on the peer-reviewed literature, consensus statements by professional practice organizations, as well as collaborative studies by the CDC, other agencies, private investigators, and manufacturers. We also support integrated efforts to collect post-market data to meet the clinical, regulatory, and reimbursement goals.

AMP is concerned that the current Recommendation 1.4 could develop a duplicative system of oversight for laboratory-developed tests and laboratories performing these tests.

Finally, effective communication and decision support. We reiterate our commitment to participate not only in pursuing the success of this project but in translating the results of this effort for the betterment of the public's health and well being. AMP remains available to the Committee to assist with or provide additional information for your thoughtful deliberations and important work.

On behalf of AMP, I thank the Committee for your time and for listening to our concerns.

DR. TUCKSON: Thanks, Michelle. That was very, very good. Eight succinct, clearly articulated points. The key to your presentation to me is essentially with your Point No. 4, which you say again is ultimately that you will work with others to assure the Congress and others that in fact everything is okay.

I'm trying to make sure; out of all those recommendations, and I'm trying to go back and remember them all, are there any of those recommendations where you are calling for a material strengthening of existing recommendations? Or, the essential aftertaste of your presentation is things are basically okay. You guys are going to work hard in good faith to keep making sure that everybody is doing right?

DR. SCHOONMAKER: Right. We do support enhancements of CLIA where there are clearly gaps in the regulatory oversight structure, particularly for the direct-to-consumer marketed genetic tests, and agree that there may be some analytes that perhaps FDA may be able to provide additional oversight for. We do support

continuing public dialogue to identify those analytes and to identify which intended uses may also require additional oversight.

DR. TUCKSON: I think I have it pretty clearly. Thank you very much. Lastly is Sharon Terry from the Genetic Alliance.

Comments by Sharon Terry

Genetic Alliance

MS. TERRY: Thank you for the opportunity to publicly comment on your report for the oversight of genetic tests. Thank you, too, to the Taskforce for your work. It has been enormous.

I speak on behalf of the board of directors of Genetic Alliance, and I know you received our 18 pages of comments so I will not belabor them here. Almost as long as Mark's chapter.

I will call out several important concerns for us and, more importantly, move to a global view of your task and product. The first step to improving oversight of genetic testing is through enforcement of existing regulatory authority under the CLIA program and applying the available funding resources to provide for additional

personnel, consultants, training, and to provide the mandated level of transparency of CLIA labs under the current statute.

In addition, it is important to take action on the identified interim steps within the agencies' discretion and to immediately implement the necessary steps for proficiency testing enhancements for genetic testing. For example, proficiency testing expansion incentives for PT reference controls, training of inspectors, and additions to the list of regulated analytes.

Two, it is clear that the mandatory genetic test registration, including all tests across the risk continuum, is necessary to provide stakeholders with information that would greatly improve the oversight of genetic tests. Making test performance characteristics and reference information, including analytical and clinical validity, publicly available should increase confidence and improve the appropriate utilization of genetic tests.

We also believe that the registry should be housed at and managed by a federal agency such as the FDA

or NIH to offer the needed capacity and independence. It would also allow the first assessment of harms through adverse event reporting.

Three, we agree that more public resources should be committed to fill in the gaps. We support the establishment of a laboratory-oriented consortium for sharing information regarding method validation, quality control, and performance issues. We believe that any such undertaking must prioritize based on clinical need, availability of information, and appropriate resource allocation.

Four, in order to maximize benefits and minimize harms, a public-private consortium of stakeholders should be created to assess the clinical utility of genetic tests, including the establishment of evidentiary standards and increasing the number of systematic reviews.

Five, we agree with the SACGHS report's concern over FDA exerting regulatory authority over clinical decision aids.

Six, direct-to-consumer access to testing must be carefully regulated to ensure the public safety.

Seven, HHS must convene the relevant HHS agencies as well as interested stakeholders to provide further input into the development of a risk-based framework for the regulation of laboratory-developed tests. In addition, HHS must take the leadership role in coordinating the activities of the federal agencies under its auspices for the benefit of public health.

More important than these concrete recommendations, however, is the overall place of tests and testing in the integration of genetics into medicine and, further, into prevention and wellness. We recommend that HHS take a broad and enlightened view of the landscape. We are at the dawn of a new age, and innovation, development, oversight, and delivery of genetic services in a coordinated manner is critical to advancing human health.

Genetic testing is a disruptive innovation, and this is a critical time for the development of new paradigms. We must avoid applying old models and methods to new technologies. HHS can and must require that federal agencies work together with one another to achieve the best possible solutions. Human health is no

place for politics and turf battles. Excuses such as "The burden is too great" or "It is too difficult" are unacceptable in the realm of health.

We, the entire genetic testing community, have dialogued a great deal over the past year. I believe we have also achieved a great deal in understanding each other's issues. It is time now to engage each other in meaningful and landmark solutions, novel partnerships, and collaborative models.

As you deliberate over the next two days, you are representatives of the millions of individuals who are suffering, sick, and dying. Not an easy task. You must keep them before you. They are your loved ones, your neighbors, your friends. You cannot offer answers or opinions from your silos or your own self interests today or tomorrow. You must push the boundaries regardless of your company, your profession, your university or constituencies and represent what is best for the public both in this country and beyond.

Before you speak, don't think of your position but instead the greater good to be gained. Focus on the intended consequences rather than the unintended

consequences. This is not a zero-sum gain. While the status quo will be destabilized in the short term, we will all win in the long term.

Finally, it is a decade since your previous committee made important recommendations that have been left to history unimplemented. Regardless of the Secretary's response, we as a community are now further enlightened by your work and have a responsibility to one another and to the world community to strive for solutions that will release the incredible potential of biomedical research. We must all remain engaged in dialogue with one another, seeking to tell the truth and discover new pathways together.

We have a historic opportunity before us. Let us commit to measuring our responses, products, and actions against the greater good. On behalf of those who wait for treatments and therapies, thank you.

DR. TUCKSON: Thank you so much. Two quick questions, Sharon. First, remind us who the Genetic Alliance is, please?

MS. TERRY: So the Genetic Alliance is a network of many, many organizations, companies,

universities, et cetera. Primarily, our greatest group of individuals and organizations under our auspices are about 650 disease-specific organizations.

DR. TUCKSON: So these are consumers.

MS. TERRY: Yes.

DR. TUCKSON: Secondly, let's just take your seven points real quick. You have provided a terrific bridge to the break and the discussion.

As we go through your seven, in terms of the recommendations that the Committee has made so far, if we go through those seven -- I'm trying to just do the math on what you said -- are there overwhelming, profound differences with the draft, where we are now, as we go into this discussion that you all are concerned about? It sounded like a lot of them you were agreeing with where we are today, and I want to just make sure that we don't lose in the seven points some things that you are really taking the draft report to task for.

MS. TERRY: I haven't seen your current draft. I believe it is different than the draft I saw. I would say we differ in our understanding of the strength with which I believe this Committee must recommend that CLIA

be enhanced, that we really look at proficiency testing. That is really, really important, and it is not strong enough in the draft that I saw.

The second thing would be the mandatory genetic test registry across all laboratory-developed tests, that it be housed at a federal agency. I'm also very clear about that in my mind. That has become very clear. One of the first commentators here from the 21st Century Medicine Coalition talked about that. We have worked together a lot with industry, a lot with universities and thought leaders, and the mandatory registry seems to be the way to get the light on the data.

As I said last time I was here, again, if we tell our kids something is voluntary, it doesn't get done. It is really time to be responsible for that.

DR. TUCKSON: Lastly, one of the things that we keep hearing from some people who comment on over-regulation is the chilling effect on innovation, thereby decreasing access to new knowledge and new tests. As the consumer community, are you chilled by those cautions around, again, especially greater attention to CLIA and so forth? Are you concerned that in fact there could be

an unintended [impact]? You told us don't focus on the unintended, focus on the intended. Are you concerned about this potential chilling effect on innovation?

MS. TERRY: If innovation is chilled, I am concerned. I come from the rare disease community, where it is even harder to get people to innovate. I think this has to be done carefully, and that is why our work with especially the companies in the genetic testing space has been very important to open our eyes to what is needed.

I still believe that enhancing CLIA and a mandatory registry doesn't chill innovation. In fact, it begins to bring a lot of stability to the field that venture capitalists, et cetera, are looking for.

DR. TUCKSON: Thank you so much. You are terrific. What a morning.

I think that we are going to, obviously, take our break. It is 20-of. You all know I have a reputation for starting on time. Every minute being precious, we will start at five minutes to the hour.

[Break.]

DR. TUCKSON: Welcome back. I want to make a

special note and a special hello to the 32 people who are so committed to what we are doing that they are listening. Even though the video is not on live, there are 32 people listening live to the audio. You are beyond terrific, and we think you are wonderful.

You need to know that the video part is actually in a delayed broadcast so that it will be up in a couple of hours and people will be able to watch it on a time delay deal. We are told that tomorrow the live video will be up in the morning. There is a video to it, but it is just going to be time-delayed. So we are appreciative of all of that.

Now to the discussion. We have heard a lot. As we go into the discussion, it is critical that we have a lot of stakeholders who have voices in this. I thought [Sharon] was very passionate about thinking through and being balanced.

There is also this issue of the chilling effect of over-action and the harm of too much action that people have been equally passionate about. So we will work through these deliberatively. Thank God we have Andrea to lead us through it. Andrea, I will help be a

traffic cop, but the floor is yours.

SESSION ON OVERSIGHT OF GENETIC TESTING

Overview of Report, Summary of Public Comments on Draft Report, and Goals of Session

Andrea Ferreira-Gonzalez

[PowerPoint presentation.]

DR. FERREIRA-GONZALEZ: Thank you, Reed. Can everybody hear me in the back. Great.

What we are going to do now is go into an overview and the goals of the oversight session. Before we dive into specific discussions and specific recommendations, I'm going to give you a little bit of a background of when did we receive the charge and what actually occurred until the point that we are to date.

As Reed mentioned, most of the meeting is devoted to the discussion and deliberations we need to have as a full Committee on the draft recommendations that have been developed to address the Secretary's charge to us on the oversight of genetic testing.

Before we begin the process, I'm going to review our charge, the process we used to draft our report, the public comments we received on the report,

some of which were just reiterated for us, and the changes we have made to the report in light of the public comments and further deliberations.

Although I'm going to be reviewing comments that pertain to both the recommendations and the report, I want to emphasize that we won't be discussing the report at this time in great detail.

The focus of our deliberations in the next two days will be to finish with the recommendations. By the end of the session tomorrow we hope to have consensus on the recommendations and approval of their transmission to the Secretary. We will also seek the Committee's approval on principle. Keep that in mind. We just want the approval on the principle of the document. That will be further, later, edited through the month of February and then submitted at the end of April to the Secretary.

I want to take a moment to highlight the Secretary's charge, which we received at our March 2007 meeting, to remind you that our final report and recommendations should address the issues that were raised by the Secretary in the charge. It begins with a request to develop a comprehensive map of the steps

needed for evidence development and oversight of genetics and genomic tests, with the improvement of the health quality as a primary goal.

I think we need to emphasize some of these issues that we have responsive to the charge of the Secretary, and we actually have done that.

The charge also tasked the Committee to evaluate existing pathways that examine analytical validity, clinical validity, and clinical utility, attributable harms if these pathways are inadequate, and the roles and responsibilities of the relevant government agencies and private sector organizations. We were also asked to consider whether genetic tests are different from other laboratory [tests] for oversight purposes.

Additionally, the charge asked several questions about proficiency testing: communication pathways to guide the use of genetic testing and new approaches or models involving the public and private sectors to demonstrate clinical validity and develop clinical utility.

Lastly, we consider whether additional or revised government oversight would add value to our

patients.

As we received the charge from the Secretary, six members of the SACHS Committee volunteered to be part of this group. We needed a mass to be able to deal with this issue, formally called a steering committee. This steering committee actually took the lead in looking specifically at the charge and, from the charge, developing the scope of what our document was going to be.

As we looked through the charge and the scope of what we actually intended to respond to the Secretary, we started devising how this document was going to be organized and divide it, actually, into different chapters.

Ad hoc members and field experts were brought in as we started to realize the scope of the charge. We needed additional individuals with different types of expertise and also federal experts, and I have listed all of them here.

I would like to thank the steering committee and the ad hoc and federal experts that devoted a significant amount of time from their personal time to

look at these issues. We had a number of different meetings, conference calls, two face-to-face meetings in July and September, and have worked tirelessly to actually come up with the document that you see today.

We have discussed the activities of the taskforce in detail at previous meetings, so I'm not going to go into detail. What happened throughout the different times is just listed here. This slide only briefly summarizes those activities.

We began drafting sections in the report in May, and we were divided in different chapters. The reason we divided into different chapters is just to be able to tackle some of the incredible tasks that we had in front of us.

We worked very frantically through the summer and the fall, and we were able to, with a conference call with the entire SACGHS Committee, put out a draft report for comments. Those comments took place from November 5th to December 21st.

During the public comment period, we received 64 sets of comments from a range of different stakeholders. I have listed here the different

stakeholders that we have received information from. You also have a summary of these comments in Tab 3 of your briefing book.

As you can see from this slide, the majority of the comments were from professional organizations. Some of them we have already heard this morning. Twelve from industry, 11 from government agencies, five from healthcare professionals, six from advocacy organizations, four from academicians, and one from one individual.

The steering group began analysis of the comments in late December. Actually, we received the packet and we were so excited to be doing this over the holidays, but I really want to thank the whole steering committee for actually taking the time over the holidays and the entire [month of] January to go through the exhaustive review of all the public comments.

We met by conference call the first three weeks in January. Every Wednesday afternoon we had a conference call, and we discussed the public comments specifically and what changes or revisions need to be made to the recommendations and even the text.

The revised recommendations were sent to the taskforce. Again, we are getting into the taskforce to get a wider perspective from individuals that had already contributed. We had a conference call on January 23rd.

In addition, we invited taskforce members to present additional comments, and we will have a member of the taskforce actually present later today.

After that January 23rd [meeting], we actually made some changes to the recommendations, responding to some of the comments and discussions that we had with the taskforce and presented this to the whole Committee.

You will remember our conference call on January 30th. That conference call was not to start discussing the recommendations but just give you an idea where we are and for us to get a sense of where are the areas that might have some further discussions or deliberations that are needed today and tomorrow.

Although most of the comments are for edits or comments for specific sections for the report, the overall tenor of the comments was very positive. Most commenters thought that the report was responsive to the Secretary's charge and provided an excellent review of

the issues associated with the oversight of genetic testing. Commenters also recognized that the development of the report involved diverse stakeholders.

Some recurring themes that also emerged from the public comments are listed in this slide. Several commenters were concerned that the report's broad definition of genetic test may slip non-genetic testing under this report. To address this concern, actually we have made changes to the text to provide further examples of what are actually considered to be a genetic or genomic test.

Many commenters agreed with the report's stand on genetic exceptionalism. For that oversight purpose, genetic tests are not different from any laboratory test. They may defer in other ways, however, such as communication of the results to the patients or even healthcare professionals.

I think it is important to note that there was strong support for the increased proficiency testing or genetic test and development of standards and reference materials needed for proficiency testing. A large number of the commenters were very positive about these

developments.

Comments for a registry of genetic tests favor a mandatory approach, but there was no clear indication where such a registry should [be housed.] A few comments articulated preference for CMS or FDA, but in reality most of the commenters did not say anything about the registry. So those that did actually make some comments, which was not the majority, did provide different places where these registries should reside.

Commenters also had concerns about direct-to-consumer advertisers and consumer-initiated testing and agreed with the recommendation to improve enforcement of the current regulations to cover this type of testing.

In addition, there was overall agreement that enhanced oversight is needed for genetic testing. FDA's authority to regulate laboratory tests was not questioned. Its risk-based regulatory approach was affirmed, although there were some comments criticizing specifically the FDA's IVDMIA draft guidance.

Commenters recognized that there is an adequate evidence for the clinical validity of many genetic tests and the importance of adding to these two evidence bases.

Although many agree with FDA roles in assessing clinical validity, some commenters asserted and favor CMS's role in this particular issue.

In addition to addressing gaps in clinical validity, commenters also called for more evidence and analysis of clinical utility and increased education efforts to enhance genetic knowledge of healthcare providers, public health officials, consumers, regulatory officials, and actually payers.

Last but not least, before increasing oversight, commenters asked that benefits and harms to patient access and cost should be considered. I think we looked at that and modified some of our recommendations in particular to those comments to make sure that the stakeholders are part of any of the recommendations that we are putting forward.

We made some revisions to the report as a result of these public comments and further deliberations not only on the steering committee but also with the taskforce, and we added public health surveillance as a key consideration in the executive summary, added an introductory paragraph explaining transient genetic

tests, added a methodology section to explain reports development -- how did we get to the development of the report -- and also revised the definition of genetic test to include genomic tests and examples of the tests excluded from the definition. We are hoping to be a lot more clear about that.

There were also other revisions of the report where we added information about the Senate Bill 1858, added the role of the states in oversight of newborn screening, added activities of the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children to roles of federal agencies in research and development and evidence, which is located in Chapter 2 under "Knowledge Generation."

We augmented the discussions in nanotechnology to include devices using extremely small amounts of materials. We added the term "reproducibility" as a key term in Chapter 4. We updated and actually corrected information about the CAP products and PT performance. We corrected information about transport of biological materials and actually augmented the list of professional societies in Chapter 4 to make sure there are as many as

we can list. But again, we can't do an exhaustive listing of all the professional organizations.

We have also added other activities that are currently underway at ACHDGDNC and HRSA to discussions of the clinical utility of the test and patient access to genetics expertise.

We added a discussion of harms due to inadequate information about clinical utility. We corrected information about Oncotype-DX. We had actually mistakenly called it FDA-approved when it is actually a laboratory-developed test. We have updated statistics for board-certified genetics M.D.s, laboratory disciplines, and genetic counselors.

We added information about privacy concerns related to direct-to-consumer testing and advertising and commercially operated PHARs.

We added ACMG-AAP-developed ACT sheets and algorithms as examples of critical decision support tools that are currently being used for newborn screening.

The next steps. Here we go to today. As you can see, at the end of February the final recommendations and the revised draft report will be submitted to the

Secretary. Today we need to further discuss the recommendations and actually come, tomorrow afternoon, to finalize the recommendations that will be submitted to the Secretary.

We will still be receiving comments on the draft report even though we will not be discussing the draft report. We will ask you to approve it or not in principle, but the edits will be accepted until February 20th to make sure there is enough time to continue the editing of that draft report.

So, the final recommendations and revised draft report [are to be] submitted to the Office of the Secretary by February 29th. Then we will continue to work on the report over March until April 16, where we will have a final review by this entire Committee, maybe through teleconference.

April 30th [is when] the final report will be formally submitted to the Secretary.

So again, just to make sure we all understand and are on the same page, our focus is to finalize recommendations by the end of the meeting. Edits to the report content can be sent to Cathy. I think we all

[know] Cathy Fomous has been incredible in support to our efforts here.

[Applause.]

DR. FERREIRA-GONZALEZ: Before we begin our discussions of the recommendations, Cliff Goodman and his team of analysts from the Lewin Group will present a comprehensive map of oversight of genetic testing that they have prepared for us.

As you will recall, the development of a map is part of the Secretary's charge. So we want to review it with some detail this morning for two reasons. I think it will frame our discussions if we have a very good understanding of this map of oversight, and it will be a good primer for the work of reviewing the recommendations.

We want the Committee to weigh in on whether the map fulfills the charge of the Secretary. So remember to keep that in mind.

Cliff actually will be joining us from Rome. We seem to be working with the people that get to travel to very fun places and we are all here in Washington, D.C. Maybe we should ask Cliff to bring us something

back.

DR. GOODMAN: I will do my best.

DR. FERREIRA-GONZALEZ: Staff is here. They have worked tirelessly to help us develop this map for the presentation.

Cliff, welcome. Please continue with the review of the map.

Presentation of the Comprehensive Map

Clifford Goodman

[PowerPoint presentation.]

DR. GOODMAN: Thank you very much, Andrea. Can you just tell me now if this is a proper tone for my voice? Is it clear enough?

DR. TUCKSON: You are very clear.

DR. GOODMAN: I will proceed, then. You should have a title slide in front of you, Slide No. 1, which says "Comprehensive Map of Genetic Testing Oversight." We will proceed to Slide No. 2.

As you can imagine, this map can be quite complicated. What I would like to do now is present it at a very high level. You see in front of you five main sectors. As a matter of fact, if you want to extend the

analogy of a map, you can think of five main continents of genetic testing oversight.

The five main continents start out with research and development on your left. Then, in the middle are three. CLIA-exempt states, which would be New York and Washington in particular. In the center is the main CLIA pathway, and at the bottom is the FDA pathway. At the far right is the sector for availability and reimbursement. Those are the five main sectors of the map.

Am I still being heard clear enough at this point?

DR. TUCKSON: You are very clear. You are completely locked into the slides. It is as if you were in the room.

DR. GOODMAN: Thank you. Thank you, Dr. Tuckson. Let's go to Slide No. 3.

You will see now on the far left the research and development sector is highlighted. What I'm going to do now, with the help of our team, is describe each of these individual sectors of the map, these five sectors, and then we will pull them all together in the final

slide. So let's proceed to Slide No. 4 now.

This is the research and development sector. We will talk about this part of the map and I will walk you through the main parts of it. We don't have time to walk through the entire bit of it.

We will start in the upper left with "Understanding Gene-Disease Interactions," with "Basic Research," and then a cycle of prototype design and preclinical development. Coming out of pre-clinical development, we are going to do clinical testing, perhaps, of devices.

You can see towards the top where it says "Test Clinical Development." You can arrive there directly from "Pre-Clinical Development," although in some cases you may have to arrive from just below where it says "Apply for IDE." That is investigational device exemption, which may apply to certain tests and test kits and so forth. That is the permission that is needed to test a device, including some tests, not all, in people.

So that is how you arrive at the clinical development of tests. Extending to the right from where it says "Test Clinical Development," you can go directly

up to LDTs, which are laboratory-developed tests. That is one route. Now, going down from there, you will see down to "IVD/IVDMIAs." This group of course knows what those are. That route is typically, but not always, typically characteristic of test kits and test systems developed by device-makers and other companies that will manufacture these. So those are two routes for devices.

Now, you will notice, quite interestingly, where it says LDTs there is a downward-pointing arrow. That downward-pointing arrow toward IVDs and IVDMIAs reminds us that some LDTs are IVDs or IVDMIAs, and these, as you will see later, are going to be subject to FDA review as well as CLIA oversight. So it starts getting a bit complicated there, but it is important to understand, especially in light of the more recent FDA guidance on IVDMIAs. Indeed some laboratory-developed tests must be subject to oversight that way.

Now, going back toward the top where it says "LDTs," you will see that this breaks off into three main directions. One is going to be the CLIA-exempt state route. The next one is the "Available for Use" route directly. By the way, the secret that you will find out

later on is [this is] the direct route for direct-to-consumer tests, which end up bypassing a lot of this oversight. That is a gap that the Committee has noted. Then the straight CLIA regulation is that third arrow off to the right.

Now, before we leave this slide, I want to remind you of a couple other things. If you go back to where it says IVD/IVDMIAs, there is an arrow dropping down from class designation. For example, when a test kit company applies for FDA review, they will put it in as a Class 1 device, Class 2 or Class 3 device, and that goes in towards, at your lower right-hand side, application for FDA approval or clearance. FDA approval is typically for the PMA route, the pre-market approval route. Clearance is typically for the 510K route.

Before we leave this slide, notice that at the bottom we have provided a pathway for co-developed therapeutics. Co-developed therapeutics may be new drugs or perhaps biologics that may be developed in parallel to certain tests, certain genetic tests in particular. Although we are not going to dwell on the therapeutics very much at all here, we wanted to note here that there

is a place in the map for that co-development. Indeed, coming out of Phase 1, 2, or 3 trials, they too will go in for application for FDA approval as appropriate.

Before we leave this slide, I just want to remind you that you will see a double asterisk at the bottom left-hand corner of this first slide which says "Functions of FDA Quality System Regulation." You will see on this slide FDA design controls are accounted for as basic research and prototype/design. Later on you will see two other functions of FDA quality system regulation, or QSR, subsequently.

That is what we are calling the research and development sector of the map. Note towards the top something that says G2, where it says LDTs. G stands for "gaps," and in an accompanying document that I think you have perhaps in hard copy, we have a list of more than 30 gaps in genetic testing oversight, which gaps were identified by the taskforce.

For example, a very important one is the one that says "GD2." That refers to insufficient clarity about FDA role in regulating laboratory-developed tests. Of course, the report goes into that in much greater

detail, but this map shows, obviously, in very short form more than 30 gaps and that is one of the more important ones that appears on this sector.

If it is okay, Dr. Tuckson, I will move on to the next sector.

DR. TUCKSON: Please do.

DR. GOODMAN: On Slide No. 5, you will see that we have highlighted "CLIA-Exempt States" at the top center.

Let's then turn to Slide No. 6. This is the CLIA-Exempt State sector. This applies primarily to New York and Washington States. We are going to start at the left, not the lower left-hand corner but the left middle that says "CLIA-Exempt State Regulation," for example New York. We will start there. We are talking here about CLIA oversight of the laboratories themselves.

That right arrow goes into a sector that has five main sections, starting with Proficiency Testing, down to Quality Assurance, Quality Control, Personnel Standards, Reagent and Equipment Inspection. This aspect of the CLIA-exempt state regulation applies to those attributes of these laboratories.

You will note that coming out of there, towards the bottom, just below "Personnel Standards," is a right-going arrow that points to "Analytical and Clinical Validity Review." Of course, if you look at this field, you know that there are some special things about the CLIA-exempt states with regard to their examination of analytical and clinical validity review.

Then you can go upwards, where there is the function of New York lab approval of non-FDA-approved tests, which is a very important function.

Upward from that is the New York State Licensed/CLIA-exempt, and then coming out from the right of that, to the right and down, is the route for availability for clinical use.

Now, in order for these tests to be available for clinical use, they do have to pass through this New York State licensed/CLIA-exempt. That is the pathway there. As a matter of fact, if you look at the lower left-hand part of the slide that says LDTs, remember this is one of the pathways from a previous sector slide. Those LDTs progress to the right and up, and those are the ones subject to analytical and clinical validity

review that do go through the New York lab approvals, non-FDA approved tests, and therefore can be provided by these New York State licensed/CLIA exempt laboratories. That is the route.

What has to happen for the test to be available for clinical use is that it has to have come from the LDTs and then be subject to the oversight of these laboratories. Once the laboratories subject it to that, it can then provide these tests. That is what we are trying to show.

The last thing to point out in this slide, which is in the right-hand corner, is of course biennial inspection. That is another aspect of oversight in these states. If a laboratory does not do well for the biennial inspection, there are certain sanctions. They may lose their CLIA-exempt status in some cases, or they might not be able to offer certain tests. You will see that the feedback loop goes back towards the CLIA-exempt state regulation function, and as a matter of fact, you can go all the way back to the "LDTs from Research and Development" in the lower left-hand corner because maybe data and information from that inspection can be fed back

even to improve test development.

So that is the look at this one. I will just mention a couple of gaps. You will see in the center, just above "Proficiency Testing," those are Gaps 9 through 11. These have to do with insufficient resources, funding, and need to develop proficiency testing for all genetic tests. Gap 10 is that no data exist on the effectiveness of PT versus alternative assessment, and No. 11 refers to PT based on test methodologies such as sequencing that has not been fully developed in the United States. So these are some excerpted gaps from the text of the report.

That is the CLIA-Exempt States Sector. Let's move to Slide No. 7.

DR. TUCKSON: By the way, you are doing just great. There is something you just said at the end I want to make sure everybody understands. The gaps that you have so specifically identified and mapped to the map all come from the body of the report.

DR. GOODMAN: Yes.

DR. TUCKSON: You are summarizing the report. I think it is important that people understand whose

words you are using. Thank you.

DR. GOODMAN: Yes. Dr. Tuckson, just to be even more clear, we did some paraphrasing and shortening, so we tried to find the kernel of the discussion of the gap to list it in short form on the accompanying single sheet. They do indeed come from the report, yes.

Let's move, then, to Slide No. 7, which is the CLIA sector, and then Slide No. 8, which describes it in more detail.

On Slide No. 8, let's start again toward the near left, which is "CLIA Regulation." You will see that that points to about five functions there. Some of these should be familiar already: personnel standards, quality assurance, quality control, analytical validity, and proficiency testing.

Now, coming off to the right here where it says "Quality Control," you will see "Inspection Survey Requirements." These can be done by CMS or its agents. Then, to the right, "CLIA Accreditation." So an important thing to consider again is the CLIA regulatory oversight of the several functions, along with inspection survey requirements, gets a laboratory to CLIA

accreditation. That is not the same thing as approving the test, but a laboratory with CLIA accreditation will be a laboratory that can provide the test.

As a matter of fact, the tests come in from the upper left, where you see "LDTs from Research and Development." Remember this was one of the other pathways from that sector. It comes across the top of this sector and down to "CLIA Accreditation." So what we are trying to portray there is the tests, as services, become available from the CLIA-accredited laboratories which have gone through those other bits of oversight, the several that I just mentioned. Then, off to the right, they become available for clinical use.

Once again, coming off the bottom of "CLIA Accreditation," you will see "Biennial Inspection," "Review of Validation Data" for all the tests, and again, an analogy towards the previous slide. If biennial inspection does not go well, the laboratory could lose its CLIA accreditation or it may not be able to offer some tests. That gives very important feedback information to the CLIA regulatory process and yet even again to the R & D process in a sense in that you learn

from biennial inspection and other sources of data that may inform test development and improvement in the future.

Before leaving this one, I want to point out some of the gaps. We don't have time for all of them. You will see just above "CLIA Regulation" at the left Gaps 3 through 8. Of course those correspond to Nos. 3 through 8 on the list. Just to name one, Gap 6. I think there is a lot of emphasis on that one, which is insufficient resources to establish analytical validity, clinical validity, and clinical utility to address gaps in evidence for an increasing number of genetic tests. That is one of the important gaps to call attention to there.

For example, towards the far right-hand side where it says "CLIA Accreditation," Gap 12, insufficient regulation of laboratory-developed tests prior to initial clinical use along the CLIA pathway. That is another one that rises from the report.

That is a pretty quick run-through of the CLIA part of the map. Let's go on, if we can, to Slide No. 9. This is where we are going to highlight the FDA sector

of the map. This is how it ties in.

Then, on to Slide No. 10. Let's start at the upper left-hand corner. Now, you will recall that we got to this part of the FDA sector from a couple of directions. One comes in from the top. There is a downward arrow to IVDs and IVDMIAs from research and development. Those can come typically from device-makers with test kits and test systems, but remember that some of those might be, for example, IVDMIAs that are laboratory-developed tests. That is, LDT IVDMIAs. Remember that they too are subject to FDA oversight in this model.

Also remember toward the left that it says "Co-Developed Therapeutics." Remember that we also have that parallel pathway for drugs or biologics that may be developed along or in parallel with the tests. So both of those converge on applications of FDA approval and clearance.

Now let's take the device part of this first. To the right of "Application for FDA Approval and Clearance" you will see "PMA" at the top. That is the pre-market approval application. Those are novel devices

for which there is not a substantially equivalent device on the market. That is usually the steepest route to take for tests.

You will also see at the bottom of that box the 510(k). Those are the substantially equivalent tests. That means that something has been on the market or that something had a predicate as of 1976.

There is also this special route to 513(f)(2), which is a way to get something called the de novo 510(k)s. That is when a device does not have a predicate on the market but it does not present a high level of risk. It is perhaps a way to not have to go through the full PMA route but using something that looks more like a 510(k). It is called a de novo 510(k).

In any case, these are all subject to, above, FDA manufacturing controls, FDA pre-approval inspections, and so forth.

Coming out of the right-hand side of that, you see to the right and down towards "Application Review," that is when it is reviewed by the FDA. Then, well, what is reviewed? Depending on the technology, it may be analytical validity, it may be safety and effectiveness.

Of course, that is a very simplified way of saying the kinds of things that the FDA is looking for. When appropriate, the technology can gain FDA approval, which is typically for PMAs; clearance, typically for the 510(k)s; and onward to availability for clinical use.

You will notice, by the way, just below and to the left of "Available for Clinical Use" is the "FDA Post-Approval Inspections." That is another aspect of the FDA QSR.

Not to forget at the bottom, of course, was that route for the co-developed biologic. The BLA is the biological license application. The NDA is the new drug application. That is what you need to submit to the FDA in order to get review of these products in order to go to market.

So again, I hope you see that this is highly simplified to show these parallel paths going through one gate first, the approval and clearance. There is really a lot more going on there.

I believe those are the main points here insofar as the FDA routes. A couple of the gaps, to the far right just below where it says "FDA

Approval/Clearance." You will see G6 and G14. We have already mentioned G6 before, about the insufficient resources to establish analytical validity, clinical validity, and clinical utility. Gap 14 is insufficient evidence of clinical utility for most tests. So remember, even when we go through this process, it is really the exception when you get good data and good evidence on clinical utility. So that is a very important gap to point out here, and I know that this is reflected in other discussions.

If we may, then, let's look at Slide No. 11. That is, as you see, the 30,000-foot level. We are going to take a look at availability and reimbursement. That is the far right and fifth and final sector here.

On Slide 12, let's start at the top. You will recall that we entered this sector from four different main pathways. One was from the CLIA-exempt states, New York and Washington. There is a route to get here by that way. Another one was that special bypass one, direct-to-consumer tests. That one is by non-CLIA-certified labs, typically. That is a pretty good bypass of the system and of course your report has called

attention to that. The third one is from CLIA regulation. We have discussed that. The fourth main one is via the FDA approval, or current way.

There are four main ways to get into this sector, and just advancing up toward the top where it says "Available for Clinical Use," that is how they become available for clinical use.

Let's drop down from there. You will see that you have DTC, which is direct-to-consumer tests, and DAT, which are direct-access tests. Remember those difference between those. The DTC tests can be acquired by consumers, tested by themselves. Direct-access testing is typically something done by consumers but it should go back to a laboratory.

Then there is clinician testing and testing by a laboratory, and so forth. Those are the several main ways that something becomes available for clinical use. You will see to the right of the DTC, DAT, Clinician, and Lab that those various agencies and organizations had various types and levels of oversight and other involvement in how these things are done. Obviously, the FDA. The FTC has a role of course. The courts do.

Certainly many professional organizations. We noted other laws and guidelines. With HIPAA. We put a question mark after GINA because obviously that is still pending.

Now, having gone through these kind of gateways to become available for clinical use, you can drop down. Some tests to the right are subject to clinical utility review. This is really a very highly select number of tests. The U.S. Preventive Services Taskforce looks at some of those. EGAPP has looked at some of those. These are good but pretty limited efforts. Most kind of go the left way, which is not really being subject to another look at clinical utility that carefully.

Coming off the bottom of that towards "Reimbursement" and the right, there is an arrow going to "Reimbursement." Obviously that is carried out by Medicare, Medicaid, private insurance, the VA, Department of Defense, and others. That goes into "Reimbursement."

We don't show a bunch of other arrows from "Reimbursement" to all the places where the money goes. We thought that would be too complicated. I think you know where those go.

Interestingly enough also, another arrow goes to "Post-Market Surveillance" off to the left. This is done largely but not entirely by FDA.

So what you have here, then, is some post-marketing surveillance. There is a lot of feedback information from that. Some post-marketing surveillance information is fed back to reimbursement because payers are interested in what happens to tests once they are on the market. It might affect their coverage and payment decisions.

Certainly, post-marketing surveillance feeds back to the left, to the research and development sector and even the FDA approval part because post-marketing surveillance information may be used to reapply for perhaps a broader indication at FDA or may change how the FDA couches its indications or labeling for marketing of tests and availability of tests.

Notice, too, that at the very top it says "Outcomes Research." I don't want to forget that. Once a test becomes available for clinical use, various organizations in the public and private sectors conduct outcomes research. The findings of outcomes research may

be fed back right to availability for clinical use. Clinicians and others may use that information to reinform their decisions about when and how to use a test.

Off to the right from "Outcomes Research," there is feedback that goes all the way to reimbursement. Remember the payers are also interested in outcomes research. It may affect their decisions. Outcomes research can go all the way back, along with post-marketing surveillance, to the R & D sector and input to FDA decisions.

So that is the overall picture of the FDA part of the map. I want to call your attention to just some, not all, of the gaps. Let's start at the top where it says G15 and G16, next to "Availability for Clinical Use." G16 is that there is a growing number of genetic tests that are offered based on inadequately validated genetic association studies. That was one thing that came out of the report.

Let's go down to the lower right-hand side where it says G32 and 33. G32 refers to inadequate, outdated systems for coding, coverage, and payment for

genetic tests and services. G33 raises the potential for misuse of genetic information in insurance premium-setting and employment decisions. That is a concern of some, and that is why I know that some people are interested in GINA, for example. So we are calling attention to a selection of the gaps that are noted in the report.

That is the FDA sector really quickly. Now, if you are brave enough to turn to Slide No. 13, Slide No. 13 is the big picture, where we put all of these five sectors together. I hope you realize why we didn't show you this first. It would have given me an upset stomach, I know, myself.

This is all of it put together. I want to say a few things about this before turning it back to Dr. Tuckson. This map does try to represent the current system. Is it complicated? Yes. Is it a simplified version of reality? Also yes. This is not a map to represent where we need to be or some would like to be or some ideal. It is a decent, high level snapshot of where we are now.

Why is it complicated? Well, it is complicated

because it has to accommodate a great, evolving diversity of testing and testing services that have evolved over time. It also has to reflect an uneven and sometimes patchwork history of legislation and regulation that have applied to testing over many, many years.

So it is not complicated by design. It is complicated because it has to account for an extraordinarily diverse range of technology and it has to be complicated in order to reflect the different historical reasons and growth by aggregation of types of oversight.

That is where we are with this map. This map still needs some tweaking and some fixing. Obviously, we welcome more input for it. We will make it better, but this is where we are now.

Back to you, Dr. Tuckson.

DR. TUCKSON: Thank you. I will give it back to Andrea in a second here. First of all, my God.

[Laughter.]

DR. TUCKSON: First of all, what a terrific job. I think the companion code for the 33 gaps is actually terrific as well. You sort of have those side-

by-side.

Two comments I think that the report is going to need as we go back and look at it. Number one, at one level this in and of itself could be proclaiming a problem. Just the very nature of something as awesomely complex as this could by itself be declared a problem. So one of the things we will need to do also is to say how different is this than the oversight of non-genetic tests, which would be kind of important. If you were to look at this in the reality of traditional medicine today, is it any less horrible than this looks.

Secondly, I think that one of the things we have to be real clear about, and again, obviously we are getting into the basis of our analysis, is who is the person responsible for making sure for the public that all of that stuff gets dealt with. Once you start to realize that it is this complex, who is driving the train? Whoever is responsible for driving the train is going to have to be also fairly explicitly known so that folks will understand where are the accountabilities for the things that exist as we deal with the accountabilities for the things that don't exist.

Andrea, take it away.

DR. FERREIRA-GONZALEZ: Thank you. This map is describing a very complex process. I think it looks very complex because we have been very comprehensive in looking at the oversight of all laboratory-developed tests and the IVD and MIA route of the clinical laboratory testing that is currently offered in this country.

I would like to open the floor to see if anybody has any comments to the oversight map.

Discussion

DR. TUCKSON: By the way, one other comment I had, as people start to rush to the microphones, is I think one of the things, also, that I wonder about -- and Andrea, I'm not sure whether we have commissioned Lewin to do this -- is a couple of illustrative vignettes. I think that [is] one of the things we probably ought to be doing as we have our debate and discussion about these recommendations.

For those of you that feel strongly about certain positions, play out a scenario so that you can actually see how this works in real life. But I think

the vignettes are going to be very important for transmitting this report.

DR. FERREIRA-GONZALEZ: I think that is a very good idea. Does anybody else have a comment? Paul.

DR. BILLINGS: Reed mentioned the issue of genetic exceptionalism, really, in relation to the complexity of this. We have two other overarching issues: public awareness and access. I would say also fostering innovation. So I think that, actually, there ought to be specific comment about how this picture relates to those issues when this is portrayed.

DR. FERREIRA-GONZALEZ: Muin.

DR. KHOURY: This is a very nice and complicated view of the real world. We can all quibble about little things, but just the fact that we have all the map laid out is a very tremendous task. My compliment to the Lewin Group for doing this.

I just want to, by way of clarification, try to understand how the LDTs, like Decode Me and 23 and Me, just go straight to the consumers, bypassing all of this. I don't quite understand how this happens right now. Maybe because they don't use it for health purposes?

Basically, there is a big hole. There is a train you can drive from an LDT directly to the consumer through all of this complicated framework. Maybe somebody can explain it to me.

DR. FERREIRA-GONZALEZ: I think that you have just identified another issue that the Committee had and that is exactly portrayed in that way about the LDT for those laboratories that are offering testing to the public without going to CLIA certification. They claim that they don't fall under CLIA statutory regulation here. So that is exactly what we have here and that is a big hole that we have identified.

DR. EVANS: Isn't that because they claim not to be offering diagnostic or medical services?

DR. FERREIRA-GONZALEZ: Remember we have recommendations on that issue. We are just looking at how we are portraying that type of test. Steve, do you have a comment?

DR. GUTMAN: Yes, I also applaud this. It is amazing. However, it is not complicated enough.

[Laughter.]

DR. FERREIRA-GONZALEZ: Do you want to

complicate it?

DR. GUTMAN: It leaves out what to us is a small but important niche line of submissions, which is the investigational device exemption, or IDE exemption. That clearly needs to be interposed. There are some technical corrections. I won't bother the Committee with that.

DR. FERREIRA-GONZALEZ: If you can give us the technical corrections, it will be greatly appreciated.

DR. GUTMAN: I will provide them. In regard to post-approval products, our surveillance program, post-approval, or pre-approval, PMAs, or pre-approved, the de novo goes straight. You don't break off to PMA. Actually, that is the whole purpose of the de novos.

We would probably take umbrage. I realize that this is hotly contested, but we would probably call LDTs IVDs as well, but they are IVDs to which we have applied enforcement discretion. So we have a variety of small things.

DR. FERREIRA-GONZALEZ: The idea is to identify the different roles.

DR. GUTMAN: The missing IDE is, for us, is a

patient protection vehicle that you need to think about when you do look at the whole map.

DR. FERREIRA-GONZALEZ: Phyllis.

DR. FROSST: I would of course like to echo the comments that have gone before me at how impressive it is to put together a map of this scope of detailing, a process that is clearly very complicated and likely to become more complicated as the map evolves.

My first question determines what my second question is going to be. The audience for this is the audience for the report, a fairly high level with, hopefully, other people in the field reading it to understand it. So the report is twofold, an in-depth analysis of the situation with recommendations for that so that a more casual reader could understand it.

My second comment would be that I think one of the most valuable parts of this in looking at everything from a 30,000-foot view is having gaps tie in with the process. As a casual user, I would see this diagram and I would flip the page. I realize this is a very non-trivial thing to be thinking about, but would it be possible to do a map of this flavor at a lower

resolution, at a higher view? Very much in the way that you broke down each chunk into chunks, can you collapse some of this granularity into a way that someone could appreciate where the gaps are without losing the understanding of what the process is?

DR. GOODMAN: I was going to say, as Andrea knows, one of the things that we are thinking about is actually showing the five sectors separately: showing most of the slides that you just saw, which is the big five pieces, and then each of the five pieces, and then finally the thing together. It sounds like you might even be talking about something at a slightly different level. We want to make it easier for the target audiences to comprehend this, yes, not just showing the one big complicated diagram.

DR. FERREIRA-GONZALEZ: I appreciate your comment. I think the value of this type of granular system is to show where some of the gaps are located. If you go to a higher level, you might lose some of that appreciation. We can take into consideration your comment. Marc wants to make a comment.

DR. WILLIAMS: I just think that we have gotten

into the philosophy of everything has to be on a one-page executive summary. When we try and distill down horribly complex issues into something that is so simplistic, it really doesn't represent reality and it gives people a false sense of security.

I think the issue more is less the map but more the engagement of actually walking through the map. As I looked at this map and tried to dissect it myself when we were trying to do the review, I found it very confusing. But to have Cliff walk through the different sectors, if you can have that type of engagement, which takes a relatively brief period of time, that is where the real rubber can hit the road.

DR. FERREIRA-GONZALEZ: Steve and then Muin.

DR. TEUTSCH: To Phyllis's point there, I think it is helpful to show here on this map, and we can probably be clearer, where the issues in analytic validity occur and where the clinical utility and clinical validity issues are so at least we can begin to see that where the gaps that we are actually dealing with in the report and trying to fix fit here. It is not like they are in isolated places where you can put your finger

directly on them. I think it is important to realize that the problems we are grappling with actually are across the spectrum of this process.

DR. FERREIRA-GONZALEZ: I think that is a very important point. We don't want to lose, for example, that the LDTs go through the FDA and other areas. You need to see the entire picture. But maybe adding, like Marc is saying, the different slides and having them walk through will help whoever is reading this report down the road to understand or actually facilitate the understanding of what we meant by this. Marc.

DR. WILLIAMS: To be responsive to Paul's comment, too, which I think is right on, I think maybe the other thing we could add to this that I don't think would add any more lines [is] we could certainly highlight which parts of the process are currently transparent, i.e. where a sophisticated consumer could actually go in and information, and those parts which are currently behind the curtain. That is a big issue in terms of our research.

DR. FERREIRA-GONZALEZ: Muin.

DR. KHOURY: I just want to build on what Marc

said, actually, because this is very, very helpful in our deliberations and discussions later on, especially around the concept of a registry. For any intended use today for any genetic test that is on the market or in this research morass here, or in this winding diagram, for consumers and providers to get the information they need, where would they go. They can go different places.

I think if there is a way, as a starter, to put out all that information together and display it to the stakeholders in a transparent way, that would be a good start in order to inform the providers and the consumers whether or not a test is ready for prime time.

Just by the way of a little correction here, if you look on the right lower corner, "Clinical Utility Review," where you have the U.S. Preventive Services Taskforce and EGAPP, actually EGAPP was designed not only as just a clinical utility review but to review everything, including analytic validity, clinical validity, of course with an eye towards clinical utility. We have actually used the EGAPP working group, from which there are a couple people here --

DR. FERREIRA-GONZALEZ: So we should put the

EGAPP in another place, too.

DR. KHOURY: Right. If there is a way to try to capture this information from multiple places and feed it, whether in a central location or distributed information, that is transparent and accessible to the public through websites, that could actually be a good start to go through this and understand how much of it is downloadable. Right now it looks like an opaque, very thick forest that you are unable to penetrate through.

DR. FERREIRA-GONZALEZ: That is a very good idea. They will have to figure out how to do it. Mara, and then James, and then Gurvaneet.

MS. ASPINALL: I would agree on the compliments on this system. I don't believe I have ever seen something as comprehensive as this. First, I would say I think it is important to make the smaller or medium changes so we truly have something that we can put a stake in the ground and say that this accurately reflects the system.

As opposed to the last comments or the related, I think we can use this map with the recommendations. So as we go through the recommendations, we talk about gaps

here, but to use this both literally and graphically to be able to say that Recommendation 17 -- I know there aren't 17, but I didn't want to prejudge it -- indeed fills a gap that is G2 over there.

So if this is an organizing principle, let's make sure to use it throughout our whole process.

DR. FERREIRA-GONZALEZ: Paul, you have noticed that you have a single page. Unfortunately, we have a single page, Mara, with the map, but you can still read it. So we will use this, and that is why we have it separate, as we go through the recommendations to go back to this map.

I have James and then Gurvaneet, and then I think we are going to try to wrap it up.

DR. EVANS: I would just suggest as a practical issue this overview is so good. When I first looked at this I almost had a tonic-clonic seizure.

[Laughter.]

DR. EVANS: But Cliff's walking through it, which probably took, what, 15 minutes was so good that I would strongly suggest having a very explicit link in the report to that presentation, which I imagine has been

captured, because I think that anybody wanting to understand this we should say would be well served by spending the 15 minutes to be taken throughout it by the hand.

DR. FERREIRA-GONZALEZ: Gurvaneet.

DR. RANDHAWA: It is a great job, Cliff. I compliment you and your team. This is sort of fine-tuning the map here, but when you look at the upper right-hand and the middle corners, the outcomes research and guideline development is very well laid out but you could consider the same thing happening at the USPS and EGAPP level, where outcomes research information is also used to inform their recommendations.

Vice versa, in guideline development, the guidelines we are thinking about, clinical utility is a part of their review before making the guidelines. So you may want to consider tweaking that a little bit.

DR. FERREIRA-GONZALEZ: One other thing is that we have here the role of the known regulatory oversight such as the professional guidelines and so forth in the area that we have on the right and middle corners of this slide. Under the DTC, DAT, and clinicians, we have there

the professional organizations and other organizations that provide guidelines, but then those actually might have to be also reflected through the CLIA-exempt state and the CLIA regulation because they also apply into how you are actually going to be performing the testing and so forth.

So there is not only the regulation currently but there are also all these other inputs from these other professional organizations or other groups that are providing these guidelines. If there is any way to also put them in these two other main blocks of the CLIA-exempt state regulation and the CLIA regulation.

I think the question we have to ask is does this reflect the charge from the Secretary on a map of the oversight. If you don't think so, please say so.

DR. TUCKSON: Well, I vote that it certainly is responsive with the appended gaps issue, which we will go through, with the only exception that I think that what it misses is a little bit of a commentary on accountability. If we can get a commentary on accountability at the levels of what is there.

Obviously you can't have accountability for the

gaps, but assigning the accountabilities of the Secretary's Office in general for driving the overall train and how explicit is that accountability, the accountability for the major government agencies. So, "The head of the FDA is accountable for." Just assigning a rational accountability.

DR. FERREIRA-GONZALEZ: Mara.

MS. ASPINALL: Just briefly, I would very much agree. I think the accountability makes sense. I just want to say on the record it is particularly impressive that you have added the right-hand side that talks about accessibility and reimbursement because that is something that has been an undercurrent in the broadest scope of the industry for a long time and you can't really look at the left-hand side without at least understanding the right.

DR. FERREIRA-GONZALEZ: If you notice, on the map everything is a circle. It is inside a circle.

MS. ASPINALL: It is perfect. Thank you.

DR. FERREIRA-GONZALEZ: We are doing good so far. We will see you later. Now we are going to move to the next presentation.

DR. TUCKSON: Are we done with Rome?

DR. FERREIRA-GONZALEZ: Yes.

DR. TUCKSON: Rome, you are done?

DR. GOODMAN: Thank you very much. I wanted to just ask our team, Laura and Crystal, to make sure to not let I guess it was Gurvaneet, Steve Gutman, and a few others out of the room without getting their handwritten corrections on their versions of the map to make sure we capture those wonderful suggestions.

We had two rules. One is we had to work in two dimensions. The other one was we couldn't cross lines. That is one of the rules on these things. We will do our best within those constraints, but thank you for the very, very helpful suggestions.

DR. TUCKSON: By the way, because you can't see us, there are 28 of us here who are waiting for the presents from Italy. So, thank you.

[Laughter.]

DR. FERREIRA-GONZALEZ: Cliff, before you leave, I think we need a round of applause. Gurvaneet is asking for that.

[Applause.]

DR. FERREIRA-GONZALEZ: This is going to be a significant contribution to our understanding of this complex issue. Thank you, Cliff.

DR. GOODMAN: Thank you very much, Andrea. Thank you for your leadership in making this map as good as it is so far, and thanks to our team of Laura, Crystal, and others.

DR. FERREIRA-GONZALEZ: Thank you.

DR. GOODMAN: Thank yo.

DR. FERREIRA-GONZALEZ: We are going to continue forging through.

DR. TUCKSON: Let me just do a quick check just so we have people's "bladditary" expectations. We are scheduled for lunch at 12:30. We will plow forward and see how we do, and we will see if we can have a natural stop around 12:30. Thanks.

DR. FERREIRA-GONZALEZ: Great.

Discussion of Final Recommendations

DR. FERREIRA-GONZALEZ: Now we begin our work to finalize the recommendations that will address those gaps. Now, in our January 30th teleconference with the entire Committee, we took a poll as to where the

Committee was on all the different recommendations and we started to identify areas that might need a lot more discussions and further information.

We decided to take revising the recommendations in reverse order. So we are going to go from the back to the front because we think actually the recommendations in Chapter 4 require a little bit more discussion. We want to make sure we don't rush through those because we still have all the other recommendations to go through.

We are going to start from the five recommendations in Chapter 6, proceeding to the four recommendations in Chapter 5, and then as to the big ones, recommendations in Chapter 4. We will be ending with the overarching recommendation that appears at the end of Chapter 2 of the report.

We expect that our deliberations and recommendations in Chapter 4 will need the most time, so we hope to be able to move through these other recommendations.

These are the questions to consider. Keep them in mind as we go through the recommendations. Changes made to the draft recommendations are going to appear in

lime green as we go through the different texts. For each recommendation, I will provide a capsuled summary and then ask three questions. I'm not going to read the recommendation. You are going to have the recommendation. Any changes that we have made from the original draft that were then changed through the steering committee and the work with the taskforce will be in lime green.

First I will ask you if you have any questions about the recommendation, do you need any more information to clarify the intent of the recommendation. At that point, we will have the taskforce members, who are sitting right over there, to [answer] questions, especially if we need more information [about] what the intent of that particular [language was]. Then I will ask if you have any edits to the recommendations to change the wording or actually the specific recommendations. When I have a sense that we have completed our discussions, I will ask you if we can move on to the next recommendation.

In reviewing again each recommendation, consider the following questions: does the

recommendation adequately address the identified problem, and is the wording of the recommendation satisfactory?

We are going to start with Chapter 6. This recommendation calls for HHS to work with relevant stakeholders to identify and address deficiencies in genetic knowledge in education of three key groups: healthcare practitioners, public health workers, and consumers. We actually revised the preamble of the recommendation to recognize the creation of the SACGHS Taskforce on Education.

To Part A of this recommendation, we have added that educational efforts should also take into account issues of medical literacy, access to electronic information, and deficiencies in public infrastructure.

Recommendation 6 also has a Part B. Part B is not new text but it appears in the section. We actually moved this recommendation from Chapter 5 to Chapter 6 because we thought it fit better here.

This recommendation in Part B calls for research and surveillance on how knowledge of analytical validity, clinical validity, and clinical utility can inform the development of evidence-based clinical

practice guidelines.

So again, the three questions we are going to be asking through the day. Do you have any questions about this recommendation?

DR. TUCKSON: Yes. This is terrific. I think a lot of this is determining how to have the form and structure. But this is fairly generic, saying people ought to have more knowledge. We just have to be attentive to saying the point of it is that people need to be able, and it is very specific. You can talk about a lot of things with tests. It now is whether or not as a rational consumer. This is about protecting the consumer. It is also about some of the uses, but it is about does a rational consumer have the information and [is he or she] being taught where they can go to understand the safeguards around how they use and access genetic tests.

There is something missing in the sense that this is a little more general than getting to this notion of ultimately saying how do you become an aware consumer of a product in addition to being concerned with how you interpret the tests and all those other things.

So there is something missing in terms of the focus of this activity.

DR. WILLIAMS: I would take issue in the sense that I don't think that we intended that focus, nor should there be, because the deficiencies are across all stakeholder groups. It is not just the consumers, it is the healthcare providers that are ordering the tests, that are attempting to interpret the tests. I think those groups are all articulated in Part A, the three key groups that we discussed, the healthcare practitioners, the public health workers, and consumers.

DR. TUCKSON: Let me try it a little bit differently. I agree with you there. That is absolutely right. But what it is saying is that HHS should work with all these people to identify and address. It doesn't say there is going to be a place where you can go to get the information.

DR. FERREIRA-GONZALEZ: Muin and then Mara.

DR. KHOURY: I'm trying to digest what Reed just said. I agree with him. I think the bottom line is this is about oversight of genetic tests. This is not about the Education Taskforce. We need something.

Starting from the back, Chapter 6, now we have done all the oversight stuff and this is now the place to go get information and educate the public, the providers, and all of these things so that the information they need for the implementation and use of genetic tests in practice can be done in an informed fashion.

Maybe we can tweak the words a little bit. Parts A and B seem like it is wonderful. It is like we need to educate everyone about genetics. We have been saying this for years. What is missing here is the management of genetics with the information that has gone through this diagram leading to evidence-based processes and guidelines. That is what needs to be put out in decision support tools and for the general public and the providers to be aware of, not genetic information in general. Am I making sense?

DR. FERREIRA-GONZALEZ: You are going ahead of, actually, what recommendations are coming. Remember that we have other recommendations about clinical decision support and so forth. Just look at all the other ones, too, to make sure we don't have it in the other ones.

But I would ask Muin and Reed, what language

would you recommend? What changes would you recommend to address this issue?

We have Mara and then Kevin.

MS. ASPINALL: First, let me deal with the specific change. In Recommendation A, I think there is one group that is not mentioned, which is the group of payers. So instead of saying three key groups, I believe it needs to be four key groups and include public and private payers as part of the group that needs to be educated, as number one.

Number two, and I'll leave this as a general comment because it comes up a few times, did the Committee think about having a timeline for implementation. I would very much agree this is important, but when you think about getting to all government agencies and interested private parties, that could be a process that could literally take generations. I think putting some parameters around actions or a timeline puts more teeth in the recommendation so that actions will have to be taken over a particular time period to actually ensure they are implemented.

DR. FERREIRA-GONZALEZ: We will take that into

consideration. Kevin.

DR. FITZGERALD: I just wanted to get back to Muin and Reed's point. To get some more specificity here, are you looking for a resource, a website or something, a "one site fits all," or are we just looking for some kind of process by which we say to the public, if you are looking for this kind of information this is how you go about getting it.

DR. KHOURY: I can make suggestions to change it right now. The third line, "Address deficiencies in genetic knowledge of education." Replace that by saying "To identify and address deficiencies in knowledge about genetic applications and practice and information on genetic tests and all of these applications." This is sort of like a "Know your genes," essentially.

What we are talking about here is the practitioners, the providers, the consumers, and the payers need to know the value of this information for practice. So instead of saying "genetic knowledge and education," just say more explicitly what we want people to know. That is the only change I would make.

DR. TUCKSON: Where is the one on decision

support? Just so I can answer your question. Who knows where the decision support is?

DR. FERREIRA-GONZALEZ: The next one. It is the next one, Recommendation 2 and Recommendation --

DR. TUCKSON: Six? Recommendation 2?

DR. FERREIRA-GONZALEZ: Yes. That is the FDA regulatory one.

So anyway, I guess I am saying, in addition to what Muin is saying, we ultimately are recommending that there be a place for guidance that helps that.

So No. 6-4 does it.

DR. FERREIRA-GONZALEZ: Maybe they can explain that to include --

DR. TUCKSON: I will stay with Muin on that part and then we will get more specific when we get to this one. Great.

DR. FOMOUS: Do we want to add in Muin's language now?

DR. FERREIRA-GONZALEZ: Yes.

DR. FOMOUS: Can you repeat that?

DR. FERREIRA-GONZALEZ: Muin, could you repeat what you said?

DR. FOMOUS: This is in the first sentence?

DR. FERREIRA-GONZALEZ: Yes. "Genetic knowledge."

DR. KHOURY: Instead of "deficiencies in genetic knowledge and education," say "Deficiencies in knowledge of appropriate genomic applications and practice." That is broad enough. It captures everything we want from this oversight mechanism.

DR. FOMOUS: Say it one more time? "Deficiencies in knowledge"?

DR. KHOURY: "Deficiencies in knowledge about appropriate genomic applications and practice," or "genetic applications and practice."

DR. FOMOUS: Genetic and genomic?

DR. FERREIRA-GONZALEZ: Yes. Yes, "/genomic."

DR. KHOURY: How about just "genetic tests"? Because this is a report about oversight of genetic tests.

DR. FERREIRA-GONZALEZ: How about "the genetic test applications"?

DR. FOMOUS: Do we want to change the number of key groups while are at it?

DR. FERREIRA-GONZALEZ: Yes, yes.

DR. TEUTSCH: I would suggest, to Mara's point, that that is just one of a whole series of decision-makers, policy decision-makers. I don't know how broad we want to make that because there are a lot of them that are making policies that influence this environment.

DR. FERREIRA-GONZALEZ: So, do we want to put the number? For example, "In practice and education of key groups in particular." Then we are not saying that these are the only four.

MS. ASPINALL: I think that is better. I did debate over Steve's point, but I think payers are so critical. When you read the rest of the list, they wouldn't be included. So I think eliminating the number and then highlighting "in particular" deals with both.

DR. FERREIRA-GONZALEZ: We are going to put "practice and education of key groups, such as."

DR. FOMOUS: I'm hearing two different things.

[Pause.]

DR. FERREIRA-GONZALEZ: That will get to the point that Muin and Reed had. Then Gurvaneet has a comment.

DR. RANDHAWA: I thought when we were initially writing what was there that we were describing a general gap in the knowledge and not specific genetic tests or applications. While that may be where we want to go, then we are getting into each specific test and each specific matter in education. Are we making it more specific or are we still about the more general where are we in terms of education deficiencies and how do we overcome that?

DR. FERREIRA-GONZALEZ: What would you recommend to change? Marc.

DR. WILLIAMS: Just to respond to that before we discuss it, I think that is a good point but I think that the other points that Reed and Muin brought up are probably more pertinent given the focus of the report. This is appropriate. It doesn't mean that those other problems don't exist, and I think we do articulate the breadth of the problem in the language of the report.

I also feel less concern that we need to be as broad here given that we have another taskforce that is going to be devoted solely to that issue.

From my perspective, I'm comfortable with the

changes that have been proposed to keep this within the context of what this report is supposed to be doing.

DR. FERREIRA-GONZALEZ: Now I think we are okay with this, but thinking back to the point that Mara brought up, the timeline, do we want to put a timeline in this?

DR. WILLIAMS: Yes, I would love to. But I have no idea how to set it. I really don't. I understand that these things can go out and they can disappear. We heard talk about the processes of this going around since 1995. But I think that probably, again, I would defer to the Education Taskforce to maybe be a little bit more prescriptive about this because I'm not quite sure I could even begin to get a handle on how you would set up a timeline for this.

DR. FERREIRA-GONZALEZ: It might be that we don't need a timeline for every single recommendation that we have. The other thing we can do is just think about this. Remember we are going to go back through all the recommendations tomorrow. With that in mind as we go through the process, tomorrow we can go back to a specific timeline.

Mara and then Kevin.

MS. ASPINALL: I was going to say exactly that. I would like to suggest that the Committee keep in mind the issue of timelines and then we can come back at the end and we will be, likely, more realistic. It may not be ideal, but I'm going to advocate that we put some parameters around this, and we can do it for the report as a whole, maybe, or major sections as opposed to one by one.

DR. FERREIRA-GONZALEZ: Since you brought it up, we are going to charge you to be looking for that. Kevin.

DR. FITZGERALD: Just a technical question. Perhaps we are going to need different input to figure this out. But, are we talking about payers with an "E" or "payors" with an O?

[Laughter.]

DR. FITZGERALD: We have to be consistent in the report. How are we supposed to refer to this?

DR. FOMOUS: What did you do?

DR. FITZGERALD: Suzanne, where are you? "Payors," right? E? We did E? Okay.

DR. FERREIRA-GONZALEZ: I think we need to be consistent.

DR. FITZGERALD: I just wanted to be consistent.

DR. FERREIRA-GONZALEZ: I'm glad you are here, Kevin, to keep us straight. Are there any changes in B? Sarah is keeping me straight here. Chapter 6, Recommendation 1, Part B. Are there any changes? Gurvaneet.

DR. RANDHAWA: It is not a change so much in the wording, but I think this recommendation is sort of broad. The issue and the processes that are inherent in creating outcomes in evidence and making guidelines based on that is very different from the issues and processes in terms of implementing those guidelines in practice and changing practice. So my only concern is this is so broad as to be not very informative. Maybe we can split it up into two recommendations, one on making the practice guidelines, how we develop the knowledge on the different domains, and then a separate one on actually the dissemination, implementation, use, and practice.

DR. FERREIRA-GONZALEZ: Marc, do you have any

comments to that?

DR. WILLIAMS: Yes. I'm sensitive to those. Obviously, I think our intent here is to try and take advantage of whatever the Secretary can do to set a research agenda around these issues, whether that be through AHRQ or NIH or some other mechanism.

But we couldn't really come to a good decision about how best to specifically articulate where this should go and as a consequence we have left it broad. I would like to be more specific. If you have some specific suggestions about what we might be able to direct the Secretary to do to move this along, that would be most welcome.

DR. FERREIRA-GONZALEZ: Reed, do you have a comment to this?

DR. TUCKSON: Yes. I really appreciate what Marc just said. I think that where the specificity is, and it is embodied in some of our other recommendations, is that the Secretary should ensure that there is adequate research resources available to advance analytical validity, clinical validity, and clinical utility for multiple purposes, including so that it would

be included in evidence-based clinical practice guidelines.

Here I think where the danger is, is that there is no such thing as evidence-based clinical practice guidelines without all that other stuff. You don't need to conduct research on how it might be. You need to say "Give us the damn research."

DR. FERREIRA-GONZALEZ: So, are we comfortable? Steve.

DR. TEUTSCH: I think one of the reasons we have wrestled with whether this is Chapter 5 or Chapter 6 is it deals with two sets of issues. One is the clinical utility and guidelines and the other is from the guidelines into practice. We could have separated them out. We decided that probably wasn't very helpful because they are closely linked, and that is why it is sitting here in this chapter.

I think it is what you are getting at, if I hear you right, Gurvaneet, that there are really two separate components. I guess we could break it at least into sentences here.

DR. FERREIRA-GONZALEZ: With the comments that

Reed just made, changes to the language of the recommendation, will that address specifically the issues that Gurvaneet and we all are bringing up here?

DR. WILLIAMS: I think it makes sense to me because the Secretary obviously can't conduct the research, but I think [he can make] the resources available.

DR. FERREIRA-GONZALEZ: Reed, can you go back and say the language?

DR. TUCKSON: Again, I have to go back and remind myself. We have a bunch of recommendations in our gap analysis. Our gap analysis specifically said "Insufficient resources to establish analytical validity, clinical validity, and clinical utility." That was a gap, so there are reasons why that is important.

What we probably want to do is find the right place to summarize to say that the gap in that results in stifling some extremely important things, one of which -- you will have a list -- is not having evidence-based clinical practice guidelines to inform the translation of this into clinical practice. Therefore, we recommend that there be adequate resources to achieve this purpose.

That is what I'm saying.

DR. FERREIRA-GONZALEZ: So the language change would be that "The Secretary provide adequate resources" --

MS. CARR: How about just "sufficient resources are provided to research and surveillance"?

DR. FERREIRA-GONZALEZ: Say that again, Sarah?

MS. CARR: I don't think we have to say "The Secretary." We can just say, at the beginning, "Sufficient resources are provided."

DR. FERREIRA-GONZALEZ: Now, we are going to go back, remember. What I'm hearing here is we also have other recommendations in other chapters. Remember we are going to go back at the end after we have gone through all the different recommendations to make sure we don't have overlap with where these should be broken or where they should be placed.

DR. TUCKSON: What I hear you saying, Madame Chairperson, is that we will accept for the moment that there will be some duplicative recommendations. We can go back and smooth the stone a little later on.

DR. FERREIRA-GONZALEZ: Remember we will be

going over this tomorrow. We are going to go back to all of them.

DR. TUCKSON: We can start catching the redundancies as we go along and then figure out when you might want to smash this together with something earlier and just have a more complete statement. We will worry about those niceties later.

MS. CARR: Is this the extent of the change that needs to be made? There was your point, Reed? Look at the preamble, remember.

DR. TUCKSON: "The Secretary should provide sufficient resources to conduct research."

MS. CARR: "The following strategy" --

DR. TUCKSON: No, the issue is not how the knowledge can inform. You don't need all that stuff. Everybody knows that that is how you do it. You can't do evidence-based clinical practice without it. You are basically saying give us the resources to advance evidence-based clinical practice.

DR. FERREIRA-GONZALEZ: Let's step back for just a second.

DR. TEUTSCH: I was going to speak to that

issue.

DR. FERREIRA-GONZALEZ: Go ahead.

DR. TEUTSCH: Because Chapter 5 actually talks about supporting the public-private partnership and getting adequate funding to do the research and surveillance and get all of this evidence right and develop guidelines. That is in Chapter 5. So it may be that we can shorten that first sentence and actually get down to the second part, which is the translational piece, which also needs adequate information and research base.

DR. TUCKSON: Gurvaneet's agency has like zero dollars. So the thing I don't want to do is ask the Secretary to give his agency a bunch of dollars to tell us how to translate this stuff into evidence-based guidance. They know how to do that. Give them the information.

DR. FERREIRA-GONZALEZ: So the idea is "Sufficient resources should be provided for the development of evidence-based clinical practice guidelines." Is that where we are?

DR. WILLIAMS: No, I think what I'm hearing is

there are really two pieces. I think this gets back to dividing it up. Again, as we get to Chapter 5, we may take out that first piece of that and reflect that in Chapter 5.

I think what Reed said is really the critical issue here. AHRQ doesn't have a lot of resources to actually do the translation. What we are really asking for is that they have adequate resources to be able to take the stuff that we recommend in Chapter 5 and create evidence-based guidelines and to study how that should be translated into clinical practice.

DR. FERREIRA-GONZALEZ: What I'm hearing is that "the conduct of research surveillance and knowledge of analytical validity" is already covered in Chapter 5 recommendations.

DR. WILLIAMS: Right.

DR. FERREIRA-GONZALEZ: If we take that part out, we are dealing with a duplicate of the two recommendations. Only develop these recommendations with that specific issue of funding for AHRQ to develop --

DR. TUCKSON: To do the translation of that into evidence-based practice.

DR. FERREIRA-GONZALEZ: Wait. We need to look at the language that we are going to put here to reflect that. So we have, "Sufficient resources should be provided for the development of evidence-based clinical practice guidelines and how that information can be translated into clear practices that enhance the quality of the care and health outcomes, including dissemination and implementation of recommended genetic tests into clinical and public health practice."

DR. TUCKSON: I would just say take out "how that information can be" and just say "how it can be translated into clinical practice guidelines that enhance the quality of care and health outcomes."

DR. WILLIAMS: You're saying leave that but take everything after that out.

DR. TUCKSON: You don't need "how that information can be." They know how to do it.

DR. FERREIRA-GONZALEZ: Wait. Hold on.

DR. WILLIAMS: Undo what you just did.

DR. FERREIRA-GONZALEZ: Hold on a minute.

DR. TUCKSON: "Sufficient resources should be provided for the" -- by the way, it would be terrific if

you could put it in the very beginning. So you would say, "Given that there are resources to enhance the knowledge of our clinical validity, utility," et cetera, then "Sufficient resources should be provided for the translation of that knowledge into evidence-based clinical practice guidelines that enhance the quality of care and health outcomes." Period.

DR. FERREIRA-GONZALEZ: Do we want Reed to work on this one during lunch?

DR. TUCKSON: Then everybody can shoot that down.

DR. FERREIRA-GONZALEZ: You did that to us, so we are going to do it to him before he leaves.

DR. TUCKSON: We got a lot done here before the lunch break.

DR. FERREIRA-GONZALEZ: With these changes and edits that we have done, remember that we are going to see them again tomorrow, are we done with this recommendation?

DR. FOMOUS: Do we want this repeated, "translated into evidence-based clinical practice"?

DR. FERREIRA-GONZALEZ: Reed is going to work

with you over the lunch time.

DR. TUCKSON: I will show it to you during the lunch break.

DR. FERREIRA-GONZALEZ: I think we are at a good point for the break.

DR. TUCKSON: Does it have to be 45? So, 30 minutes. Go clog the line. If you see a member with a tag, let them in before the other people from HHS.

[Lunch recess taken at 12:36 p.m.]

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A F T E R N O O N S E S S I O N

[Reconvened 1:13 p.m.]

Discussion of Final Recommendations (Continued)

DR. TUCKSON: On the board is the new thought. The operative part of the recommendation is the first sentence. "Based upon increased research regarding analytic validity, clinical validity, and clinical utility, sufficient resources should be provided for the translation of this knowledge into evidence-based clinical practice guidelines that enhance the quality of clinical care and public health outcomes."

Now, apparently the Committee's sentiment may have gone beyond that to what is reflected in the second sentence, which I personally believe is not within the domain of this taskforce but in another taskforce somewhere else. But intellectual honesty prevails upon us to put this here for the Committee to tell us no, this is what we darn well meant.

"The Committee recommends the Secretary ensure the availability of information regarding the clinical use of tests to determine the adequacy of information and its translation to ensure that the adequacy of

information and its translation meets the needs of improved clinical care and outcomes."

In other words, you are saying you want to monitor how the tests are actually used to be able then to have it as part of the feedback loop for oversight. I believe that you are actually talking here about the regulation of the practice of medicine and not oversight of tests. But there are some who feel that in fact, no, you want this information about how it is actually used and how well are these tests being translated into clinical practice as a part of the oversight mechanism.

So you need to tell us, Committee, if that is what you really meant and you feel strongly about that.

DR. FERREIRA-GONZALEZ: Marc.

DR. WILLIAMS: This came out of the idea that as we discussed testing in the report we talked about testing as a process that doesn't just end with a laboratory test being done but there is communication before the test is done, after the test is done, that there is adequate understanding of how the test information should be used, and that it has an impact in appropriate care. What we were trying to capture here is

the idea that we do need to understand this.

It also reflects the sentiment that has come out and will be discussed in previous chapters about the whole idea of post-market gathering of information. Some of this will relate to appropriate use, not just if you use it right does it work.

So we thought it was reasonable to reflect this here. However, on our little break, there is also the possibility that this group will be proceeding with another taskforce that had been put on hold as part of our visioning process where this would, I think, arguably fit much better.

DR. TUCKSON: With that very cogent analysis, and this is, I think, much ado. I don't feel strongly about falling on the sword about this point. Quickly tell us if you want it in or not. I'm more than fit to keep it in.

DR. FERREIRA-GONZALEZ: If you want it out, raise your hand.

DR. TUCKSON: Move it quick. Which way do you want it? In? So, all the "ins" put your hands up.

[Show of hands.]

DR. FERREIRA-GONZALEZ: No, out.

DR. TUCKSON: Okay. Those are the "ins." Now the "outs."

[Show of hands.]

DR. TUCKSON: So we have two "outs."

DR. EVANS: The reason I think it should be in is simply that it says "The Secretary should ensure the availability of information." That doesn't address practice.

DR. TUCKSON: Paul, you and I are going to be overruled. Andrea doesn't get a vote because she is chair.

[Laughter.]

DR. FERREIRA-GONZALEZ: Since when?

DR. TUCKSON: It is in, and we are moving forward. Next issue.

DR. FERREIRA-GONZALEZ: What have we decided?

DR. TUCKSON: It is in. You won. Go.

DR. FERREIRA-GONZALEZ: Oh, lordy. Lordy, lordy.

[Laughter.]

DR. FERREIRA-GONZALEZ: Recommendation 2.

Recommendation 2 calls for FDA to engage relevant federal agencies' advisory committees to the secretary and other stakeholders to gather perspectives on the appropriate regulatory framework for clinical decision support systems. The only change that we made to this recommendation was to add a reference to the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children as another advisory committee that should be engaged in the discussions of the appropriate framework.

Do you have any questions about this recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Do we have any edits to this recommendation?

[No response.]

[Pause.]

DR. TUCKSON: Let's just make sure, folks. Even though we have a lot of FDA-CLIA mish-moshing to do, you are starting with this one because this is off to the side a little bit. You are saying this is not center. You are basically saying the FDA should then prepare

guidance articulating the basis of its authority to regulate clinical decision support systems as opposed to actual drugs.

Because the basic assumption in this is the FDA is the key organization here.

DR. FERREIRA-GONZALEZ: They claim to have statutory authority.

DR. WILLIAMS: That was what was brought forward in our discussion. They have in fact exerted statutory authority over this area. We have thought about this probably in the smaller construct of decision support that is associated with interpretation of a test result, so an IVDMIA that has an algorithm that runs to be able to interpret the result.

However, there are clinical decision support systems that are running in clinical practice that we also have indications that FDA may or may not choose to exert support over. So this is to reflect the fact that we need clarification of exactly what their intent is.

DR. FERREIRA-GONZALEZ: Steve.

DR. GUTMAN: You need to just tell me a little bit. You can ask, and obviously, as a committee, your

request will be respected. But there are two different issues on the table. One is to explain the basis for authority. I think that that strikes us a little bit as anomalous because we have actually been exerting authority for decades, but not impossible. I'm certain someone who has a great legal mind could in a sentence or two explain that it meets the definition of a device. That strikes me as a legal authority. I might even be able to do that, but I'm not a lawyer so I won't.

The second I think is more profound because I think we have a long history of grappling with the thorny issues of software and trying to communicate to stakeholders where they are. There is relatively little interest in writing a sentence saying it is a device. There is great interest in trying to, either as an independent agency or in collaboration with stakeholders, create more clarity in terms of what being a device might mean.

For us, for example, we would characterize laboratory information systems as devices. They have historically been Class 1 exempt. The good news is they don't require any pre-market review by FDA. The bad news

is they actually have to work, and if they don't, we will come in and take action.

DR. TUCKSON: We have to move this one fast because we have bigger ones ahead.

DR. GUTMAN: We think this is a pretty big one.

DR. FERREIRA-GONZALEZ: This is really big.

DR. TUCKSON: The word here is clinical support systems in general or those that are related to drugs and devices? Is that what this means?

DR. GUTMAN: I guess drugs and devices are combination products. So it is both, yes.

DR. WILLIAMS: Actually, it is beyond this. There has been experience within the clinical decision support community of free-standing clinical decision support for clinical practice, specifically in our institution with glucose control in an intensive care unit. We have had FDA basically say cease and desist relating to dissemination of this protocol because this is a device and we are not treating this as an exempt device.

This has been discussed at the AHIC as well. This is a very big concern because we do not understand

where FDA is in fact going to choose to exercise control over the range of --

DR. GUTMAN: But what I'm trying to say is I think it is different. I don't know that that is easy, but I think that is something that we do owe our stakeholders.

DR. TUCKSON: So we do need to clarify it. I wish you hadn't chosen an example of glucose but had chosen an example of how a patient or a doctor works through the decision tree on treating diabetes.

DR. WILLIAMS: That is where the discussion line goes. If a physician can reasonably do this on their own, then that is considered to be low risk. But, where do you define that.

DR. TUCKSON: The only question is the word "then." Does it have to be sequential or can it be simultaneous?

DR. WILLIAMS: I would think it would be simultaneous.

DR. TUCKSON: The word "then" makes it do all this other collaboration and then FDA is going to do something. It sort of falls off the edge of the earth.

Why can't that be part of it.

DR. FERREIRA-GONZALEZ: Where is the "then"?

DR. WILLIAMS: It is in the second sentence.

DR. TUCKSON: "FDA should then prepare a guidance." As part of this collaborative process they should prepare the document.

DR. WILLIAMS: Yes.

DR. TUCKSON: So just lose the "then" and we are all right. Go ahead.

MS. ASPINALL: Two comments. I don't think it is a big deal either way, but I thought the "then" was after engaging all of the others, then they should do it. So they should make comments before they engage.

DR. FERREIRA-GONZALEZ: That is part of the process FDA is developing.

DR. TUCKSON: So you have a lot of people talking but you don't know what the FDA authority is. You need the FDA authority to follow the conversation and everybody is working together. Otherwise, you have to reconvene everybody else again.

MS. ASPINALL: I have another point. I'm not sure if this is the right time, but it is sort of a broad

point around this to maybe inform this process. The assumption in the report, and I think industry-wide, has been that any regulatory authority in any way comes under device regulation and that the assumptions all over the map are all about within device and which part are device and which part aren't.

I'm going to suggest something, and maybe it is bigger than we can handle in the report given the historical nature of it. But I have to say I wonder, when device regulations came about they weren't an asterisk under drug regulations because drug regulations were first and device regulations came thereafter. We are now talking about regulation in an area, whether you believe there should be more or less, but an area that in my mind is a separate, independent industry.

While we have become accustomed to many definitions that these are truly in some way devices or there are some parts of tests that are devices, I think the average person would have said no, a device is something much different from a test.

Maybe we can come back to this at the end, but just given Steve's comment I wanted to mention it as

really thought-provoking. But whether, in the midst of this, some of the challenge we have is that there should be regulation that is truly specific to diagnostics and that it is not an asterisk in some way under a different industry but something that is distinct and representative of the strong, independent industry. When I say "industry," I don't mean commercial, profit, not-for-profit, research, academia, universities.

It really is a separate area and classifying it as devices, I have to tell you, I believe will never going to work. It is going to be piecemeal from what is there.

DR. FERREIRA-GONZALEZ: Marc.

DR. WILLIAMS: I think just the pragmatic response to that is while I don't disagree, the reality is that as we raise these issues this is how it is currently working. The interpretation of the statute I believe dates back to 1976, which of course means we are interpolating an awful lot about what was really intended given that decision support for the most part and genetic testing for the most part really wasn't around. That is what we are working from.

So we wanted to try and start from where we are, but I don't disagree that maybe, as we look at a bigger picture and a bigger version, that maybe we need to go there.

MS. ASPINALL: I appreciate the practical nature of it, but in this moment of time when we have the opportunity to think about that, I don't want to completely lose it before we finish the report.

DR. FERREIRA-GONZALEZ: Do you have a specific response to that?

DR. GUTMAN: It is directly related to that. When you parse out "diagnostic," you have to realize that it is not just in vitro diagnostics. It is radiologic, it is echocardiographs, it is, frankly, demographic information. It is much broader than just the lab. It is not your father's Oldsmobile.

MS. ASPINALL: No, I think that that is fair. In the broadest definition, and it is broad, I would still say it is different from devices. But there are some that include it and many that do not.

DR. FERREIRA-GONZALEZ: I think it is something that we can keep in the back of our mind as we go through

the recommendations. I think it has a lot of value what you are bringing up, Mara. Thank you.

MS. ASPINALL: Remember it.

DR. FOMOUS: Did we decide to lose the "then"?

DR. FERREIRA-GONZALEZ: That is the question. Any more edits? Are we okay with this?

DR. WILLIAMS: A clarification. Before the word where you have your cursor, where "FDA" is, just before that, I would just say "As part of this process." I think that gets at Reed's comment that it is not sequential but it also doesn't put the second sentence just kind of hanging out there, which is it is not related to that process. I think it is important to link them but not necessarily sequentially.

DR. FERREIRA-GONZALEZ: We are ready to move to the next recommendation? Recommendation 4.

DR. TUCKSON: Three.

DR. FERREIRA-GONZALEZ: I really want to finish. Recommendation 3 recognizes the need for genetic expertise to support the best genetic testing practices and requests that HHS act on recommendations in the 2006 SACGHS Coverage and Reimbursement of Genetic Tests and

Services Report. We did not make any changes to this recommendation.

So, we do have any questions about this recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Any edits?

[No response.]

DR. FERREIRA-GONZALEZ: Can we move to Recommendation 4 now?

[Laughter.]

DR. FERREIRA-GONZALEZ: Recommendation 4 requests that HHS allocate resources to AHRQ, CDC, HRSA, and NIH for research and development of clinical decision support tools and resources. We have made no change to the wording from the draft report here.

Then we revised this recommendation to include engaging providers and payers in education efforts and to provide incentives on protections in order to ensure participation in the design, dissemination, and implementation of clinical decision support.

DR. WILLIAMS: Andrea, just a comment. That paragraph was added in response to a number of public

comments that expressed concern about these issues. So this was in response to those comments.

DR. FERREIRA-GONZALEZ: Do we have questions about the recommendation? Gurvaneet.

DR. RANDHAWA: Just a clarification here. In this recommendation, is there a specific sense to tie in the clinical decision support to clinical guidelines? If so, is it the sense of the Committee that the clinical guidelines as they are being developed or formulated currently need to be cognizant of how clinical decision support tools are developed and so have a better linkage with that?

DR. FERREIRA-GONZALEZ: I think AHIC is actually specifically working on those.

DR. WILLIAMS: Yes, I think that is a really important point. The clinical decision support proto-recommendations overarching the entire AHIC are specifically looking at developing ways that guidelines can be constructed so that they are much more easily computable.

I don't know that we need to add that level of detail here, unless you really feel strongly that we

should.

DR. RANDHAWA: I think I'm coming more from the perspective of having worked with some of the guideline developers. I know there is a great deal of interest in the informatics community. I'm not sure it has percolated up to the guideline developing community in that how they formulate the guidelines they need to be cognizant of how they are being used downstream.

DR. WILLIAMS: That is true. We are trying to begin to develop that engagement.

DR. FERREIRA-GONZALEZ: Remember that in the report we are saying that these should be looked into in other activities that the Secretary is using through the Personalized Healthcare Initiative.

Do we have any more edits to this?

[No response.]

DR. FERREIRA-GONZALEZ: Can we move to the next recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Recommendation 5 requests that HHS set up efforts to assess implications of direct-to-consumer advertising and testing and

implementation of strategies to protect consumers. We revised these recommendations to include social stigmatization and privacy concerns to potential negative impact of direct-to-consumer testing.

We also added HRSA to the list of the relevant federal agencies that should be involved in issues related to direct-to-consumer advertising and testing.

Do you have any questions about this recommendation?

DR. WILLIAMS: Again, just to emphasize that these were added specifically related to public comments. There was actually some data which will be added into the report indicating some concerns about how the information was being collected from people and that either DNA information or information relating to the types of tests that were being ordered might be available to people that purchase lists for contact and those sorts of things. That was really compelling and, to a large degree, disturbing, and that I was not aware of.

DR. TUCKSON: Again, I'm trying to remember going back to the earlier recommendations, so you will have to let me know whether there are going to be some

that will get more specific.

This just sounds very weak to me. At the end of the day, I thought we are supposed to say stop screwing with people. This is saying he should step up his efforts. We are not telling him how. Don't we need to be more specific?

I don't know [about] you all, but the stuff that I heard today on the phone worried me, by the way.

DR. WILLIAMS: I will take a shot at that. I think you are right. The challenge that we have had, and this is reflected in the gap analysis, is that it is not absolutely clear of that alphabetic list of agencies there who really should take ownership of this.

I think that you are absolutely right. What we could probably do is to add language to indicate that this is something that really needs to have specific oversight but that the Secretary has to decide which of the agencies under his or her purview is going to have the primary responsibility for this.

DR. FERREIRA-GONZALEZ: Reed, there are differences in direct-to-consumer advertising and direct-to-consumer testing. Here is geared to direct-to-

consumer advertising.

DR. TUCKSON: Right.

MS. ASPINALL: And consumer-initiated genetic testing.

DR. FERREIRA-GONZALEZ: And consumer-initiated genetic testing. But we have other recommendations that say some of these consumer-initiated are not currently under CLIA [and] CLIA needs to be, maybe, revised to see if those will be under the CLIA regulation. So we have in Chapter 4 other recommendations specific to this. Will that actually respond to some of the concerns that you have?

DR. TUCKSON: Go back and put this in context with the stuff that we continue to applaud, the collaboration between FTC and FDA. Is that sufficient here? We don't reference that, by the way, here.

We have been praising that collaborative as being something that deals with this problem. I think we should reference that somewhere, that we recognize this is going on. Then, I guess, by de facto, are we saying that that combined effort is okay and that we don't need to codify that anymore?

DR. WILLIAMS: I think the point that you made we should definitely include in the report in terms of the collaboration there. Maybe, as I look at this, what we should do is to say something more to the effect of HHS should convene relevant federal agencies, e.g., a parenthetical statement, states and consumer groups to assess the implications and decide who has oversight authority.

That is a little bit more directive than just saying "and if necessary." I don't know if that is getting at your [point.]

DR. FERREIRA-GONZALEZ: Let's go to Mara and then Paul.

MS. ASPINALL: I like the way Marc is going, but I would agree with Reed. I know it comes up later, so it may be that at the end we need to harmonize them. But I wonder if we need to be more specific and say at a minimum "to ensure that these tests are covered by CLIA and/or any future regulatory system."

DR. FERREIRA-GONZALEZ: Yes, that is a separate recommendation.

MS. ASPINALL: I know, but I guess --

DR. FERREIRA-GONZALEZ: Remember that recommendation is going to be before this one. It is Chapter 4, that recommendation.

MS. ASPINALL: Right, and we are doing it backwards.

DR. FERREIRA-GONZALEZ: Remember that.

MS. ASPINALL: I understand that it is there. I just wonder whether we need both. I don't know. I can't quite harmonize them now as we are doing it this way, but I think that if that is the case, does this really say anything that is very significant that it wouldn't just say harmonize under the one under No. 4. I'm not sure we need both from my reading to date.

DR. FERREIRA-GONZALEZ: Paul.

DR. BILLINGS: My English isn't always that good, but does direct-to-consumer advertising of genetic testing and consumer genetic testing "has" the potential or "have" the potential? That is one question I had. I'm not sure what the proper English is.

DR. TUCKSON: Anybody with a bow tie should know that kind of stuff.

MS. ASPINALL: Can I ask the fundamental

question? Do we need this recommendation?

DR. FERREIRA-GONZALEZ: Let Paul finish.

DR. BILLINGS: That was my trivial point. What I don't understand about this is, this is in a study of oversight of genetic testing and this is about direct-to-consumer advertising as it relates to genetic testing. So, one, is this genetic exceptionalism? Are we really objecting to direct-to-consumer advertising of anything to do with testing or maybe direct-to-consumer advertising in health care, potentially? What really are we trying to get at here?

DR. FERREIRA-GONZALEZ: Some of the issues that the Committee discussed are not just the direct-to-consumer advertising but it is the truth of the advertising that you do. If you are going to do advertising for a specific test and you make claims that a test is meant to [do something], then it is under the review of the FTC.

DR. BILLINGS: Does the advertising cause social stigmatization and privacy concerns? Are we saying that that is a necessary and proven result of direct-to-consumer advertising? I wonder about this.

DR. TUCKSON: One of the reasons we got to this was Francis Collins brought in this Nutraceuticals for the Millennium. Remember that one? It was this really odd, off-the-wall thing.

Now, Steve, I don't know. In the collaboration between FDA and FTC, do we now know based on all this kumbayah that we have been describing earlier for the last two meetings about what is going on between FTC and FDA -- so you have the answer.

MS. CARR: I just wanted to point out that the Office of the Secretary is actually getting the agencies together to do more collaboration. They are having another meeting in a couple weeks. I think FTC's Matt Daynard is going to be participating in that meeting. CDC. NIH is involved.

DR. TUCKSON: That is helpful. Let me just ask you real quickly. Because we have given you all this praise about you all coming together and doing things together, is the problem solved or is there something else that needs to get done?

DR. DAYNARD: Addressing the problem is just beginning, of course. But I think it is important to

note in the recommendations that the collaboration is working and HHS needs to ensure that it continues to work.

As far as it goes, the advertising issue is going to be additionally addressed not only by the FTC, and I will let Steve respond to this also, but [by the FDA.] If the FDA decides that it has jurisdiction and in its discretion will pursue, for example, that some proprietary software is a medical device, it therefore will have jurisdiction over advertising as well, and it will make the collaboration even more important.

So I do think it is important to have something like this definitely in the report, but HHS should do what it is doing.

DR. TUCKSON: I hear uncertainty about whether or not they have oversight or not.

DR. DAYNARD: I can't speak for the FDA.

DR. FERREIRA-GONZALEZ: Steve and then Paul.

DR. TEUTSCH: I think one of the concerns is how strictly should this be regulated. I think part of the concern is, and we have talked about it with FDA, if they are health-related there is a higher bar than normal

for most types of advertising. But like what we have heard earlier from 23 and Me, if they don't even consider this health-related, then why would FDA regulate it?

We recognize that all of this has potentially substantial risks and there needs to be oversight of the advertising at a higher level than you might otherwise for routine consumer products.

DR. FERREIRA-GONZALEZ: If this health-related testing comes under CLIA or the FDA, some of this advertising will be dealt with through that realm.

DR. TUCKSON: But if the manufacturer can self-declare. If I decide, hey, you know what, I'm just having a good time. This ain't really about health. Then you can't regulate me. I have decided to take myself voluntarily out of it, but I didn't take myself voluntarily out of selling this thing to people.

DR. FERREIRA-GONZALEZ: We need to start coming back. Mara and then Marc.

MS. ASPINALL: My point is simply just what Reed said: to make sure that everywhere we do this, and again I'm not convinced we need two separate recommendations, that we make it clear that both the

advertising and, more importantly, the testing itself needs to fall underneath some regulatory umbrella.

DR. FERREIRA-GONZALEZ: Marc.

DR. WILLIAMS: The language that I would propose, given what I'm hearing, is that we could say that "The Committee recognizes the ongoing efforts of collaboration to address these issues. We ask the Secretary to explicitly add direct-to-consumer advertising for genetic tests and consumer-initiated genetic testing as issues for consideration by this collaborative and would request an update about the issues for further deliberation," or something to that effect.

DR. TUCKSON: Let me give you a counter one, just to play devil's advocate and try to find some way to polarize you so you make a decision.

"The Committee is concerned at the public being preyed upon by unscrupulous people who will market their products to an unsuspecting public that is ill prepared to understand some of the complexities of these things and who can be harmed as a result. Therefore, we recommend to the Secretary immediately conclude the

effort that we understand is underway to determine jurisdiction between the FTC and the FDA," and anybody else that has to be done, "and that you report back to this Advisory Committee within six months as to the answer so that the fundamental purpose by which we were convened is dealt with." Thank you. No fooling around.

DR. FERREIRA-GONZALEZ: Paul.

DR. MILLER: I think this is a really important conversation. The only thing that I would add is that I think it is really important, given the intensity of the feelings around this table about this issue, that we come up with something that is concrete, directed, and an action item to recommend.

Anybody who has been around the block in Washington knows any recommendation that basically says you should convene a group and talk about it some more isn't really a recommendation. To the extent that we actually can come up with something concrete to say to move the Secretary or move the process along that is a deliverable, I think that it is time well spent to come up with drafting one such deliverable.

Reed, you came up with an idea, a soft idea,

but maybe we can make it a little harder.

DR. DAYNARD: I just had a suggestion that if you do keep this recommendation you change the word "advertising" to "marketing" because the FTC's hook is advertising and only advertising. Our charge is not the safety of the American public as it would be the FDA. You are talking about broader than just advertising. You are talking about bringing this test to market, which involves the FDA and CMS, et cetera.

DR. FERREIRA-GONZALEZ: Do we want to work a little bit offline on recommendation language for this? Mike.

DR. AMOS: I just had one comment on Reed's strawman recommendation where you said "and do harm." We have to have data to back that up.

DR. TUCKSON: Potential.

DR. AMOS: Because I don't see where the information that comes from this type of thing would potentially be any more harmful than somebody making a health decision based on some Nutraceutical advertisement. You have to differentiate. You have to really clearly support that with data if you are going to

say we are thinking it is doing harm.

DR. TUCKSON: Or the potential thereof.

DR. AMOS: It has to be stronger than that. If you are going to make a recommendation this strongly, then you really have to have something to back you up that says there is really harm being done.

DR. FERREIRA-GONZALEZ: Marc.

DR. WILLIAMS: Well, the specific issue that came up that really crystallized this for me was this. If somebody sends in a cheek swab because they want to look at diabetes susceptibility testing or something of that nature, there is evidence that those [lists of those] individuals that are tested for potential diabetes susceptibility are being sold to people that are marketing diabetic devices and other things.

Now, they would characterize that as providing information to consumers who really espouse a need for it, but I'm not sure that on the front end when the person is sending in that cheek swab that they have been adequately informed that this information is going to be used to basically target them.

Again, you can define that as harm or not, but

I think there is some evidence that that does in fact happen.

DR. DAYNARD: If you have such information, Marc, I would certainly like to know about it.

DR. WILLIAMS: I will see if I can pull it together.

DR. FERREIRA-GONZALEZ: Focus on what we need to actually make recommendations. What are we going to do with this recommendation.

MS. ASPINALL: I guess I wanted to get to Marc's example because I think the bigger harm comes from the test is wrong and somebody says they don't have diabetes susceptibility and therefore they go about doing higher risk behavior rather than selling the advertising piece, which I understand is harm. But from the health perspective, I think it is focused on that piece.

So I come back to what Reed put together to take a stronger stance on saying, one, that HHS needs to take some action; two, that all tests that are direct to-consumer must be covered by the current regulatory environment. We may not want to deal with that here, whether it is CMS or FDA or otherwise, but I think that

we need to take that stance.

If you look at some of the public comments, I think there were at least six of them, in my quick tallying, that also said exactly that, that we need to have stricter regulation around direct-to-consumer testing.

So I'm not quite with the wording Reed had, and maybe we can take that offline, but I'm pretty close.

DR. FERREIRA-GONZALEZ: Cathy.

DR. FOMOUS: I think a lot of the suggestions that I have heard are really terrific, but in my mind, they seem to apply more to our recommendation in Chapter 4. So I'm thinking maybe we can think about that wording and apply it to the recommendation in Chapter 4.

I actually have a question for Marc for this recommendation. When I read it, my impression is that you are saying there is a gap in what we know about the impact of all of this. We are making some assumptions here and we don't have the knowledge to really know what kind of impact direct-to-consumer marketing and testing has on consumers.

In my mind, that is what this recommendation is

trying to get at. Are there harms being done. That will guide us going forward. What are the positive aspects of this type of testing and what are the negatives.

So to me, the recommendations were very different, and a lot of what I have heard really applies to what we have in Chapter 4.

DR. FERREIRA-GONZALEZ: Sarah.

MS. CARR: I just want to add to that that this recommendation in the way Cathy just expressed it, if that is the intent, has been the Committee's position for several years. In an earlier letter we called for more data on the public health impact. CDC has been working on that. We heard last July or November an update from CDC on its work. So that does seem to be what we are after here.

There is also a role for the states -- Judy Yost can speak to this better than I -- in terms of who can order and who can receive test results. I don't think it is solely a federal matter as to what the regulatory scheme would be in this area.

Then I also think we have, from a regulatory standpoint, addressed it more in Chapter 4.

DR. FERREIRA-GONZALEZ: We have Paul, Gurvaneet, and then Reed.

DR. MILLER: To the extent that we have gone around and around, I think the issue is on the table. I think that where we are is to basically have an offline conversation to look at Recommendation 4 vis-a-vis this, see if it can be collapsed together, and then maybe come back tomorrow.

DR. FERREIRA-GONZALEZ: It is going to be covered in No. 4.

DR. MILLER: Yes, exactly.

DR. FERREIRA-GONZALEZ: Maybe we need to tweak No. 4 a little bit. I think we need to keep in mind some of the issues you are bringing up.

DR. TUCKSON: If I can just add one thing, if we are going to do that. I think that is rational. Could I just get two seconds of a summary of the collaboration between FTC and FDA that we have been talking about so far? Just tell me what is it that you all are doing. What area are you working on?

DR. GUTMAN: Aside from the public advisory that we put forth, actually I can't comment on anything

else that we might be doing.

DR. TUCKSON: Can you remind us of what the advisory said?

DR. GUTMAN: It said that these are unsubstantiated tests and you should beware. It was made as public as we possibly could.

DR. TUCKSON: Matt.

DR. DAYNARD: That is accurate. I think we can say that the FTC is looking at the area specifically to see whether there are representations being made about genetic test services that warrant pursuit in investigations.

MS. CARR: And you are relying in FDA.

DR. DAYNARD: In part, yes.

MS. CARR: In part. There has been that exchange, maybe not recently, but where you were providing --

DR. GUTMAN: No, it is ongoing. You would be surprised at how clever the feds are at communicating with each other.

DR. TUCKSON: When we get to Section 4 we will revisit it, as Paul said.

DR. FERREIRA-GONZALEZ: We can look at Recommendation 4 in the next piece and have it right on the side.

DR. TUCKSON: Yes, we can do that. I just want to make sure I'm summarizing what I'm hearing for when we get there, and then we can get off this.

DR. GUTMAN: Not that we have even been specifically named. I know how horrifying it is, the thought that we might actually regulate. But this is, from FDA's perspective, very nuanced. I think there are legitimate things here which are medical devices and which have implicit enough or explicit enough claims that drive you to think they are medical devices.

I think in this universe there is stuff that we wouldn't, under our current statutory definition, call medical devices. I don't know that Judy's group would call everything. I won't mention any, but gender identification tests are not, from either CMS or FDA's perspective, currently medical devices.

DR. TUCKSON: So we have a big gap in understanding. Then the FTC point of view, Matt, you just made. You made an explicit point earlier. Define

the limits of your purview?

DR. DAYNARD: With genetic testing, as with any product out there, health care-related or not, it is what the advertising claims and whether they have competent and reliable scientific evidence in relation to health care advertising to support what the claim is. It doesn't matter what the device is, what the product is, what the service is. It is all the same.

DR. TUCKSON: When you go after them, or when you investigate because you are concerned about the scientific validity of their statements, where do you go to get that answer of the science?

DR. DAYNARD: I'm a lawyer. I make it up.

[Laughter.]

DR. DAYNARD: Just kidding, just kidding. I go to Steve Gutman and his staff and I go to private experts and I go to NHGRI.

DR. TUCKSON: I want to be disciplined and nail it. At the end of the day, it doesn't matter whether or not FDA has oversight over it. You can go to them and say "I want to understand the science of it." Then they say, "I will tell you what we understand about the

science," whether or not it is in your regulatory purview or not. You are providing a consultative science opinion to the FTC. So you are good as long as it is about advertising.

DR. DAYNARD: Absolutely. We do coordinate.

DR. TUCKSON: You are not good on, you said, marketing.

DR. DAYNARD: To the extent that it is something other than advertising, that is correct.

DR. TUCKSON: Thank you. Did everybody sort of begin to understand something about the fact base?

DR. BILLINGS: Can I ask one other question about the fact base? So, aside from the advisory which has been referred to, have there been specific actions against companies in this area?

DR. DAYNARD: Nothing public. All investigations that we might have are non-public. So unless my next phone call will be from a jail cell, I have to tell you that.

DR. FERREIRA-GONZALEZ: We need to start wrapping up this and move forward. Mara, you have a comment. Then Gurvaneet.

MS. ASPINALL: I guess it is a placeholder to come back to Steve's comment about the current regulations of CLIA around health-related testing because the gender issue is a very interesting one, as I understand, not regulated as health. But we know families are using that to look for X-linked diseases. So while gender in and of itself may not be health, it is being used very much in a health-related way to make determinations around a pregnancy. So I think we need to reevaluate that.

DR. FERREIRA-GONZALEZ: That issue is in Chapter 4. Gurvaneet, and then we are going to move forward. We are going to leave the way we are currently the recommendation. After we review the recommendation in Chapter 4, we will look at this right there.

DR. RANDHAWA: Thanks. This is sort of responding to Reed's albeit provocative contrarian here. I'm not a constitutional scholar or legal scholar by any means, but the concerns that I heard here were more public health, health outcomes, whereas I don't see any mention of health or public health in that paragraph at all.

So whether it is gender testing, whether I came from India or if I have genes from Africa, paternity testing, nothing is there to help per se. I don't know to what extent this Committee or HHS will be regulating that.

To some extent, I think that is part of the constitutional right, is for a person to make their own determination of what is harmful and what is not. So I think we should be careful how we frame this and not be overstepping and thinking of a very broad definition here.

DR. FERREIRA-GONZALEZ: That is a very good point.

DR. TUCKSON: We will need to be very attentive again on one of the criticisms that we had of the first draft, how we define the word "genetic testing" as it relates to this function, and what is in and what is out.

MS. ASPINALL: And health-related testing. We may want to suggest a new definition.

DR. HANS: We said earlier we would take a look at this map when we are doing this. I would just say, if we are going to be redrafting, look at the map and which

knowledge gap this is supposed to be attached to. We seem to have drifted.

DR. FERREIRA-GONZALEZ: We are moving to Chapter 5, Recommendation 1. It calls for HHS to create and fund a public-private entity to assess the clinical utility of genetic tests. We revised this recommendation to include examples of evidentiary standards and levels of certainty for different situations, and we also added data from electronic medical records as a source of data for research.

Part B of the recommendation calls for the development and funding of a research agenda that will address gaps in knowledge of analytical validity, clinical validity, and clinical utility on population health impact of genetic tests. The only revision in Part B involved movement of a section to Recommendation 1 in Chapter 6.

Do we have any questions about this recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Any edits?

[No response.]

DR. FERREIRA-GONZALEZ: Can we move on to the next recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Recommendation 2 for Chapter 2 requests HHS to act on recommendations in the 2006 Coverage and Reimbursement of Genetic Tests and Services and asks public and private healthcare payers to develop mechanisms, such as coverage with evidence development or phased reimbursement, to facilitate the collection of clinical utility evidence for high priority tests and applications.

We revised this recommendation to include determining whether mechanisms to collect clinical utility evidence enhance or hinder innovation, understanding of effectiveness, and proper utilization.

Do we have any questions for this recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Do we have any edits?

DR. TUCKSON: I'm just trying to understand, re-reading it again cold now, the recommendation "to continue." Public and private healthcare payers should

develop mechanisms, such as coverage with evidence development or phased reimbursement, to facilitate the collection of clinical utility evidence.

I'm not following the trail here. We are saying we want to collect information of clinical utility evidence through reimbursement.

DR. FERREIRA-GONZALEZ: Steve.

DR. TEUTSCH: This is really an extension of what CMS has proposed to allow innovative products to get on the market and that there be a process that, if they agreed to get paid for it, that there will be evidence collected along the way so that we will know about the clinical utility and a subsequent final decision can be made. It is a way to try and get the evidence generation underway for some of these technologies. It is just a mechanism.

DR. FERREIRA-GONZALEZ: James first, and then Muin.

DR. EVANS: This is also known as conditional coverage, right? It is a potentially important mechanism to try to prevent the bar being so high in terms of clinical utility -- which we don't have for 90 percent of

what we do in medicine anyway, right? -- before things get covered. It is a chicken and egg issue.

DR. TUCKSON: It is basically saying we are encouraging coverage even when the evidence is not there. By the way, once you cover it, we can then have a larger base of evidence upon which to make further decisions. It looked like it was saying we were going to solve the evidence problem by covering.

DR. FERREIRA-GONZALEZ: If you don't actually cover, the tests will not be offered and we can never get to the point.

DR. TUCKSON: With a little language tweak we will be okay.

DR. FERREIRA-GONZALEZ: So I have Paul.

DR. BILLINGS: Was this meant to be only for high priority tests and applications, or is this a general recommendation?

DR. FERREIRA-GONZALEZ: I think it is a general recommendation but we thought that maybe starting with the high priority first.

DR. BILLINGS: And then, does the last sentence again add more barrier, essentially? You are saying that

they ought to look at effectiveness and utilization and the hindrance or fostering of innovation. Does that sort of muddy the water, essentially?

DR. TUCKSON: What it definitely leaves unsaid in this recommendation is any mechanism of who pays for the collection, where does it sit, who houses it, how do you do it. It is a muddy issue, and I think it is something we have to attend to here.

Muin used to argue a lot, I think, for CDC being the place where you put the money for post-market surveillance. This is the same sort of deal here. It is sort of hanging out there.

DR. FERREIRA-GONZALEZ: Marc.

DR. WILLIAMS: As we discuss this in the report, there are some examples. Again, I think that if you get to Paul's point, there are different levels. For the ultra-rare tests, a program like the SET program has been brought forward through the CDC. The intent there is that we may never get the amount of evidence that we would like to have to meet a bar, so this is a process by which we are going to actually encourage these tests coming to market with the express intent and funding for

collection of that evidence.

I think on the other end of the spectrum you have something like, let's say, a pharmacogenomic profile for Warfarin where the impact on that is potentially for hundreds of thousands of people, where I think you could reasonably expect utility studies to be done before that test is introduced into the marketplace.

Then, in the middle ground might be something like has been done with the Children's Oncology Group where you are dealing with a collection of things that are somewhat rare and the only way to collect sufficient data -- and in the genetic realm probably newborn screening is a good example of this -- is to collect it under sort of a consortium arrangement. But all payers are covering for children's oncology knowing that that data is being collected and we are learning new things from it.

So I think that this shouldn't be looked upon as a "one size fits all" and maybe we need to tweak it to reflect the fact that different models may be appropriate but that the intent is that we don't want to just set a high bar so that most things don't come to market or a

low bar so that everything comes to market and we don't learn anything.

DR. TUCKSON: But at the end of the day, what this recommendation basically winds up is putting the onus on public and private payers to develop the mechanism for creating the information, organizing it, and doing something with it. I just don't see how that is going to happen.

DR. FERREIRA-GONZALEZ: Steve.

DR. TEUTSCH: I don't know that they actually have to do the evaluation. For instance, one of the examples that CMS had was for lung volume reduction surgery for emphysema. They agreed to pay for the procedures as long as it was part of a clinical trial so that at the end of the trial we would know whether that was an effective procedure and there was something learned about exactly who benefitted and who didn't.

In fact, in that case it was a fairly limited amount of benefit for a very selected group. They continued to pay for that group, but essentially nobody availed themselves of that service.

But it is for a high priority. You can't do

this for very many things. So it is for a fairly selected number that you would think are likely to be of important public health or economic impact.

DR. FERREIRA-GONZALEZ: Mara and then Muin.

MS. ASPINALL: I agree with what Steve said in terms of looking at it, but I think, as Reed said, there is no mechanism to do it now. I think the challenge is laboratories themselves can't do it because the fundamental piece of this is looking at outcome data and laboratories don't have access to outcome data.

In the report itself, that is implied in the fuller piece of the text. Maybe we can bring that out in the recommendation. I haven't formed the words. But I think it is important to acknowledge this is not just shifting the burden but there has been discussion about laboratories doing this sort of evidence under HIPAA regulations and which otherwise laboratories cannot do.

So I think there is a reality here that needs to be at least acknowledged that this is not an optional thing. If we want to get this data, payers have to be part of the system. If you believe one of the things we have talked about in the pharmacogenomics report, this is

not just for academic purpose. These tests will actually reduce inappropriate care and reduce cost for the system. So there should be enough incentives for payers to want to do this.

DR. FERREIRA-GONZALEZ: Muin.

DR. KHOURY: I think this is a complicated issue. Maybe we should put Recommendation 1 and Recommendation 2 together.

DR. FERREIRA-GONZALEZ: I was going back to that.

DR. KHOURY: Part of the current dilemma, which I call the evidence dilemma in genomics, is that clinical utility is the last information that is to be collected. Many payers won't pay until you have clinical utility. If you don't pay, you don't get tested. So it increases disparity and discourages development of new applications.

So if there is a public-private stakeholder group that would come together and oversee these discussions, so to speak, and then set the parameters for what is enough to meet a certain threshold beyond which you move a certain application from being research to

being conditionally covered under a controlled research and practice environment in which you do those clinical trials.

Obviously you can't do it for everything, and the payers shouldn't pay for everything. It has to be a shared burden between the public and the private sector.

That is part of our dilemma right now. The clinical utility piece is missing for most genomic applications in practice, but you need at least a good analytic framework, good clinical validity, and proficiency testing. Then if there is enough biologic plausibility, perhaps a few applications can move. Certainly for rare diseases, if you don't do that, the rare disease environment is not going to be implemented.

So at least there is a process for the rare disease environment to be done, but for the common genomic applications, we are still struggling with where to draw the bar. Where do you put the threshold. I think, putting it with Recommendation 1 to work together with Recommendation 2, we can make more progress.

DR. FERREIRA-GONZALEZ: I think in Recommendation 1 we already recommended a sustainable

public and private entity of stakeholders to assess the clinical utility. So this will fall within the clinical utility of the test where you add these other things of evaluation of the clinical utility by providing additional issues of payment with condition of payment and so forth.

DR. TUCKSON: I think that would be good. If we can roll this in with No. 1, that is good. I will tell you, I have sat on too many IOM groups and every kind of group you can think of where all the health plans and CMS are sitting around trying to figure out who is going to pay for these kinds of essentially health service research types of initiatives.

We finally, after a lot of effort, just got this Center for Comparative Effectiveness funded, which was an enormous effort. It is funded. It is funded at like a toe in the water level, but they didn't get where they need to go.

So my point only is that we have been through this a bunch of times. This is that again. If we don't say that CDC or AHRQ is going to step up and be the agency to pull this doggone stuff together, then you are

not going to get it. Maybe you can roll it into the first one where we say there needs to be this whole group that actually gets funded to do several specific things, one of which is this.

DR. FERREIRA-GONZALEZ: Steve, do you have any comment on that?

DR. TEUTSCH: In my own mind, these are quite separate things. The first one creates the public-private group that is actually going to develop a lot of the information. This one actually harkens back to the reimbursement issues and the need for evidence on utility by payers. Then the question is, what do they do, and how do we begin to make those things work.

That seems to me a little bit different. I don't know that we would include this reimbursement stuff in the first part of this recommendation.

DR. FERREIRA-GONZALEZ: The reimbursement fits from the data that will be generated from this public-private partnership in developing the infrastructure to evaluate how you determine the clinical utility. So this will be, maybe, another component of that group, kind of the back end.

DR. TUCKSON: So we are going to pick a couple quick ones. Again, it is a little dangerous to keep postponing things, but I think we are talking about trying to see if we can, with an appropriate bridge ala Steve's comment, lump this into No. 1.

The one thing you have to be doggone sure is you can't call for too many separate funding things in this report given that the government ain't got diddly-squat in terms of money left.

DR. FERREIRA-GONZALEZ: I think we have Mara and Gurvaneet.

MS. ASPINALL: I agree with Reed. We can't ask for too many, although I see it Steve's way. I think it should be kept separate because it is specific to the reimbursement area. I don't think we lose anything to have it separate. We are not asking for any more. Recommendation No. 1 is a particularly lengthy one. So I think it gets lost in the midst of No. 1. Leave it as a separate one.

DR. FERREIRA-GONZALEZ: Then, would you want to recommend the creation of a stakeholders group for this?

DR. TEUTSCH: This is just talking about

mechanisms. It could vary by payer. It doesn't need a stakeholder group.

MS. ASPINALL: I don't think so. To me, it stands on its own. It is all part of No. 5, and it is highlighted separately and will get more focus this way. We are not asking for any more or less money by combining it. So I would leave it.

DR. FERREIRA-GONZALEZ: Gurvaneet.

DR. RANDHAWA: I think it is useful to combine the comments that have been made before for the purpose of the public-private entity that establishes an infrastructure. That is certainly one recommendation, and this is a different recommendation which focuses on the actual implementation of research for different tests that we are thinking about. The question then becomes who exactly is going to be paying for it.

Reed's observation did resonate with me that there is no need just for the payers alone to have the burden of being singled out here because what we have been discussing so far is where we stand right now in our infrastructure. The clinical labs don't have access to the outcome and to pay also from the payers. But that

isn't really true if you are thinking about electronic health records being used more often and the capacity of collecting de-identified data that is pretty rich in outcomes as well as lab information.

Although we are not there yet, AHRQ has already funded two projects on the Distributive Research Network Initiative, which is actually doing the same thing, looking at electronic health record-based information which resides in different databases, perhaps clinical labs, prescriptions, or in hospitals.

So I think where we go in the future, there may be more entities than just the payers alone that can fund these kinds of special research topics and not just focus on one group.

DR. FERREIRA-GONZALEZ: So, your recommendation, then?

DR. RANDHAWA: My recommendation actually would be it would be useful to have it in a separate recommendation but add not just the healthcare payers but other folks who may be interested in clinical utility to make use of the mechanisms that we are constructing in the first recommendation.

DR. FERREIRA-GONZALEZ: I think there is a sense in the Committee that we will leave the recommendation as is, adding some of the changes that Gurvaneet has just recommended. Do we want to work on the wording now? Do you want to add, Gurvaneet, the edits?

DR. RANDHAWA: Give me some time to work on it.

DR. FERREIRA-GONZALEZ: We will do it during the break. Just keep a tally of who is doing what during the break.

So, are we ready to go to the next recommendation? Recommendation 3 requests that HHS conduct public health surveillance to assess health outcomes, surrogate outcomes, practice measures, and the public health impact on genetic tests. We did not make any revisions to this recommendation.

Do we have any questions about this recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: Do we have any edits?

[No response.]

DR. FERREIRA-GONZALEZ: Let's go to

Recommendation 3, the first part of Recommendation 3.

DR. TUCKSON: So I guess as the flow goes forward, is this different than stuff we have already talked about? Haven't we talked about this? What is the difference here?

DR. TEUTSCH: It is certainly similar to the one we stuck at the end of No. 6 that we talked about before. This is really using surveillance to make sure that the utility is realized.

DR. TUCKSON: I thought we already did this.

DR. TEUTSCH: The other option is to do what you suggested and get rid of the sentence that we added in No. 6 where we had some disagreement and leave this one, if you would prefer that.

DR. FERREIRA-GONZALEZ: The idea is to look at the one in Chapter 6 and this one in Chapter 5?

DR. TEUTSCH: Isn't that what you are referring to?

[Pause.]

DR. TUCKSON: Which one are we on?

DR. FERREIRA-GONZALEZ: I think it is 6-1. Yes, it is 5-3. How about 6-1? 6-1-B. We talked about

this and we added that.

DR. TEUTSCH: That's right.

DR. FERREIRA-GONZALEZ: That is where there is redundancy, because we added this.

DR. TEUTSCH: If you take that out there, you can leave the one in No. 5 because it has more specificity. A little bit more.

DR. TUCKSON: Do they have to be in different places?

DR. FERREIRA-GONZALEZ: No, they don't have to be in different places.

DR. TUCKSON: Let's keep them together because you will make the reader crazy.

DR. FERREIRA-GONZALEZ: No, no. We are talking about deleting this part of Chapter 6, Recommendation 1, the part we added. So Chapter 6-1, Part B, there is an overlap with Chapter 5, Recommendation 3. The reason is because we added some of the language to this.

I think we need to decide to do we keep it in 6-1-B or we keep it in 5-3. Marc.

DR. WILLIAMS: Actually, to speak to Reed's point, I think that what we could do here is if we keep

this recommendation from No. 5-3, Recommendation 3, Chapter 5 in, then we can basically just in 6-1-B say we reference this recommendation, the recommendation in Chapter 5, Recommendation 3. Just say we need to have that information provided for translational purposes, and then that's it. It does refer to the quality improvement piece.

DR. FERREIRA-GONZALEZ: Exactly. So, do we want to make changes to this one, then?

DR. FOMOUS: Do you want to start with the changes here first?

DR. FERREIRA-GONZALEZ: Yes.

DR. WILLIAMS: Just get rid of the last sentence and cross-reference. "See also Recommendation 5-3."

DR. FERREIRA-GONZALEZ: We are going to do the cross-reference to the recommendation in Chapter 5. Now we have dealt with the overlap. Going back to Chapter 5-3, do we have any edits for this one?

PARTICIPANT: Excuse me. Did you lose a little bit on the availability of the data with that deletion? I think that last sentence spoke to making sure that the

data was clearly available for people's use. I don't think 5-3 specifically states that. It almost, I would think, worked out to take that last sentence and actually move it as a clause to No. 3 under Chapter 5, Recommendation 3. Make it one, two, and three. Or put in some statement about ensuring that the data is available.

DR. FERREIRA-GONZALEZ: Steve.

DR. TEUTSCH: This just gets into the definition of surveillance, which is the collection, analysis, and dissemination of data to those who need to use it. What I'm hearing from Greg is that may not be the definition that is widely understood. So if you feel there is a need, you can include it.

DR. FERREIRA-GONZALEZ: So, Steve, what you are saying is it is already implicit?

DR. TEUTSCH: I think it is there. It is in the standard definition of surveillance that is used. If it needs to be clarified, you can add something, but it is there.

DR. FITZGERALD: That can go in the text, right?

DR. FERREIRA-GONZALEZ: Yes. So we can put this in the text.

Can we move to the next recommendation? Chapter 5, Recommendation 4 asks HHS to advance appropriate use of interoperable patient-level data for research and to enhance the quality of decision-making. We revised the recommendation to include implementation in the efforts to advance the use of interoperable patient-level data.

Do we have any questions about this recommendation?

DR. TUCKSON: The only challenge we have is AHIC is in a transition mode and will not exist under those terms, I don't think, by the time this comes out.

DR. FERREIRA-GONZALEZ: Is there an AHIC 2?

MS. ASPINALL: Why not.

DR. TUCKSON: They are moving to a public-private partnership. What you might want to say is "SACGHS and AHIC (and/or its successors)".

MS. ASPINALL: Yes.

DR. WILLIAMS: Cathy, just to fix the parentheses problem there, take out "particularly." Lose

those two parentheses, take out "particularly," and say "and other workgroups addressing," and then lose beyond. Leave the close parentheses after "successors." Then get rid of that line.

DR. TUCKSON: Move it. That works.

DR. FERREIRA-GONZALEZ: So, can we move now to the further recommendations? Are we done?

What we are going to do now, before going into Chapter 4, Recommendation 1, we are going to have public comments.

DR. TUCKSON: Are we?

DR. FERREIRA-GONZALEZ: I'm sorry.

DR. TUCKSON: Comments from who?

DR. FERREIRA-GONZALEZ: We have completed two chapters, going through them. We have to go back. Yes, Muin.

DR. KHOURY: My only plea to the group is to try to [keep in mind], after we take a look at all the recommendations, even if we implement all of them, how far will they fix our current broken system.

DR. FERREIRA-GONZALEZ: After the break we might go back to see the map. Sherrie was telling us to

keep that in mind.

We had earlier mentioned our steering committee added experts and ex officio members that had specific expertise to form the taskforce that worked through the entire document. Throughout the development of the document we have been tapping back into the knowledge of the different taskforce members to seek their advice continuously.

So as we go through also the review of the public comments in going back to changes and edits to the text and the recommendations, we will also seek the advice of the taskforce members.

Again, to give them another opportunity to provide input directly to this Committee, we have invited all the taskforce members that might have comments to the public comments or any changes that we have made to the report to come and talk to you and tell us about what they feel about the current state of these final recommendations and the draft.

One of our taskforce members took us up on that offer and decided to come and address the Committee. We are looking forward to Kathy Hudson providing us some

comments.

DR. TUCKSON: So in addition to those centering comments, we are very excited that Kathy wanted to come and present some comments. We know that the areas of her comments are germane to where we are getting ready to go. Therefore it seemed to make sense to stop what we are doing here and get those comments as we now proceed through in an orderly way the rest of our agenda.

So, good. Thank you.

Comments by Kathy Hudson

SACGHS Oversight Taskforce

DR. HUDSON: My name is Kathy Hudson. I'm the director of the Genetics and Public Policy Center at Johns Hopkins, and I was honored to be asked to serve on the Oversight Taskforce. I really want to commend the Committee for its expeditious work in moving through all of the issues that were included in the final recommendations, and I appreciate your endurance today as you work through all that.

I particularly want to acknowledge the incredible work of Sarah Carr and Cathy Fomous, who have worked tirelessly to pull this together.

I would like to comment on three issues that are raised in the recommendations and comment on those. First, the recommended enhancements in the CLIA, the Clinical Laboratory Improvement Amendments; secondly, the recommendation for a registry; and third, say just a word about direct-to-consumer genetic testing. I recognize that the revised recommendations haven't yet been discussed, so this is a little bit of a challenge.

In the draft report for public comment, the taskforce recommended an expansion of proficiency testing and not the creation of a genetic testing specialty. You heard from some of the public this morning that there are still a number of people who are interested in the creation of a genetic testing specialty.

A specialty is a framework that was created by CMS in order to implement CLIA, and currently, it is really the only way that CMS has of putting in place new proficiency testing requirements. But the statute certainly doesn't require that, and it is not the case that the creation of a specialty necessarily would require that laboratories perform PT.

Previous advisory committees have attempted to

work within the existing CLIA specialty structure and have made recommendations over the years to create a genetic testing specialty. I think the taskforce was correct in ascertaining that the thing that we really want is more proficiency testing and therefore let's just move outside of this framework and get to what we really want, which is PT.

It has also been clear over the last year that CMS does not want to create a specialty, so banging your head on that particular wall again may not make much sense.

We strongly support the revised recommendation that requires that laboratories that are performing tests for which a CMS-approved PT program exists should be required to enroll. The key issue there is going to be what PT programs does CMS in fact approve, and there may be some devil in the details there, but I think this will go a long way. There will be a market to create PT programs for tests that are offered on a widespread basis.

Implementing this recommendation will require changes to CLIA regulations, which will of course be

subject to public comment before they are finalized. We believe these changes are straightforward. In fact, we have drafted a model regulation that would fulfill both the requirements of the report and we believe avoid concerns about genetic exceptionalism that have been expressed in public comments. We would be happy to share that model MPRM with the Committee.

DR. TUCKSON: Excuse me. Before you go further, just so we are hearing you clearly, who is "we"?

DR. HUDSON: "We" is the Genetics and Public Policy Center.

DR. TUCKSON: Genetics and Public Policy Center.

DR. HUDSON: Is "we," yes. I'm speaking of my role as a member of the taskforce but also as --

DR. FERREIRA-GONZALEZ: When you are here, you are here as a member of the taskforce.

DR. HUDSON: Okay. I will try to differentiate between me and "we" and "they" and "us."

[Laughter.]

DR. HUDSON: The second issue I would like to address is the recommendation to create a genetic testing

registry. The draft report included a recommendation for the creation of a voluntary registry, perhaps as an extension of gene tests. As Mark Smith of the California Healthcare Foundation has said, there is no such thing as a voluntary universal anything.

The taskforce and the steering committee clearly reviewed those comments, where a majority of the people who made a comment about this issue recommended that the registry be mandatory. I think the taskforce has responded to those public comments. So that is an important addition.

Several commenters have urged that the registry be housed by and managed by a federal regulatory body, and in considering what agency should have lead responsibility, a number of key issues have been raised. I think this is where, probably if the taskforce had had more time, we could have gone into these issues in greater detail.

What functions are going to be carried out by the registry. Will they be facilitating data submission. Will they be involved in any quality control. Will they have a stick with which to demand that data be submitted,

and will there be penalties for non-compliance. These are issues that still remain but certainly that the Secretary has the authority to put in place.

The other question that has been discussed is whether the various agencies or the Department in toto has sufficient authority to require the kinds of information that are envisioned to be within the registry. It is important to recognize that many of the authorities that the agencies have are actually authorities that are held by the Secretary and he delegates them down. So it may be possible for him, the Secretary, to use some creative redelegation of authority to get the job done.

In the discussion of the taskforce of what agency would be the most appropriate home, there was lively conversation. In one iteration, CMS was indicated to be the appropriate home for this registry because they already do collect some information, although as somebody mentioned, it is difficult to retrieve that information.

It is certainly possible for the Secretary to figure this out and for this Committee to punt to the Secretary and not name a specific agency, but I think

wherever this registry is housed we should look for an agency that has documented experience and expertise in creating and running publicly accessible registries.

So FDA certainly has lots of experience in maintaining publicly accessible and useful databases. CDC maintains a number of registries. NIH manages huge numbers of publicly accessible databases that allow timely and easy access to trillions of pieces of interlinked information.

If I am speaking as a taskforce member, I might not then be able to share comments on DTC, some of which grew out of the conversation that just preceded, so I will take guidance from the chair.

DR. FERREIRA-GONZALEZ: You are here as the taskforce member.

DR. HUDSON: Fine. I will withhold my comments on DTC. I would like to make one point, though, that in the map that was put up where it had a separate line for DTC non-CLIA certified, that the CLIA statute applies to laboratories that are providing assessment of health irrespective of how they are marketed. So I don't think there is a distinct pathway there. I think that may be

misleading.

DR. FERREIRA-GONZALEZ: That line is specific, and maybe we need to be more clear. It is for direct-to-consumer advertising by laboratories that claim they are not under CLIA regulations and they can directly market these tests or offer the tests to the public.

DR. HUDSON: So that is a problem in enforcement. There is no permissible pathway.

DR. FERREIRA-GONZALEZ: Exactly. That is why some of our recommendations are going to deal with that specific issue.

DR. TUCKSON: Great. First of all, thank you for your comments. They are very helpful, and we are going to move right on. If you will sign up for the public testimony part so we can get your DTC stuff in, that would be great, Kathy. Thank you.

All right. Let's move right into the next section. We are going to really move.

Discussion of Final Recommendations (Continued)

DR. FERREIRA-GONZALEZ: Chapter 4, Recommendation 1. Recommendation 1 in Chapter 4 proposes steps to support and augment the CMS action plan in lieu

of the CLIA genetic testing specialty. We revised Part A of this recommendation to call for CMS to require proficiency testing for all high complexity tests for which PT products are available. We did not revise Part B or C of these recommendations.

So, do we have any questions about this recommendation?

MS. TURNER: Just a reminder comment. With the change of "cannot be achieved immediately," there is a "may" before "cannot." I imagine that "may" should be deleted.

DR. FERREIRA-GONZALEZ: Thank you.

DR. TUCKSON: So this is back to the issue of the genetic testing specialty, which everything falls on. Could I just make sure I got the reason that we are not recommending the genetic testing specialty? Why did we decide not to do that?

DR. FERREIRA-GONZALEZ: Genetic testing today is covered under CLIA. There are specific personnel requirements under CLIA that fall under high complexity laboratory testing. In addition, it is kind of a moving target. Trying to put something that is an evolving

field into a specific cubbyhole might be problematic down the road.

As we have already in CLIA specific issues to deal with high complexity testing, the personnel requirements, quality control, and so forth, we felt that this already covered that particular rule. So what we saw is that the only issue that was not covered for genetic testing under the current CLIA regulation was the proficiency testing. By making these changes to the proficiency testing, we actually solved some of the major concerns related to the lack of specialty and genetic testing.

DR. TUCKSON: Was that pretty much, again, the unanimous position of the taskforce? Is that where we are? Given that we have so many comments that were critical of this, I just want to make sure that I know how to assess the public comments on this.

DR. FERREIRA-GONZALEZ: Marc.

DR. WILLIAMS: Our starting point when we were first crafting this, I think, was really to follow the direction that SACGHS had previously given to support creation of a genetic testing specialty. But over the

course of the time we discussed this, with input from our representatives on the taskforce and CMS. By really getting down to the points that Andrea brought up, which are what is the real issue and what do we really want to accomplish here, I think we recognized that if we fell back to "We just want you to make a specialty" that we would once again mire ourselves in the mud.

By doing this, with the support of our colleagues on the taskforce from CMS saying "We think that this is the way to go," we might actually be able to accomplish what we want to accomplish and avoid the problems that would be encountered in terms of trying to create an entirely new specialty.

I can't speak for everyone on the taskforce, but I think everybody was at least comfortable with that direction going forward. I don't recall anyone that stood up and said this is just absolutely unacceptable, although you are completely correct to point out that there were specific public comments that did go to this issue. We did consider those, but we ultimately decided there were not compelling enough reasons to redo this to ask for creation of a specialty.

DR. FERREIRA-GONZALEZ: Another thing to keep in mind is that, as I call it a moving target, what we were starting to see is what is a genetic test. It is not just what we have thought in the past, nucleic acid-based technology. Our definition is more broad and encompasses current specialty areas within CLIA.

So actually, the genetic testing cuts across current specialties that are listed in CLIA. Putting all this different genetic and genomic testing that is covered as a high complexity laboratory test and just fixing the issue of the proficiency test, then we can cover the majority of the issues that were brought up to us as concerns with genetic and genomic testing.

DR. TUCKSON: I guess it would be helpful for some of us, and we don't have to wordsmith it here, to nail down what the gaps are. At the end of the day, if you had to say, "We are agreeing that there are some key gaps. Those gaps are:" Is it possible to succinctly summarize the gaps?

DR. FERREIRA-GONZALEZ: Related to the CLIA specialty?

DR. TUCKSON: No. For a number of years CMS

has been planning to address gaps in the oversight of laboratories that conduct genetic tests. Again, all of the gaps in the oversight could have been done with the addition of a genetic testing specialty. However, we are saying CMS has changed direction and is now addressing, again, these gaps. So, what are the gaps again?

DR. FERREIRA-GONZALEZ: Well, some of the gaps were not only the proficiency testing that we have already identified but how they were actually reviewing genetic testing laboratories. CMS has actually developed a plan to develop more guidelines for the inspections and how to inspect genetic testing laboratories. Maybe Judy Yost can fully talk about the gaps, too.

MS. YOST: I think it is very important to recognize that the majority of the issues that you are dealing with here are not covered by CLIA, first of all, at all. Secondly, to craft regulations, I think, as Andrea was indicating, for technology that is so dynamic at this point in time would clearly cause that little chilling effect that we talked about earlier and really limit and prevent for future development.

Instead, if you step back from that thought and

look at, as Kathy Hudson indicated, what is it you are really looking for to do within that authority, you can get there from here. The only place that you would have to do regulation would be for the PT, which we have already committed and agreed to do because we could look at all the PT needs across the country, not just for genetic testing.

But you can get to personnel requirements through professional standards. You can get to quality control. There is a CDC group that is working on genetic testing quality control. Those recommendations can go into our guidance to laboratories. Believe me, anytime we place something in there, people do it. They follow it.

We have an example where we have already included a clinical and laboratory institute standard for microbiology cut points for antibiotics. It has become the standard of practice across the country. Everybody uses it because it is available to everyone and it works.

So we are trying to look at what are the needs that are necessary and use existing mechanisms and information to get there rather than spend six years

doing a proposed and final rule on all of these different areas. Then you don't know what the outcome will be.

DR. FERREIRA-GONZALEZ: The first two recommendations, Reed, talk to some of the issues that were identified for the need of the genetic specialty.

DR. TUCKSON: So we can go ahead and start drilling into these recommendations and see where they take us. I guess the question that was confusing is, it gave me the sense that all of the problems in this space could, by some people's recommendation, be addressed by the magical creation of a genetic testing specialty. Then when you start going through the recommendations that come forward, there are things that are well beyond just a genetic testing specialty.

So we set it up as if there was this magic wand. If you don't agree with the magic wand, you are a bad committee. What I think we want to make sure we do is to make sure we are saying the concern is [this.] The solution to those that we recommend is [this.] I think we got a false dichotomy.

But with that as an editorial comment, let's zip through these and see what we are saying.

DR. FERREIRA-GONZALEZ: Do you want us to put in text something like that specifically?

DR. TUCKSON: Eventually I think we will have to come back and try to put an organizing framework that says the problem that this recommendation is addressing is, boom. The solutions are, boom.

DR. FITZGERALD: To that end, again, if you go back to that oversight map and the gaps that were identified on that oversight map, you can look right off the top. I think they have them down under Gap 3, or Gaps 9, 10, and 11. There is already some organization to that that will be wherever this is going to be.

DR. FERREIRA-GONZALEZ: So it is not just in a single recommendation that we addressed the particular issues that speak to what others are calling for the specialty to solve some of the gaps.

DR. TUCKSON: Again, we are doing a challenge, and again, it is fine. We are working backwards. It is contextual. We have been taking this big mosaic and taking it in pieces: piece, piece, piece. This piece is what, is what I'm trying to [understand.] How did we define this piece.

DR. FERREIRA-GONZALEZ: If we go, I guess, to the Genetic Testing Oversight Map, these recommendations in Chapter 4, Recommendations 1 and 2, will deal with the G3, G9 to 11, and let me get my list.

DR. TUCKSON: So the notion is how do you describe what is common about G3 and G9 through 11? In other words, what is our bag here?

DR. FERREIRA-GONZALEZ: No. 3 is inadequate CLIA requirements for proficiency testing. No. 9, insufficient resources, funding, and means to develop PT for all genetic tests. No. 10, no data exist on the effectiveness of PT versus alternative assessments. No. 11, PT based on test methodologies such as sequencing have not been developed in the United States.

DR. TUCKSON: So this is a bag almost exclusively around proficiency testing. That is what we are talking about.

DR. FERREIRA-GONZALEZ: Recommendation 1 deals with a piece of proficiency testing. As we move forward to the other recommendations we are going to deal with other pieces that were of concern to people asking for the CLIA specialty.

DR. TUCKSON: So let's go ahead and see what the solutions are fixing the proficiency testing problem.

DR. FERREIRA-GONZALEZ: So again, you have the green there. We have revised Part A of this recommendation to call for CMS to require proficiency testing for all high complexity tests for which PT products are available. In No. 2, we have also added "in order to promote the development of new PT products and facilitate performance assessment efforts" to the language of that particular recommendation.

DR. TUCKSON: That would be everything.

DR. FERREIRA-GONZALEZ: Everything. It just goes beyond.

DR. TUCKSON: If you have any high complexity test for which proficiency test products are available.

DR. FERREIRA-GONZALEZ: Yes.

DR. TUCKSON: If they aren't available, you must use an alternative assessment methodology, as is already required.

DR. FERREIRA-GONZALEZ: Yes. It is already in CLIA. Alternative assessments.

DR. TUCKSON: So the only thing that is not in

CLIA now is if you have a high complexity test for which it is available. If it is not available, there is something to do.

DR. FERREIRA-GONZALEZ: Yes.

DR. TUCKSON: So if you have a PT available, you currently get a ride. We are now saying no more rides.

MS. ASPINALL: Just for a limited number right now.

DR. TUCKSON: Right now the operative word is "high complexity." We will come back to that. All high complexity tests, as a result of this, now must have proficiency testing.

DR. FERREIRA-GONZALEZ: The way CLIA is now, it is explicit about PT for 83 specific analytes, or regulated analytes. What we are doing is taking out the 83 specific analytes to talk about every high complexity test.

DR. TUCKSON: And the 83 stay in.

DR. FERREIRA-GONZALEZ: No, we will take the 83 out.

MS. ASPINALL: Basically, 83 is not a filter

anymore. Is that what you are saying? The 83 analytes was a filter that kept people out. We are taking that filter off. More tests are going into the funnel.

DR. TUCKSON: So more tests are going into the funnel. But at the end of the day, no high complexity tests now will go unregulated. We have closed the door. Nobody slides.

DR. FERREIRA-GONZALEZ: For PT purposes.

DR. TUCKSON: For PT purposes.

DR. FERREIRA-GONZALEZ: For PT purposes, if you are doing high complexity testing, you must do PT if it is available. If not, you have to do alternative assessment. Mara.

MS. ASPINALL: I don't want to get back into the other discussion, but theoretically, if there is a DTC test that is not considered health that is high complexity, and I can't mention one.

DR. FERREIRA-GONZALEZ: We will deal with that. We need to bring them back in.

DR. TUCKSON: We will do that with the definition. Good for you, Mara.

Now, let's just go back through the basics

again. Just for the average person to get how we write our language, what does the proficiency testing on this guarantee? And what doesn't it guarantee?

DR. FERREIRA-GONZALEZ: Well, the proficiency testing will assure that the laboratories that are performing specific testing, either FDA, CLIA, or laboratory-developed tests, will actually have a process to check that they are putting appropriate results, or the correct results. So it speaks to the analytical validity of the test.

DR. TUCKSON: Now, the high complexity bar; is there something important that is not being stated that is lower complexity that slides under the radar, comes out, and bites me in the butt?

MS. YOST: I think in the long run the analysis has to really look at all testing that is being performed and determine how best to describe the tests that should be covered by proficiency testing.

Clearly, there are 2- or 3,000 different tests that a laboratory may perform. Not every laboratory does. The majority of labs in the country are very small and probably do a menu of 20 tests because they are

doctors' offices and they do patient-related testing for that particular visit. But for the larger laboratories, they do have huge menus that constitute thousands of tests.

You want to use tests that are going to test the laboratory, challenge the laboratory, so that if you do one test on a machine that does 25 different tests simultaneously with the same method, you only have to do one of those for PT to get whether or not the lab is doing it correctly. You don't have to do all 25 of them.

So you have to come up with a way to craft that proficiency testing requirement to allow for challenging the laboratory to ensure the accuracy of its testing but not making them do it just because.

DR. TUCKSON: In your answer, Judy -- I need the Committee to make sure as we try to get this nailed -- it sounded like you said there was a ride for somebody that got a free pass.

MS. YOST: Right now there are 83 out of those 2- or 3,000 tests that are currently in the regulation. But anything else that the lab does, as Andrea indicated, the lab still has to do that alternative assessment twice

a year.

DR. TUCKSON: You mentioned something about big folk and then little folk.

MS. YOST: We have different sizes of laboratories. We have 200,000 labs in the country, and probably 80 percent of them are very small: clinics and doctors' offices sort of stuff.

DR. FERREIRA-GONZALEZ: Those will be moderate complexity or low complexity?

MS. YOST: Right. But a lot of the tests that currently are under PT are moderate complexity right now. So we can't leave them out necessarily because they are used as diagnostic tools in laboratories.

DR. TUCKSON: Is it true, from what you have said, that even with this recommendation there will be some laboratories that are performing genetic tests that will not be covered under CLIA for proficiency testing?

MS. YOST: If a genetic test is not high complexity. Under this recommendation just on its face.

DR. TUCKSON: Therefore, just to make sure from the Committee's sense, why are we comfortable that non-high complexity tests don't need to be reviewed?

DR. FERREIRA-GONZALEZ: I think today we can say with some certainty that all genetic tests are high complexity tests.

MS. YOST: Right now. It depends on how you define it.

DR. TUCKSON: We seem to have some uncertainty.

LT COL McLEAN: I'm just very concrete. Could I have an example of a high complexity, medium complexity, and a low complexity test? Is PKU sequencing a high complexity test? I would say yes. So, what is low complexity?

DR. FERREIRA-GONZALEZ: There are certain people saying what is a low complexity genetic test.

MS. ASPINALL: I guess it goes back to the fundamental issue, which is definition of genetic. It is not inheritable, but maternal serum screening is probably not genetic. Most people think about it as low complexity.

DR. TUCKSON: As we try to figure out the answer to Scott's question, let me ask CMS. Why would you be comfortable giving a pass to some category of test? Human beings get the test whether it is complex or

non-complex. It is still my life.

MS. YOST: I didn't say I was. What I did say was that we need to look at the whole range of tests and determine what are tests that are appropriate for PT. If you want all high complexity, maybe that is one criteria, but then the second might be other types of medically useful types of tests that currently may not be listed there but are used in high volumes in laboratories as diagnostics.

DR. TUCKSON: Let's just take the posture that you would want the authority to evaluate tests for which PT are available and, for when they are not, alternative assessment.

MS. YOST: That is essentially what the plan is to do.

DR. TUCKSON: So we should take out the word "high complexity."

MS. YOST: Well, are there tests that the Committee would say we don't think should go through PT. We are going the other way. We are starting with the big pie and we are going to narrow it down so we can identify which tests are appropriate for proficiency

testing since all non-waived tests are currently regulated in some fashion under CLIA.

DR. TUCKSON: Judy, I think I understand. I think I see where you are. Let me make sure. Outside of the field of genetic tests, are there tests that are provided to the American people that have not been tested? That are not under some degree of oversight? Is there any laboratory test that is given to Americans that are completely devoid of oversight? You can just do whatever the hell you want to do and put it out on the market.

MS. YOST: There are the waived tests under CLIA. The waived tests under CLIA basically only require that you follow the manufacturer's instructions. There are no other requirements for those.

DR. TUCKSON: What would that be?

DR. FERREIRA-GONZALEZ: The waived tests are FDA-cleared.

MS. YOST: All laboratories are regulated as long as they meet the definition under CLIA in some fashion. But it depends on the complexity of tests that they perform how stringent the requirements are.

DR. TUCKSON: I'm talking in this case tests, because that is the word we use. So there are tests that you waive. An example would be what?

DR. FERREIRA-GONZALEZ: But they are FDA-cleared. They are usually FDA-cleared tests that have been waived.

DR. GUTMAN: In order for a test to be waived, it first has to be either FDA-cleared or approved. So it has to meet the FDA evidentiary standard. However, whether you swear by it or add it, it is our standard. It then has to go through a second process.

DR. TUCKSON: So it wasn't just because you said "I don't care."

DR. GUTMAN: No, no. I can assure you that is not the case.

[Laughter.]

DR. TUCKSON: Let's keep this right on focus because we have to roll.

You have to speak English here. Are you saying that there are some tests that you are prepared to let this Committee go forward recommending that do not get an FDA waive pass and that you are not doing your number on?

If you are saying that is okay, I want to know why. To me, this is pretty straightforward. This is a no-brainer. You take out the "high complexity" and you say "tests in the field of genetics." You don't do it anywhere else, so why do it here?

I just want to understand why. Are you making an economic problem, that you don't have the manpower to do it? Is it that people are lazy? What is it? Why not just do it? What am I missing?

DR. FOMOUS: Are you asking to take out "high complexity"?

DR. TUCKSON: Yes. Or tell me, why is it in there?

DR. FERREIRA-GONZALEZ: Reed, the waived testing, the manufacturer has to go through FDA clearance and then has to demonstrate specific criteria that is very hard to screw up with the test. Is that correct?

DR. GUTMAN: Yes. Waived testing wouldn't be a very good setting for proficiency testing because you are making the assumption that you are dealing with untrained users. We are looking for simple technologies that are highly well calibrated and highly well controlled.

But that begs the issue. That is waived. Let's take waived off the table. I think the question you are asking is moderate versus high complexity. Where I'm not so sure is whether you are mixing FDA-cleared versus lab-developed tests. Lab-developed tests theoretically shouldn't be on the market if it is operating outside of a high complexity lab, although I think there are loopholes and it is possible for moderate complexity.

DR. AMOS: What about the term "all non-waived genetic tests"? Is that appropriate?

DR. TUCKSON: Yes.

DR. AMOS: Does that cover it?

MS. ASPINALL: I think that is closer, but do we need the word "genetic"?

DR. AMOS: Yes, because that is part of the definition.

MS. ASPINALL: I think there is a tremendous debate.

DR. AMOS: That is what we are talking about here.

MS. ASPINALL: Sort of. But we talk here about

high complexity tests, some of which are genetic, some of which are not. The definition of genetic, many tests are low complexity and may be genetic. So I like "non-waived," but I don't think we need either "genetic" or "high complexity." If a test can have a PT, it should.

DR. FERREIRA-GONZALEZ: I think for the waived tests, the way it gets approved --

MS. ASPINALL: Non-waived.

DR. FERREIRA-GONZALEZ: Non-waived, non-waived. The idea we are wrestling with here is changing this recommendation to "CMS should require PT for all non-waived tests for which PT products are available."

MS. ASPINALL: Yes.

DR. TUCKSON: And, if it is not available, you have to go down Road B.

MS. ASPINALL: Yes.

DR. TUCKSON: I think what we are agreeing to here is nobody gets through scott-free. The FDA may decide to go through some rigorous rigmarole, which we will come back to later, that says you get waived. But they have been dealt with. Somebody has grabbed them by the neck, analyzed the hell out of them, and said, "Okay.

You get waived."

Then you have everything else that is left. If you are not waived, you are going through PT if there is PT available. If there ain't no PT available, you are going to go down Route B. But nobody gets through just because.

Is that accurate? Have we missed anything?

DR. AMOS: Yes. Where does "research use only" testing come in, Steve?

DR. GUTMAN: Hopefully it doesn't have anything to do with anything anybody here is talking about.

DR. FERREIRA-GONZALEZ: Let's leave that out. Let's leave that out, please.

DR. TUCKSON: So we have closed the door on all these things. We will come back to getting specifically into what does it mean. I don't know how good Route B is.

DR. FERREIRA-GONZALEZ: As a further recommendation, we are asking for research. So the idea is we are going to change [the recommendation to] "CMS should require PT for all non-waived tests for which PT products are available." So, "In order to promote the

development of new PT products and facilitate performance -- efforts, HHS should fund studies on the effectiveness of other types of performance." That really goes to your point, Reed.

I think it has been proven that alterative assessment works, but we don't have the data. So we are asking them to fund some studies and also to look at other ways to do PT and more of a technology and methodology based like they do in Europe. There you have PT that is based on sequencing and you send your specimens. You have to sequence and get the right sequence, and then anything that actually is in your laboratory sequence space will be sufficient or covered for the PT testing.

DR. TUCKSON: I would only modify it slightly. Instead of the word "determine whether," to say "to ensure that." You have to set out with your goals.

DR. FERREIRA-GONZALEZ: You need to keep in mind, too, if we look at genetic testing, some of this testing is for rare disorders. So we are not going to have vendors that are actually going to develop PT products. It is just not feasible economically. We have

to have a route where we are assuring that the laboratory is still checking the analytical performance of the assay is working well.

DR. TUCKSON: I think this is good. Are we being mamby-pamby on this thing? Are we doing what we are supposed to do? Somebody said we are being [mamby-pamby.] Are we being too timid?

DR. FERREIRA-GONZALEZ: No. I don't think we are timid. I think we are really very aggressive.

DR. TUCKSON: Are we killing innovation?

DR. FERREIRA-GONZALEZ: No. Again, Reed, I think what is very important here is that if there are no PT products available there is alternative assessment. So there are other ways to get to this. We are not hampering the innovation of the testing. If your first one brings in a test that you have shown clinical validity, you can develop alternative assessments and continue to offer the test, but we make sure that the laboratory is checking into the analytical.

DR. TUCKSON: So, when are we going to get to the FDA part and the Route B part? The Route B part we are getting to now. We are not just saying that just as

some little jive thing but that is going to be real. That is what that says, right? That Route B is real.

DR. FERREIRA-GONZALEZ: Yes, it is real. We are currently doing it.

DR. TUCKSON: Then we are going to eventually come to the resources for the CMS to be able to do it, which we will come to in a minute, too, right? Okay.

DR. STRAUBE: On your previous slide, the third sentence. Immediately following it, it says "In principle, genetic tests and/or other high complexity tests should be required to undergo PT." That probably should be changed in light of the change we just made in No. 1.

DR. FERREIRA-GONZALEZ: We change things here and there and then they get out of sync. So tonight that is what we are going to be doing, reading this. Everybody has homework for tonight, to read this.

DR. TUCKSON: I see what you are getting at with the studies of the effectiveness and we are going to make. There is an implied aspiration here which I would like to make more explicit. They should be as robust and therefore you want to study to make sure that they get to

that level of robustness. It is just a little weak.

So, think about it. It could be the alterative assessment is as robust, is what I'm being told.

DR. FERREIRA-GONZALEZ: Yes, Mara.

MS. ASPINALL: Just a suggestion in terms of timing. Maybe getting through it all and that going back. Because we have to go back in terms of timing and putting things on the map.

DR. TUCKSON: Just keep that in your mind, folks.

DR. FERREIRA-GONZALEZ: But we also have to have in mind that actually there are different volumes of different tests. So there have to be other forms of evaluation.

DR. TUCKSON: I understand.

DR. FERREIRA-GONZALEZ: So let's go to Part B, that will deal with some of the issues specific to specialty and CMS. CMS should consult or contract with experts in the field to train inspectors of genetic testing laboratories. Training by such experts will enhance the inspectors' understanding of the technologies, processes, and procedures utilized by

genetic testing laboratories and equip them to assess compliance with CLIA requirements. In addition, CMS should identify and evaluate innovative alternative mechanisms to inspect genetic testing laboratories.

So this gets to the point that CMS had already put in place and where they are going to hire more inspectors and actually train them to do that.

DR. TUCKSON: The College of American Pathology says everything is fine now. We are saying go further.

DR. FERREIRA-GONZALEZ: No, we are saying continue to implement. We are behind CMS in the implementation of these specific changes to the process of educating the inspectors and getting more inspectors. But even though they have already undergone the process of doing this, we want to make sure it is in the recommendation to assure that it really moves forward. It is just a reaffirmation of what they are doing.

No. C is, as recommended in the 2006 Government Accountability Office Report on Clinical Laboratory Quality, CMS should use revenues generated by the CLIA program to hire sufficient staff to fulfill CLIA's statutory responsibilities, and the program should be

exempted from any hiring constraints imposed by other agencies.

DR. TUCKSON: So let's go to No. B. The question is, what is the standard. I'm trying to push here. What No. B doesn't say, or does it say, the bar right now for inspection we are okay with. Are we actually okay with the bar now? Are we saying that the current inspecting process is A-okay?

DR. FERREIRA-GONZALEZ: No. What we are saying here is that the inspectors require additional training to deal with genetic testing laboratories.

DR. TUCKSON: So we are saying they need more training. The bar should go up. And that, they should also identify and evaluate innovative alternative mechanisms to inspect genetic testing laboratories that meet a higher standard.

DR. FERREIRA-GONZALEZ: No, that is not a higher standard. Today there is no training of the inspectors to inspect genetic testing laboratories. Mara.

MS. ASPINALL: To be fair, it is a strange analogy but sort of a CME idea. It is working reasonably

now, but we want to make sure that those who are in this field are up to date with new and evolving science. I think about it as CME. Let's make sure that these folks are continuously trained and up to date without fundamentally changing the whole system.

DR. TUCKSON: I'm really appreciative for that articulation because that is what I want to make sure that I understand that I'm signing on to. Are we signing onto basically saying that the CME, the status quo today, is pretty okay, that we are okay with that, we just want more of it, or are we saying it needs to go up a notch and that if you are going to find alternative mechanisms you want things that are at least as good, if not better than today.

But the bottom line is, are you okay today. I'm trying to understand whether or not our public comments in any way challenge that assumption that it is okay today. I'm not sure I know what they are saying.

DR. FERREIRA-GONZALEZ: I think there are concerns about the lack of knowledge of some of the inspectors about genetic testing. This will solve some of the issues. We will have a work force in CMS that

will be knowledgeable how to inspect the genetic testing laboratories. But there is the same bar. We are just adding more education to the current inspection process.

MS. YOST: Let me please speak in defense of them, please. These are all experienced laboratorians with multiple years of laboratory experience before they become inspectors. We teach them about the regulations. We teach them how to interpret the regulations, what to look for in the laboratory to ensure that the laboratory is meeting the regulations. We teach them how to interview. We teach them how to go through the laboratory and observe testing and gather information, analyze that information to determine whether the laboratory is in compliance.

We teach them on a very broad-based level so they can go into a toxicology laboratory, into a cytology laboratory, into a histology laboratory and be able to identify does that laboratory have qualified people.

DR. TUCKSON: I've got you, Judy.

MS. YOST: This is very specific knowledge that we are asked to share, and we have already done it. We have started that process.

DR. TUCKSON: So look, you are doing fine work. You are working your butts off.

MS. YOST: Yes, we are.

DR. TUCKSON: I appreciate that. You are saying what you need to say. I'm going to let it go from this, and I'm not on a soapbox. I'm trying to get absolute clarity here. A very proud government official should be proud of her agency and her people. Have we heard significant testimony in front of this Committee that says the status quo, even though it is terrific, needs to be better? All I'm asking is, have we heard people say it has to get better than it is today. If so, are we dealing with it?

Now, I'm seeing people shake their heads that say that our testimony from external people is that we don't have any critical people screaming mad about today. They just want more of it and so forth. Is that what we are hearing?

DR. FERREIRA-GONZALEZ: Yes.

DR. TUCKSON: You all have read all that, every little detail?

MS. YOST: I have a little summary of the

comments and looking for A, B, and C. Very few people commented on it. The few that did were either positive or neutral, and there are very few that were very negative --

DR. TUCKSON: Therefore, we are going to do some things to make it better. We are going to add more training. We are going to do all the wonderful things that Judy has said. Let's move on. Nobody seems troubled.

DR. FERREIRA-GONZALEZ: We are adding here that CMS should be exempt from the hiring freeze to make sure there are enough inspectors and resources.

DR. TUCKSON: Now, do they have enough resources today?

DR. FERREIRA-GONZALEZ: No.

DR. TUCKSON: No. So, where is our recommendation to add more?

DR. FERREIRA-GONZALEZ: No. C. We are telling them to use the revenues from the CLIA program.

DR. TUCKSON: Why aren't they doing it now?

DR. FERREIRA-GONZALEZ: Because there is a hiring freeze.

MS. YOST: We actually did get exempted from the hiring freeze. Because we are user-fee funded, we have been removed from the normal CMS [hiring freeze.]

DR. TUCKSON: Done. Anybody have any other comments about this?

[No response.]

DR. TUCKSON: Done. Move. Next. Next, next.

DR. FERREIRA-GONZALEZ: Recommendation No. 2 requests that funding be assured for the development of reference materials, methods, and samples for assay validation, quality control, and performance assessment along with other steps to address gaps in analytical and clinical validity data.

We did not revise Part A or B of this recommendation. We revised Part C to include that an initiative for enhancing public reference databases should encourage robust participation and need to consider mechanisms for anonymous reporting and protection from liability for encouraging information sharing.

Do we have any questions about this recommendation?

DR. AMOS: Andrea?

DR. FERREIRA-GONZALEZ: Yes, Mike.

DR. AMOS: Do we want to stick on this one first and then go back? I have a specific comment on No. A.

DR. FERREIRA-GONZALEZ: Okay. Go back to No. A.

DR. AMOS: One of the things that needs to be clear is that there are really two types of standards. There are standards for the analyte for a specific test, but there are also platform standards for microarrays or mass spec. Those are being developed.

So what I recommend is that we change the wording after the last line, where it says "for assay." Following "assay," it should say, "for assay analyte and platform validation, quality control, performance assessment, and standardization," to emphasize the point there are two different types of standards.

So it should be "assay analyte and platform validation, quality control, performance assessment, and standardization."

DR. FERREIRA-GONZALEZ: Your next comment? Did

you say you had another comment, Mike?

DR. AMOS: That was it.

DR. FERREIRA-GONZALEZ: Any other comments?

[No response.]

DR. FERREIRA-GONZALEZ: The next one, Part D, I just wonder. It says, "HHS should support the development and dissemination by professional organizations of additional standards and guidance for applying genetic tests in clinical practice." The intention of this Part D of the recommendation was to encourage professional organizations to also develop professional guidance with respect to personnel training in interpreting genetic testing.

Maybe we can either add here in Recommendation 2-D, but maybe it has to go back to Recommendation 1, that CMS can draw from these professional organizations' recommendations to develop interpretative guidelines for the inspectors so they have a better understanding of who actually is appropriately trained to be directing different types of testing in this country.

MS. YOST: We would love to do that, but we would love to have all of your help to do that.

DR. FERREIRA-GONZALEZ: When you say all our help, what do you [mean]?

MS. YOST: We need your expertise.

DR. FERREIRA-GONZALEZ: That is why we are saying [we are] looking for professional societies to develop these kinds of professional guidelines.

MS. YOST: We will be happy to incorporate them.

DR. FERREIRA-GONZALEZ: Mara.

MS. ASPINALL: I think this is an absolutely critical recommendation because we know that, if you look at the adoption of tests, they happen only after professional societies recommend them.

What I would ask Judy or the Committee, can we be more specific as opposed to just what we have there at D, I think, that says we should support it? How can we be more specific and give that more teeth to make sure that it happens.

DR. FERREIRA-GONZALEZ: We have in Recommendation 2-D that HHS should support the development and dissemination of professional organizations of additional standards. So we are asking

HHS to do that. But then what we need to ask is CMS to use these professional guidelines to develop interpretive guidelines for their inspectors.

MS. ASPINALL: I'm going back to the first sentence. What does "support" mean? How will they support? Is it money? Is it time? Is it access to data that comes about to be able to do it? Because many professional societies will say, "Good concept. We don't have the structure to do it. We don't have the samples to do it. We don't have the time or resources to do it." Can we be more specific to ensure that the connections are made?

DR. FERREIRA-GONZALEZ: Some of the problems that we have as a professional society is that we don't have enough resources to develop the process. So one of those could be support in money for the professional organizations. But I think working with the members of the different knowledge-generation agencies in coordination with the professional associations in development of these guidelines could be very important and have a major impact.

MS. ASPINALL: Joe just said provide the

necessary support. I just want to get to a level of specificity that doesn't just say that HHS, with all good intentions, met with the societies and said, boy, we would really like you to do that. The societies are still stuck with the inability to get it done quickly.

DR. FERREIRA-GONZALEZ: There are two changes to these recommendations. One is that HHS should provide the necessary support for the development and dissemination of professional organizations of additional standards.

I guess we can do the change of the interpretive guidelines back in Recommendation 1. So we go back to No. 1-B. In No. 1-B we are talking about the inspection process and enhancing the training of the inspectors. Maybe we can put that particular here. We can say CMS should work with professional organizations to develop interpretive guidelines regarding personnel requirements for the interpretation of different genetic tests.

MS. ASPINALL: I was thinking that it mixed up No. B, which was, I thought, just focused on the inspectors and that it broadened it too much in terms of

that. I guess I was thinking just deal with it in No. D, not change No. B, which I thought stood very well on its own.

DR. FERREIRA-GONZALEZ: I have it in either place. The idea is to tell CMS to use these standards to develop interpretive guidelines for their inspectors. So we can put it in No. D.

MS. ASPINALL: Although, I wonder. Maybe that is a way to put teeth into it. Either HHS or CMS, maybe if they have specific tests that they actually ask specific organizations to provide guidance within X period of time.

DR. FERREIRA-GONZALEZ: Yes, because I think that this gives CMS the means to go out to professional organizations and bring them in to work with the interpretive guidelines, not waiting for HHS to provide funds for this development. That is what I thought in No. B.

MS. ASPINALL: I think that is right. I just think No. B was the issue about training the inspectors. So I wouldn't put it in No. B.

DR. FERREIRA-GONZALEZ: You what?

MS. ASPINALL: I wouldn't put it in No. B. I would leave it in No. D.

DR. FERREIRA-GONZALEZ: But I think maybe we need to have a better understanding of what the interpretive guidelines are. Judy, interpretive guidelines gives more explanation to how you interpret the CLIA regulation for the inspectors to be used.

MS. YOST: This is a very narrow context. I think that probably it could go in either B or D, but in D it is much broader because, for CLIA purposes, you are really just looking at guidance to help both laboratories and surveyors be able to meet CLIA requirements or assess CLIA compliance and ensure quality testing as your bottom line.

So, wherever you think that fits better. I kind of assumed that in D. That is where I saw that. But this is a broader context because you are talking about applying the test in clinical practice. We are not going there for CLIA purposes.

DR. FERREIRA-GONZALEZ: That is C, clinical practice.

DR. TUCKSON: All right. D, that's it. Next.

MS. ASPINALL: So, can we put that same phrase in D? So B is all training inspectors and D is all professional organizations.

DR. FERREIRA-GONZALEZ: Yes. Again, the interpretive guidelines is to provide information to the inspectors.

MS. ASPINALL: I think it is more than just the inspectors and D allows it to be more than that.

DR. TUCKSON: So let's make sure. Mara, you have a good sense. Why don't you play with it, tweak it a little bit if you need to to try to tighten it up. This is not a major issue. Let's try to move on to the big ones.

DR. FOMOUS: So we are taking it out of B? Is that the final consensus?

[Pause.]

DR. FERREIRA-GONZALEZ: So, do we have any other edits for Recommendation 2? Any edits to Recommendation 2?

[No response.]

DR. FERREIRA-GONZALEZ: Can we move on to the next one?

DR. BILLINGS: Go back. Go back to C. "For example, and may a need to consider mechanisms"? Do you see what I'm saying? It is just an editing thing. "Such an issue should be structured."

DR. FOMOUS: What line is it on?

DR. BILLINGS: The last line in C. "Such an issue should be structured to encourage robust participation." I would question "robust participation." But, "for example, and may a need to consider."

DR. FOMOUS: "And may need." It is supposed to be "may be a need."

DR. BILLINGS: Whatever. I don't know what it is supposed to read. Whatever it is.

DR. TUCKSON: Fix it later. Let's go.

DR. FERREIRA-GONZALEZ: So we go back to Recommendation No. 3, supports a mandatory system of genetic test registration that uses CLIA registration data as a foundation. Wait, wait, wait.

DR. TUCKSON: "May," "maybe," we are not talking major policy here. We are just talking grammar. They will fix the grammar.

DR. FERREIRA-GONZALEZ: They will fix the

grammar. Remember we are going to go back to this tomorrow.

DR. TUCKSON: It is 3:40. I want to get the big issues grappled with.

DR. FERREIRA-GONZALEZ: Do you want to have a break now?

DR. TUCKSON: No, no break. No. Oh, wait a minute. Wait a minute. Hold on. Time out.

I'm worried about the time. Ten minutes.

[Break.]

DR. TUCKSON: Let the record state that Judy Yost carried the flag marvelously for her team, despite repeated questioning on the part of the chairman. She held firm.

All right. We are going to press on. We are going to press on to the really hard stuff.

DR. FERREIRA-GONZALEZ: We are going to go to Recommendation 4 first and then come back to Recommendation 3. Just to keep it interesting.

Recommendation 4 asks HHS to convene relevant stakeholders to provide further input on FDA risk-based regulatory framework for laboratory-developed tests and

consider models for assessing laboratory-developed tests that will not be subject to FDA review.

We revised Part A to expand the list of stakeholders and include laboratory-developed tests offered directly to consumers. We also added that the FDA risk basis should consider intended uses of laboratory-developed tests and likelihood of harms to patients or consumers if test results are inaccurate, susceptible to misinterpretation, or if the test is misapplied or extended beyond the proposed intended use.

We also revised Part B to offer alternative assessment models for the infrequently performed laboratory-developed tests.

So, do you have any questions about this recommendation?

[No response.]

DR. FERREIRA-GONZALEZ: This is a recommendation that actually received a lot of comment, and we have different points of view from the different public [commenters.] Mainly the taskforce has different views on these issues. Furthermore, the public comment has provided different views of this particular

recommendation, from everything regulated under FDA to actually leave it as it is in the current model, and some have it in between. Mara.

MS. ASPINALL: I know there will be much comment, but I will open it up with one issue on the addition. When it says "for infrequently performed LDTs," I don't think we should have the statement "such as those for rare diseases."

DR. FERREIRA-GONZALEZ: "Such as for rare diseases." We can put "rare diseases."

MS. ASPINALL: Excuse me?

DR. FERREIRA-GONZALEZ: We can put "rare diseases."

MS. ASPINALL: Well, no, I actually think "infrequently performed" is better than "rare diseases" because there are many rare diseases that are tested very, very frequently, whether that be PKU, whether that be cystic fibrosis or other things. Even though they are rare, the testing is very common.

But I think the issue is the infrequency of testing that is relevant, not the disease itself. So yes, I would delete that phrase.

DR. TUCKSON: Before we get into all the debates, can I just make sure that we all have the same background? Basically, why is it infeasible?

MS. ASPINALL: No, at least I was not getting to "infeasible." I think there is a different issue. I just wanted to say I think the purpose of that, and as I have talked to the Committee, it is about infrequently performed. The frequency of the disease itself is not relevant. It is about tests that are only done a dozen times a year.

DR. TUCKSON: I'm back at the fundamental Recommendation No. 4 preamble. The whole launching pad for this recommendation is that we agreed that applying the same regulatory framework to every genetic test is infeasible given the number of tests in use and in development and the cost and resources that will be needed to support such a structure.

So we are basically saying you can't do everything because it is infeasible practically to do it. Therefore, you have to make some tradeoffs. Also, by the way, if you tried to make everything fit, like the camel fits into the eye of the needle, you are going to

delay patient access to important new technologies and also delay an important step forward in defining the type of LDTs that would be subject to pre-market review, i.e. some won't be.

Now we are basically accepting that. We are saying, "Okay, public. You can't do everything, and we agree to that." So I want to make sure that we agree that it is infeasible, and it is okay that everything doesn't get FDA'd. Now the issue as you go forward is to decide what things it is okay not to have the highest level of scrutiny. Is that what this argument basically makes?

DR. FERREIRA-GONZALEZ: Yes. I have another comment, too, that has come to light as we go through the Genetic Testing Oversight Map that actually is now very, very clear. It has to do with some of the language that we have in the second sentence of the preamble, where SACGHS supports FDA regulation of LDTs and the flexible risk-based approach that agencies take to prioritize their review.

Now, if we go back to the Genetic Testing Oversight Map, you can see that for the laboratory-

developed tests that will go through the FDA, laboratories will have to comply with FDA manufacturing control, FDA pre-approval inspection, and quality system regulation. At the same time, the laboratories also will have to go through inspection for CLIA, where some of the same issues will be again inspected by the laboratory.

So it seems that there is an overlap that is very onerous for the laboratories.

DR. TUCKSON: That is one of the things I think we are going to have to figure out a way to say. We need to be clear. Are we saying that there is an insufficiency of rigor problem or a gap problem or a duplicative problem? So there are three different things that can be going on here. I think we are going to have to be real disciplined about how we think through these.

On the one level, you could be saying you have two systems regulating the same thing. Sometimes you are saying that there is nobody regulating either one, FDA or CLIA. Then sometimes we are saying that we are making a judgment about the sufficiency of the review by FDA by sort of saying that not everything goes through the highest level of scrutiny and some things triage out.

When we start through this, let me make sure I understand. Of these recommendations that are coming in this section, are they speaking to all of those scenarios?

DR. FERREIRA-GONZALEZ: There is one speaking to this scenario for the testing that will go directly to the consumer without any CLIA oversight. We have a separate specific recommendation to deal with those particular tests. So that, take it out of this equation for now.

DR. TUCKSON: I think that one thing we want to be able to do in the preamble to these recommendations is to declare which bucket is the recommendation speaking to. When we look at this whole thing, is there any sense within the totality of these recommendations in No. 4, and again I come back to my one-note song here, that there are any free passes? Is there any hole where somebody gets to drive a truck untouched in this group?

DR. FERREIRA-GONZALEZ: Marc. Steve also had a [comment.]

DR. WILLIAMS: It seems to me that as we look at the subgroups after the preamble that we end up with a

situation similar to the waived versus non-waived test. Here we have tests that FDA exerts pre-market review on and those that it chooses not to. We then recommend an alternative pathway for those that FDA declines to apply pre-market. So there would be oversight for those tests that would avoid that pre-market review.

So the sense I have is we don't have a hole. They have to go A or B. There is no way to get around those two.

DR. TUCKSON: There may be a C where you get, somehow or another, FDA'd and CLIA'd.

DR. WILLIAMS: Right. Actually --

DR. FERREIRA-GONZALEZ: No, no, no. There is no C.

DR. WILLIAMS: Speaking to that, in A when we are talking about convening a group, I think one of the things we should articulate in that recommendation is that we specifically say "to avoid duplicative things." So that should be in A where we have this group coming together.

DR. FERREIRA-GONZALEZ: I will put it in the preamble. But I think Mara and Steve have comments to

this.

MS. ASPINALL: Two things. One is I completely agree with Marc that there is no C, and a lot of the public comments say that. We can't have duplicative, overlapping, and non-consistent regulation. That would make C difficult.

But, you state that the FDA has taken the important step forward through the, I assume, IVDMIA with the pre-market review. Are we going to talk about whether we agree or disagree with that as a piece of the pre-market? Is pre-market review, in the way that has been articulated in the guidance, a good or bad idea?

DR. FERREIRA-GONZALEZ: There were a lot of discussions in our taskforce regarding how the risk base has been allocated for the IVDMIA. Part of the preamble is saying that that is why we have to bring the stakeholders together to further elaborate that particular concept of what constitutes risk base and how much weight we give to technology.

Is there anything specific you want to discuss about the IVDMIA?

MS. ASPINALL: I guess we have heard in the

comment and discussion here everything from agreement to tweaks to fundamental rethinking of the pre-market review. So I think that we need to have a recommendation one way or another that says we agree with the guidance as stated today or we don't or we think that the philosophy of the guidance is correct but needs to be implemented over a period of years or a period of X. [Don't] just have it as a preamble because it is not clear to me whether that says we agree or disagree.

I would give you my opinion, but I wanted to start with the process issue.

MS. CARR: Can I ask for a clarification? When you say are we agreeing with the pre-market review laid out in the IVDMIA guidance, are you saying does the Committee agree with the nature of the review?

DR. TUCKSON: The sufficiency.

MS. CARR: Is it, or is it what they have chosen to subject to pre-market review?

DR. FERREIRA-GONZALEZ: The overall question is, do we require pre-market review of laboratory-developed tests.

MS. ASPINALL: To be fair, I have been involved

in some of the discussion about this, but I think that for the clarification of the report itself, given this is one of the absolute key issues that is fundamental to it, we should clarify whether we answer your question, Andrea, either way. Do we agree that IVDMIAs or other LDTs should have pre-market review as stated. Should it be different.

DR. FERREIRA-GONZALEZ: There were discussions in the taskforce and the outcome or the majority view was that the tests that had a high risk should have some pre-market review through the FDA. Those are the tests that don't fall within this high risk according to the FDA. Moving forward in reviewing this, it will fall under this other public-private partnership that will actually do pre-market review.

So the recommendation says yes, there is a need for pre-market review.

MS. ASPINALL: But you are defining the pre-market review as a public-private partnership in a way that the FDA and the current guidance does not?

DR. FERREIRA-GONZALEZ: No, it is according to the risk. It will be one route or the other route.

DR. WILLIAMS: I don't know. The way I understand it, and maybe this is incorrect, but I think what we are saying is we agree that there needs to be a risk-based strategy. There was a lot of concern and a lot of discussion about how we interpreted FDA's assessment of the risk, and we thought that there needed to be input from other stakeholders to basically take more time around the risk issue to make sure that we are actually doing the risk stratification properly with the appropriate input.

So I see that as being appropriate and appropriately represented in the preamble and that basically A of the recommendation says this is a group we need to pull together to really look at getting input from to decide how to do the risk and how to decide which ones get pre-market and which ones don't.

So I think we are endorsing the concept but we have some concerns about the details of which that concept will be applied. This was our response from the public comments. These are the groups that say we think we need to have input. Of course, FDA has already received some input from some of these groups, also. So

I think it reflects the ongoing process.

I don't know if Steve wants to comment.

DR. GUTMAN: I want to chime in, sure. A couple of things. First, even within the IVDMIA subgroup there are risks. It is not all Class 3, Class 2. There is actually being potential for Class 1 or Class 1-exempt products because we are not driven particularly by technology. Certainly the transparency issue is important to us, but it wasn't the technology per se. If you want to look at our webpage, we have approved expression arrays, microarrays, multiplex assays. We are not afraid of technology and its intended use.

So I would argue that even in the construct of IVDMIAs it can be parsed with some perhaps difference of opinion but some subtlety.

In terms of the issue that Andrea raised a couple of iterations ago, we are cognizant of the fact that there are QSR and CLIA differences. In that document, the IVDMIA document, we do in fact commit ourselves to working with Judy to try and resolve any differences or build off of strengths or minimize redundancy.

I view that, actually, as a red herring. I actually think there are more similarities than differences and that the differences just need to be explained in a user-friendly way so that labs that are not only offering services but making products, because that is what I would characterize them as doing, might want to have design controls or caps or things that perhaps a regular lab might not want to have.

I think the most important thing to me, frankly, as a regulator -- but maybe not as a regulator, maybe as a patient, since I'm increasingly becoming a patient -- the most important thing to me is what Reed said, which is, is there A and what is the option to A? Is it a free pass; is it half price; is it three-quarters; is it a dime on the dollar?

Let me tell you what FDA's standard is, really quickly. You don't want to hear it because you have heard it before, but I'm going to tell it to you again. There is an investigational phase. So it comes in and it either has patient safety protections like these weird things called informed consent and IRBs. If it has risk to patients, [it has] these weird things like an actual

submission to either the IRB or to the FDA. So it has investigational protections.

Before it can actually be commercially put on the mark and say "I am a legitimate lab test," it has pre-market review of discrete analytical performance, discrete clinical performance, and I would take umbrage with the term "plausibility," but I would argue it is correct to say we don't do evidence-based medicine in the way that Muin does. So we don't require that we demonstrate what the impact will be in 10 years on the healthcare system.

Then we have all kinds of interesting post-marketing controls. One is a requirement that they make product consistently and, if they don't, that they recall and notify players who were using the product.

And, we have MDR reporting. So when something goes wrong, you have to report it to FDA. Usually companies are anxious to work with FDA and fix what has gone wrong. Sometimes they are not so anxious. They are anxious to bury it under the rug, and we get into very colorful disputes with them and threaten action.

My first choice is, I tell them, that's fine.

I'm going to put out a press release and let everyone know what is going on. Usually that works. Companies become very interested in cooperating.

That is the A. That is the A. It comes with research, it comes with pre-market, it comes with quality during the production, and it comes with post-market. That is the A.

Your job, or your job to give to HHS, is to figure out what the B is. I as a patient, not as a regulator, am fascinated with hoping that the B will at least be 50 cents on the dollar, not a dime on the dollar.

DR. FERREIRA-GONZALEZ: I'm confused.

MS. ASPINALL: I had you until the 50 cents versus 10 cents. I'm sorry.

DR. GUTMAN: You have to come up with something that is an alternative to what FDA does. It doesn't have the IDE. Or it can be just like FDA and you can simply create an FDA at your place. But it can be substantially equivalent to FDA and have the same functions, or it can be novelly different from FDA.

I forgot the most important thing because it is

my personal passion, which is our obsession with labeling the truth. I can assure you our truth and the manufacturer's truth are not the same. Labeling the truth, and then putting the whole damn review in a place where every person can either swear at us or swear by us, but they can swear because it is in the public domain and it has been quality controlled.

Not to suggest any particular company lives on hype, but every company has the best and every company has pristine data and every company has the best claim. Of course that is business.

DR. TUCKSON: Steve, remind us again of which things in that scenario you just gave --

DR. GUTMAN: You have to choose. That is your job.

DR. TUCKSON: No, no.

DR. GUTMAN: I think they are all important.

DR. TUCKSON: You went to the wrong part of my question.

DR. GUTMAN: Sorry.

DR. TUCKSON: You jumped right when you should have jumped left.

DR. GUTMAN: You hit a nerve. I'm passionate.

DR. TUCKSON: Which things are outside of the FDA? That is what I don't understand.

DR. GUTMAN: Well, cost for sure. A letter with my name on it isn't a guarantee that the company will make a dime. They are often surprised or horrified or delighted. Reimbursement is outside. Actual use, as I think you said earlier. Practice standards, information, and articles will drive use. Off-label use.

DR. TUCKSON: I think you answered it, but let me make sure. In other words, you have the FDA process and then you said if there was another process. Why wouldn't everything be in the FDA process?

DR. GUTMAN: If you are going to have a registry, then the question I would ask is how do you know that the registry actually has correct information? Of course, what they are levelling at us, appropriately, is how will the FDA be nimble and quickly make changes to products. Well, the same question applies to the registry. How do you allow it to make quick changes and still make sure that those are legitimate changes?

DR. TUCKSON: I'm sorry, Steve. You are so

good and smart. I'm not sure how we jumped to the registry train.

DR. GUTMAN: I thought that was B.

MS. ASPINALL: We asked a question before that.

DR. TUCKSON: You laid out a process for the FDA, Steve. Then we laid out a process perhaps as an alternative to the FDA. I'm just asking the very stupid question, why isn't everything in the FDA?

DR. GUTMAN: I'm asking the same question.

[Laughter.]

DR. WILLIAMS: I think it can be clarified very easily. The language in B says "for LDTs that will not be subject to FDA review." What Steve is saying is they are all subject to FDA review, therefore we don't need B. But that is not what we heard at our meeting.

DR. TUCKSON: Thank you, Marc.

MS. ASPINALL: Lots of people have said and discussed that things that are non-FDA today have been under CLIA and CMS, and we heard people say that regulation is sufficient. We heard other people say that regulation is not sufficient. I think that is very much the heart of the issue.

DR. TUCKSON: Which is exactly my opening question.

DR. GUTMAN: FDA does have to be careful what it wishes for.

DR. FERREIRA-GONZALEZ: I was going to say that, Steve, in light of some of the current reports on the infrastructure and the current ability to review these type of applications, what is realistic for the agency. That is what we are proposing these are the model to, to be able to offload some of these things.

DR. TUCKSON: Everybody is really, really precise now. First of all, at one level, our job is to be practical and not ridiculous. However, our job is also, as I understand it, to define the optimal state and then you work backward from there.

I would love for us to be able to make one statement in our Chapter 4 Recommendation 4, mother, God, and country table setting. The optimal situation would be that all ta-da gets whatever. You say this is what ought to occur. That is what we want.

However, after doing meticulous homework and so forth and so on, the FDA says ain't no way in hell you

are ever going to get enough money to be able to actually do this in real life. For every test, the same thing.

We were impressed by that, although we are not scared to recommend what is important to the American people. But we also are practical people, and it seems there has to be some tiering, some hierarchization. But everything gets something, and the rules of hierarchization are the following.

I think that is what we are trying to say. I'm trying to see how our recommendations say that.

DR. AMOS: I actually think that we don't have enough information to make a recommendation on this just yet because we have not done a thorough economic assessment of the impact to markets, to innovation. The group that we have is not really qualified to do that.

DR. TUCKSON: Great point. Unfortunately, the null hypothesis doesn't exist for us.

[Laughter.]

DR. TUCKSON: We are in the position of having thought about it as best we can and making recommendations. So what you have said is that maybe what you are doing is tempering the degree of zeal or

certainty and so forth, but at the end of the day, we can't avoid it. We have to make the choice. We have to make the call based on best input.

Back to this. Can we just simply define the optimal state?

DR. FERREIRA-GONZALEZ: I think we also have to keep in mind that we have the laboratory-developed tests and you also have the laboratory or the laboratorians that offer the test. It seems to me there are two sets of regulations, that some of them are overlapping and some are not, that could be overly burdensome to the laboratory. We can actually maybe stifle some of these innovations by over-regulating this system.

DR. TUCKSON: I understand. I guess what I'm asking the Committee and all of us is, look, we can get caught up in 8 million machinations of everybody's special interest and every reason why the FDA people are going to get pissed, the laboratorians are going to get pissed, Uncle Sue is going to get pissed.

At the end of the day, can't we just clean the slate and say we are not worried. At one level, you have to start with I'm not worried about everybody's special

interests. I'm worried about the people. You have to say to the American people this is the optimal situation and then from there you work backward.

DR. FERREIRA-GONZALEZ: Muin.

DR. KHOURY: I think the end of your tenure, boss, here we are seeing the great side of you.

[Laughter.]

DR. KHOURY: So, what do we want. Let me put this public hat on. We want good tests that pass through a certain amount of standards that have analytic validity, good clinical validity. I think Steve just described the gold standard, so to speak, that FDA process. What he is challenging all of us is to design the Plan B where you get 50 cents for the dollar or 10 cents for the dollar. That is what we need to think about.

Now, people are selling stuff that is not validated out there, and you drive a train through the whole process here, from here down to the consumers, going around all of the railroad. You don't even have to go through CLIA, I think, if you go this way.

So, could we design, with Steve's help and with

CMS's help, together? This Committee can make that recommendation, describe what the ideal is, which is truth in advertisement and minimum standards of clinical validity, analytic validity, quality control, clinical utility itself. That will depend on clinical trials, and maybe more creative ways of coverage with reimbursement can happen.

But you need a threshold below which stuff shouldn't be just going to the market. That threshold could be defined in the FDA process or some other process or a public-private partnership coming together, or stakeholders. But this is a group where I think we can make it happen.

DR. TUCKSON: By the way, Andrea, as you take it back over and keep driving us through, if it turns out that the best we can get, at least in terms of our statement, is to write down what Muin just said, the public deserves a threshold that you can't drive a truck through. The way you do that is you have to close this door and that door and that door.

That is what this Committee is saying. We may not be able to get to the level of specificity that you

absolutely want, but then therefore here is what you have to do to get to that level of specificity. Even though it is not the optimal report, at least it is a pretty damn good report. But above all, let's clarify where those holes are and close the door.

DR. AMOS: Reed, I agree with everything Muin said, but there is another piece to it. We want people to continue to develop the new tests and new technology. You have to balance the regulatory zeal with the commercial realities.

DR. TUCKSON: By the way, just to put that issue to rest, I'm glad you did that. That is a sober analysis. I have enormous, as you can tell, private sector interest and sympathies myself. I believe in that.

Let me make sure, though. Does anybody believe on the private sector side that unless you get a free pass of no oversight, [there is no other] way you are going to be innovative? In other words, are there any innovationists in the room who also say, "I believe in innovation so strongly that I should never have to pass any scrutiny"? That doesn't exist, either.

DR. FERREIRA-GONZALEZ: It doesn't exist either because today we have CLIA.

DR. TUCKSON: So there is no innovationist, I believe, who will stand up in public and say "No one should ever look over my shoulder." I just want to make sure. That issue is off the table.

DR. WILLIAMS: Didn't we hear that this morning in public comments? From one of our public commenters I think we heard exactly that this morning.

DR. GUTMAN: That is what 23 and Me said.

DR. TUCKSON: So we had one. Other than one?

DR. FERREIRA-GONZALEZ: I don't think they called for no oversight. They claimed they don't fall within the current oversight.

DR. TUCKSON: Yes.

MS. ASPINALL: I heard them say that today they don't know where they fit in the system, but I thought she specifically said we welcome appropriate oversight.

DR. TUCKSON: They just said that the rules don't apply to them.

Anyway, the bottom line is I think it is really important that we get this sense of balance. But I think

balance does not mean that the Committee needs to be scared into apoplexy that says that you stifle innovation the moment you say "oversight."

DR. AMOS: But your question was what is the optimal state. It has to consider the whole picture. It really has to consider both sides of the equation.

DR. TUCKSON: Got it. So, too much. Now let's move forward. Can we all acknowledge the general tone of Muin's comment that what we want to try to do and now what we are moving toward is from that sort of basic sense that there should be review. Now the question is, what is the nature of that review and by whom.

DR. FERREIRA-GONZALEZ: I think Steve has a [comment.]

DR. TEUTSCH: It follows from that. What I see in these recommendations is that minimum threshold is a risk-based threshold that should go through FDA. That is what we have come to as a Committee. Above some level, and we need a group to decide what that level is, it should go through FDA to protect people adequately, economics or no economics. Then we are talking about the things beneath that level that need to have another

system which is going to be the one that oversees the LDTs.

I think we have that first level of review in here. That is my sense.

DR. TUCKSON: Let's define that first level of review.

DR. TEUTSCH: We are going to convene a group to figure out, given a certain level of risk of a test, above that level it should go to FDA review.

DR. TUCKSON: Now, let me just ask you. If FDA is doing it today, why do we need to restudy and why are we unsure of the adequacy of the review that they are doing today?

DR. FERREIRA-GONZALEZ: There have been some concerns.

DR. TEUTSCH: What we have is the IVDMIA guidance, which we say it should not be based on the mechanism of the test, it should be based on the risk of the test.

DR. TUCKSON: Steve, you are not doing that today?

DR. GUTMAN: We are doing risk assessment. We

are doing risk assessment in general for commercially distributed tests. The classification is actually a matter of public record. You can go in and look at our databases and see where virtually all the common tests, whether they are Class 1, Class 2, or Class 3. Most new tests will either be de novo Class 2 or Class 3.

So we are doing it, but we are doing it only for commercial tests, with the exception that IVDMIAs we did say we thought that the --

DR. TUCKSON: So for the commercial test there is no risk stratification today.

DR. FERREIRA-GONZALEZ: Yes, there is.

DR. TUCKSON: Then, why can't you just roll that over? So you know where I'm headed, and I think it is pretty obvious, this report calls for 18 commissions, 43 studies. The Secretary needs to allocate money to Bob, Joe, and Sue to study something or another. At the end of the day, what are you left with here?

I'm just trying to take out as much uncertainty as we can. If we are doing it today and if it is all right, then keep doing it.

DR. GUTMAN: Since we do have a risk-based

program that we have been operating for 32 years now, it would be our preference not to scrap that and start with a new risk-based program. The program has been refined, and I'm not suggesting the program couldn't be refined further, but the idea of starting over again strikes me as novel but unnecessary.

[Laughter.]

DR. FERREIRA-GONZALEZ: Mara.

MS. ASPINALL: I won't disagree with the fact that it may be novel, but I think, Reed, in clarification to your question and then moving on, what we are talking about are LDTs. What we are talking about are laboratory-developed tests which are not commercially distributed in the same way as I think what Steve is talking about is. [These are] not IVDs and are typically looked at more as a service than a product in casual conversation.

I think it is very critical for us to recognize the differences with an LDT both in terms of time, effort, money to create it, the work that is behind it. Not the technology itself because I would agree that it cannot be technology-based. I also think we can't

predict the technologies five years from now because they are changing.

But regulating a service is very different than regulating a product. The difference between CLIA and FDA, which goes back a few moments ago, is that CLIA, for the most part -- some may argue with this -- regulates the laboratory. Because there are a number of different LDTs going through that laboratory, FDA is regulating, on the other side, the tests themselves.

So that was the issue about fundamental overlap but not quite equal in terms of how this regulatory scheme is. I would say we need to recognize that a laboratory-developed test is not the same as a commercial kit with instructions and that by definition is made to be in everyone's hands and relatively simple to do going forward.

We need to, in the same way, have regulation that makes sense over all LDTs, and I would say not genetic versus not genetic, and at the same time recognizes the need for innovation because laboratory-developed tests have been the engine of many new tests. Many of these laboratory-developed ones start out, get to

market relatively quickly, and then with the adoption and sometimes the innovation and lowering of cost, eventually become the commercialized tests that Steve was talking about.

I think it is absolutely essential that we maintain that system because that is the engine of many of these new tests and technologies, particularly in the field of personalized medicine becoming available to patients.

DR. TUCKSON: As you said that, I recognize that there is a difference between the two. The issue then becomes is that difference so distinctive that it demands different assessment rigor. I appreciate not stifling the role small LDT plays.

The Genetic Alliance folk we asked this question of. I remember what Sherrie got to with this answer, which is making me think about this again.

So what we are recommending then is that somebody else figure out what is the optimal level of scrutiny for the laboratory tests? Even though there is a difference, Mara, I guess I'm still struggling with why would there be a difference in terms of its oversight?

MS. ASPINALL: I think that is the fundamental piece of the debate. I agree with you. I think we should take a stance and not say it is then yet another committee to do that.

DR. TUCKSON: There may be a difference without a distinction from an oversight point of view.

MS. ASPINALL: I would say there is a difference in the oversight, the need for oversight, the timing of oversight, and the access of information that is available to the lab doing it.

DR. TUCKSON: Steve, the process that you use now for the IVDMIAs, the things that you use now, describe that process so everybody has the same knowledge base.

DR. GUTMAN: Well, we have actually cleared only one IVDMIA. It went through a Class 2 de novo, so it was viewed as a moderate risk device. It had a prognostic claim, so that would have also made it a moderate risk device rather than a predictive claim.

We respected the fact that it was a very complex device. It had, I think, 70 or 72 different signals. So rather than do extensive analytical studies

on each of the signals, we used the signature itself as the signal by which to determine performance characteristics. We did insist that the signal be reproducible and robust over time over operators so that we felt that if you got the signal you would always be getting the same signal.

We had no way to analytically credential this particular signal, so we credentialed it in the clinical outcomes that the company had reported and performed. So it was a very unusual submission. It shows, I think, the flexibility of our review process.

DR. TUCKSON: Did it cost the manufacturer a billion dollars to go through your process? Is that the thing that is going to kill off the poor lab people?

DR. GUTMAN: Well, no.

DR. TUCKSON: That is not the issue?

DR. GUTMAN: Again, I would argue that what would cost the companies the most money -- and Mara will know this and can agree or disagree -- is actually to do the studies that will demonstrate that they add value and will make my colleague from CMS happy, or somebody from BlueCross BlueShield happy. So I think those trials are

the more expensive.

But I can't say it is a no-cost deal because we do ask annoying analytical questions about precision and repeatability.

DR. FERREIRA-GONZALEZ: I think it is important to realize that there are a number, for example, of academic medical laboratories that don't have the resources of the private sector that could think twice in developing this type of testing just because they will have go through this process. We might be hampering some of that innovation because of this.

DR. TUCKSON: Muin.

DR. KHOURY: I just wanted to follow up on Steve's comment and your question, Reed, about does it cost a billion dollars to get to that point. While we don't want to stifle innovation, you [could] put something prematurely out there that could hurt people and things that might make sense or no.

Just going through the EGAPP recommendation that just came out in December, plus the EGAPP working group going through six or seven, many of them established, genetic tests, there is some missing

information on both analytic and clinical validity. If you had to do it all over again, you would want to have that information while you are innovating because, at the end of the day, when you review things at the FDA level or in the EGAPP working group or the taskforce reviewing the data, the data has to be there.

So just the fact that there is no data, one can say there is no data. But if you rush it through the system, there will be premature release of technology.

DR. TUCKSON: You make a good point. The opposite of that point is a well-meaning nut in a laboratory who creates something that hurts people. I didn't have the money to figure out whether it would hurt anybody but I have terrific intentions, and therefore I released it. You wouldn't want to stop me, would you? Yes, we would. So there is a balance.

I guess where it winds up is -- and I'm just going to try this on you all and you tell me whether we can do better than this -- is the best that this recommendation can do is to take Muin's earlier comments about turning off all holes and that there should be a minimum threshold that everybody should get. That is the

ideal state.

No. 2, we believe that the FDA model for reviewing whatever it is, is a good template that may not be able to be applied to all, but a high level of review by the FDA assures for the tests that meet the following criteria this is something that you really want to apply that rigidness to.

For things that don't reach that level of scrutiny but recognizing everybody has to go through something, we do call for some process in an urgent way that at least accomplishes a minimum threshold defined as [whatever.] That is what we are at least coming out of this thing with.

Now, maybe we can go further than that, and maybe our recommendations speak to how you lay that out. I'm putting a strawman up for you all to hit at.

DR. FERREIRA-GONZALEZ: I don't think that is very different from what we are recommending.

DR. TUCKSON: Let's go through the recommendation.

DR. FERREIRA-GONZALEZ: Muin.

DR. KHOURY: Given that you just said all of

this, Reed, I think what would be important in that process is to put out the data that currently exist for the truth in advertisement. That is how we get back to this concept of the registry. Maybe we will revisit that point when we get there.

But basically, as part of this process, it is time to put the data out.

MS. ASPINALL: Muin, I think that that is exactly right. The devil then becomes in the details. The recommendation in concept, as Marc spoke about a while ago, that the FDA should exert some authority in this area but not do it in a way that stifles innovation is where the registry [comes in.]

And, I think it is fair to say the Committee moved from a voluntary registry to where the overwhelming public report was in terms of a mandatory registry. Some of the proposals, and I was involved in one, talk about having that for at least a period of time before there was any more formal FDA pre-market review just given the massive change that this is for the industry.

DR. FERREIRA-GONZALEZ: Are you recommending that in lieu of, for example, some of the moderate risk

and lower going through review, just using the registry to convey that information?

MS. ASPINALL: Understanding Steve's comment about ensuring that the registry itself was accurate and up to date, which I think is an important issue, it has to be, the same way it is now, the burden of the companies or the universities or the laboratories to put that information up and, like today, the FDA can say "We have a problem with what you are saying." We talked about the FTC in terms of inappropriate advertising.

I think that that is a very important, at a minimum, relatively immediate -- like months to a year -- process. We can put up a registry, have full transparency with an industry, which I think is critical, and then from there evaluate where we go.

The other piece that I heard is some folks saying there are a dozen or two tests that would fit IVDMIA and a few hundred that would fit LDTs. I heard other people say no, there are a few hundred that are IVDMIAs and a few thousand that are LDTs. I can't say. My bias is there are probably more rather than less, but everyone has a very legitimate argument that says why

their position is right.

So I am concerned today to put in a pre-market review, one, because it stifles innovation; two, I don't know what we are getting into in terms of the number of tests. So having an aggressive mandatory registry. This is Sarbanes-Oxley. The people who are putting it in need to sign off to say "I agree with this. It is truthful." I don't have a problem with that.

And, that we recommend a very prescribed registry for which every piece of information is the same so some company can't interpret it one way and another laboratory interpret it another way. Use that as the baseline. Put that in very quickly so that we have the full transparency and, with that, have the data to then potentially go on to have a more aggressive FDA process.

DR. FERREIRA-GONZALEZ: What you are saying, again, is that there is a different model, then. The first approach will be to have a mandatory registry for a narrow section of laboratory-developed tests, however we define this narrow section.

MS. ASPINALL: Well, narrow or not so narrow. Several of our folks said it should be broad.

DR. FERREIRA-GONZALEZ: High risk or whatever.

MS. ASPINALL: Or just all LDTs.

DR. FERREIRA-GONZALEZ: After a year or two of this, then we will have enough information on what we are actually talking about to be able to gauge the best route to go about doing the evaluation of the quality and the analytical validity and clinical validity of these tests as they go through the market.

MS. ASPINALL: Yes. To me, the beauty of the registry system and having that information available is that we can see it in our lifetime. It can happen relatively quickly. I heard a number of groups, and to be clear, I'm involved in some of them, that have said a registry is something that is doable. Not every group, but many of them have said, if you are going to have a registry, make it mandatory.

DR. TUCKSON: Mara, let me just make sure that we put this straight. The registry is a set of information that describes what? The status of its review? None of it. Just the analytical validity.

If you describe your ideal state, everybody gets something.

MS. ASPINALL: Yes, although I would say virtually everybody has something today. But under this system, everybody absolutely has something. But everyone has something today with a very few loopholes.

DR. FERREIRA-GONZALEZ: Now, let me make this clear. What you are recommending, then, is at this point that we do not make any assertion about the FDA role in the pre-market review but to create this registry with the specific data elements that allow us to get a handle on what the current testing is. From that, move forward to decide what model might fit with these laboratory-developed tests for pre-market review or not.

MS. ASPINALL: Right. What I heard Marc say earlier is the Committee talked about the principle of ensuring complete review and the principle of having the FDA involved I think is very important. But how to implement that, to me, is where innovation and practicality -- whether the FDA can do it over the right period of time and this actually gets enabled despite some legal issues, et cetera -- make this an alternative that allows us to move forward with something specific but doesn't cut off the FDA coming in at a point.

DR. TUCKSON: So here is what we are going to do. Let's go back through the recommendations and let's see what will change. I think that there is some tweaking needed on the preamble on Slide 4, Recommendation 4. The preamble stuff defines the mother, God, and country, but let's skip that for now. Go ahead.

DR. FERREIRA-GONZALEZ: Wait, wait, wait.

DR. TUCKSON: I don't want to wordsmith it, but it is something.

DR. FERREIRA-GONZALEZ: It is not a matter of wordsmithing. It is a concept. Maybe as they go through this registry there could be a role for FDA and CMS to work together to look at these types of things.

MS. ASPINALL: Many of the proposals say that. I think that is important.

DR. TUCKSON: Mara, describe, then, in your mind the relationship between the registry and the review. I don't think you mean the registry is a substitute for review. The registry is an assist to the review. It is also an assist for transparency. But the registry in and of itself does not protect you as citizens.

DR. FERREIRA-GONZALEZ: Well, it does protect.

DR. TUCKSON: How?

DR. FERREIRA-GONZALEZ: Because it starts forcing all the laboratories that develop laboratory-developed tests to start putting information out there.

DR. TUCKSON: Right. But the information has to be analyzed by someone.

DR. TEUTSCH: Someone has to vouch that the information is correct, on the analytic validity, and what we know about the clinical validity of these tests that warrant them being used at all. Right now we don't even have that.

DR. TUCKSON: That is essential for review. But you can't say to Mrs. Jones, average citizen, "Hey, Mrs. Jones, go to the registry. Look up the clinical validity. Now go have a conversation with your doctor." The patient is saying "I'm assuming this thing works."

DR. FERREIRA-GONZALEZ: Hold on. Let's say this. Analytical validity is covered under CLIA. So the problem is the clinical validity; is that correct?

DR. TEUTSCH: Exactly.

DR. FERREIRA-GONZALEZ: Now, we [can] put in

the registry, where we have all this testing, all this information, but also we heard from Mike Watson today -- he just left, unfortunately -- about this database they are developing to start gathering this clinical validity information that can be even linked or built in together within this registry. Then we get to the piece of the clinical validity. If there is no sufficient clinical validity within this registry of the tests assessed through this database, then CMS or whoever can go back and say to the laboratory, "Your test here has no clinical validity."

DR. TUCKSON: So, who puts the pieces together?

DR. FERREIRA-GONZALEZ: Muin has a comment.

DR. KHOURY: Today many of the pieces are available. If as a consumer want to get this 23 and Me or whatever test, it is very hard for me as a consumer or provider to get all these pieces. I know I can get them if I work very hard at it.

These EGAPP reviews I come back to because there is quite a wealth of experience from these several reviews that are ongoing. Steve can attest to that.

It takes a long time to assemble the existing

information on analytic validity and clinical validity of the tests, and these are sort of low-hanging fruits in the EGAPP market. So by requiring that formal registration in one place or in a virtual place, whether it is NIH, CDC, FDA, CMS, or some kind of a virtual place, you can develop a registration process where people put in that information for people to evaluate.

Now, evaluators can evaluate it at any given point in time. The FDA process can kick in if they want it to kick in. An EGAPP-like process can kick in. It becomes, really, part of the data collection that will help the assessment of the validity of that information, but by requiring that form and then refining the data elements, we are helping the test developers say this is the kind of data we want, but also, we are helping them invest in the research that is needed to get that data. We are also helping the NIH and other funding bodies to do that research.

So this could be done under the auspices of the public-private partnerships if we want the buy-in from the private sector to steer the registry in a way that avoids mandatory but with strong steering from the

private and professional organizations, et cetera. We can all work together to try to begin to populate this so that we can achieve, in the long run, that kind of idea that Steve has described.

DR. TUCKSON: That is the key thing. Again, the registry is information necessary for people to make the evaluations.

I want to make sure I understand the sense of the Committee. The Committee is not saying that it is okay, that the public is protected because there is a registry. Go look it up on the registry, Ms. Jones. Do the calculations, run the math, and you will decide whether you are fine. At some point, the registry is information that is used but there is some agency protecting the public that is saying it is okay.

That is all I'm trying to get to. Am I missing the sense of the Committee?

MS. ASPINALL: I don't know. My sense is it actually is a mix. To be fair, I think that many who have advocated for a registry -- and I won't say it again, but I have been involved in some of those efforts -- would say that it is probably best suited for

virtually most of the tests that go through physicians. So it is not Mrs. Jones who goes to the registry, although she could. It would be a physician who goes to the registry, who would presumably understand the information that is listed under Test A, B, and C for the same condition.

So I think that this works best in those circumstances and that the level, I would imagine, of scientific rigor here is not necessarily based for a consumer. It is based for a physician so we have more complete information on analytical and clinical validity in that area.

I think the concept behind that is get it up and get it done because it doesn't exist now. So at an absolute minimum, when we talk about professional groups or other organizations, you just can't get that information now.

DR. TUCKSON: Steve has his hand up. One sense I get is, no one here is arguing against the necessity of a registry. That is important. I still want to try to make sure that we are getting to consensus that, okay, you have the registry. That is important. Let's fight

for that. But, are we also saying you can stop there or are we saying you go further? Steve.

DR. GUTMAN: I have two points. First, don't underrate Mrs. Jones and her doctor, Dr. Smith, because her doctor may actually know less about the tests than Mrs. Jones in 2008. So the deal is there is a lot of ignorance among doctors about, in particular, lab tests. If you haven't read the Rand Study in the New England Journal of Medicine in 2004, please read that because it is very sobering.

But that is the deal. You have crystallized it for me. FDA actually isn't opposed to, frankly, having moderate or moderately high or maybe high or certainly low risks put into a registry. In fact, that would be the only way we could survive.

What I was trying to say about the dime on the dollar is exactly what I think Reed is struggling with. I have seen too many bad data sets, either inadvertently bad or deliberately bad or something in between, where they pool data. It is too high in this one, it is too low in this one, and you pool them together and you have a statistical gold mine. I have seen matrix changes. It

was under Judy Yost's authority, not mine. She said, "Can you send us the data?" and they said, "We will send you the 14 samples right away."

I'm telling you that that is what makes it credible. If the professional societies and the public-private partnerships step up and act in a pseudo-FDA way, then you can say to Mrs. Jones or to Dr. Smith this is a credible registry. It has been quality-controlled by an amalgam of the ACMG, AMP, CAP, AACC, ASM, maybe FDA or CMs. It is audited to make sure they know what they are doing and maybe make sure they didn't own stock in the ones that they evaluated.

But that is tricky. I'm not sure this Committee needs to resolve that, but I certainly hope in the recommendations that pass forward to HHS there is a desire for accountability in it and not just be registry, it be quality control of material entering that registry. I don't give a damn how it is done. I just would like, as a patient, to see it done.

DR. FERREIRA-GONZALEZ: But the quality control of the testing that comes in the registry is under CMS. The quality control is already checked by CLIA in the

different reviews.

DR. GUTMAN: But CLIA samples. CLIA doesn't look at every single test. They come in and they will look at a lab with a dozen home brews and they will look at one or two and they sample in the middle of their review of personnel safety, quality assurance, the check on environmental. How can that possibly be?

DR. FERREIRA-GONZALEZ: Mara, then Scott.

LT COL McLEAN: I just want to point out that a really excellent registry is wonderful but it doesn't make it safe. The safety is still a wild card depending on what is happening with the clinical encounter. Just like a scalpel, if he is not a good surgeon you certainly can get cut.

MS. ASPINALL: I guess I like Steve's idea in terms of having a registry as a public-private partnership in some way with key organizations that are also putting their reputation on the line and saying that what is in this registry means something. I think having a registry like that, not immediately going to pre-market review but having a process that leverages the FDA time and CMS's time and has some key organizations that work

together to do that. Again, one of the groups suggested something like that.

But I love Steve's idea to do that because that may, at least as we learn more about this industry, be able to fill the gap of getting the transparency and having all the tests together, which I think we all recognize is valuable. On the other hand, make it a registry with teeth that we know that if it is on that registry with a check mark that some group of professional organizations has gone through. It is very similar to the CAP inspection system.

DR. TUCKSON: Steve, tell me why this can't be again. This is the last time I'm going to ask this, and then I'm done with this thing. You have, in some definition, a high priority set of tests for which there must be pre-market review. FDA says, I have to review this thing. I'm going to turn to the registry. Look at all this terrific stuff in the registry. My job is so much easier now. I'm here to ascertain that about this test. Terrific.

Plan B is we make some decision that says because of some nature of the test it doesn't need FDA,

it needs an alternative mechanism, but something is there for real oversight to review the test. They go, oh gee, look at this registry. It has lots of information in it. This makes our job so much easier. We will do what we do.

Third, Dear Doctor, if you are interested in knowing a lot more information beyond the fact that it has passed judgment, whatever that judgment is, and this is a legitimate test to unleash on the American people, go look at the registry. Oh my God, this is terrific. Look at all this interesting stuff.

I don't understand why the discussion keeps going do a registry and stop. FDA is off the hook. Everybody is off the hook. All you need to do is do a registry, return to your homes, everyone is safe.

[Laughter.]

DR. TUCKSON: I'm missing that leap. I just think if you have the registry, everybody else gets to do cost effective doing their job.

DR. GUTMAN: I'm a very transparent guy. I play poker by putting all my cards on the table. I think whoever gets stuck with this registry is getting a day

job that is hard as hell because my job is a day job and a night job and it is hard as hell.

So if ACMG or AMP or AACC or COLA or whoever actually ends up quality-controlling the material and starting to discuss with the sponsor, "This precision study wasn't done right," wow, they have entertainment.

DR. DAYNARD: My problem is I haven't heard anyone assume the authority for reviewing LDTs and taking action against those who --

PARTICIPANT: FDA has it.

DR. DAYNARD: LDTs? I mean IVDs. I don't mean IVDMIA. I haven't heard anyone assume that authority.

DR. FERREIRA-GONZALEZ: If you have authority over MIA, they are LDTs.

DR. DAYNARD: I'm simply a mid-level official so I probably shouldn't say this, but the agency has a long history of being risk-based. So of course, the idea of looking at risk, you may argue what is high versus highest versus moderately high versus slightly moderate. You can argue about it, but the idea of a risk-based approach to regulation is inherent in the reg itself. Our Class 1 products are largely exempt and subject to

QSRs. Our Class 3 products generally go to a formal and public panel.

I certainly don't want all of these tests because it is not possible. I do think the high risk tests belong in FDA.

DR. FERREIRA-GONZALEZ: Muin.

DR. KHOURY: The devil is in the details, obviously. But if the LDTs become part of the registry and this is mandated somehow and people start submitting data according to a specific format that is compatible with the IVDMIA, whatever we want to call it, there has to be some peer review process before it goes into the registry, or at least a check for initial glitches.

Now, people who are doing systematic reviews at the end to see whether or not the cumulative data makes sense, like EGAPP has been trying to do over the last five years, that could be done by an independent group or an FDA process if it is leaning that way. But I could envision a situation that requires a lot of thinking and a lot of groups coming together under this public-private partnership sort of umbrella.

But we cannot just take anything that people

send to the registry as fact and then say to Mrs. Jones, "Go check the registry." It has to be peer reviewed. It has to have somehow gone through an initial validation process before we accept it as fact.

DR. FERREIRA-GONZALEZ: Like you say, the devil is in the details. If we are going to say that you have to put everything in the registry and everything has to be reviewed before we actually publish it in the registry, you will completely stifle everything. There has to be some kind of a process where we put stuff in the registry and there is a body of a public-private partnership that starts looking at this. It has to be funded and all these other details. But we have to be cautious when the devil is in the details.

DR. KHOURY: Right. There is some difference between NIH now requires for genome-wide association data or the sequences for the genome. Now everybody who is funded by NIH has to put their data in the NCBI DBGAP, which is the raw material from which people can do other studies.

The problem with genetic test development is you have a lot of data that is proprietary and you have

competition between many, many groups. The way NIH did this with DBGAP was by saying everybody needs these data and these are pre-competitive type data. We need to know Gene X in relation to Disease Y.

So, could we construct a similar situation where instead of talking Test A from Company A and Test B for Company B, to develop an overarching data point on analytic validity and clinical validity of these classes of test by this group or that group or that group.

DR. FERREIRA-GONZALEZ: This is similar to what we heard from the College of Medical Genetics today. They actually developed a database where these data will be put together.

DR. TUCKSON: It is 5:05. We need to resolve this section before we leave for break. So as you all make your comments, let's start figuring out how we get to actual concreteness in the recommendations. We need to have people put on the table what they want.

MS. ASPINALL: I think I'm getting there. First comment: why don't we suggest the registry has a user fee, as many registries have, as the current IVD companies have. Either way, I think it will work out if

we recommend a user fee-based registry, which takes away the issue of is there enough funding to get this done, with a public-private partnership that approves things going into the registry with various organizations.

Maybe then the FDA has the ability to look at that registry and say we still have a question over what went into this registry. But the FDA, working with four or five professional organizations, has the ability to say these are the five things we want you to ask, these are the five things we need to check off. I'm not saying it is five.

Move forward in that way for a period of at least three years where we get the information, we get the transparency, we get it funded by companies with the lab tests, and we do a quality system so the registry itself, I completely agree, has to be respected as accurate.

DR. FERREIRA-GONZALEZ: Now, what you are saying that the FDA can go and start reviewing some of these tests, we are still saying that the FDA would have regulatory authority over laboratory-developed tests. That is the fundamental issue that we need to deal with

for this recommendation. We can say that maybe the FDA doesn't have exactly the regulatory authority over LDT, but maybe it has to be kind of an interagency or so forth. That is the fundamental question we need to answer.

Now, we can say, then, after that that the FDA can review the high risk, or the FDA should for now hold off, let the registry develop, and as the registry develops, work from the registry because we will have built all these data elements and so forth. Work from the registry to actually exercise the authority over a number of these tests if they have questions about it. Marc.

DR. WILLIAMS: I am reluctant to even leave them here because I think we are so far out to sea I despair of ever getting back to shore. We have spent a lot of time talking about the registry, which I see as a means, not an end. I think that the fundamental question was very well stated by my colleague, whose name I can't read because it is tilted the wrong way. But, who has ownership of saying yea or nay?

This is a report on oversight. The issue that

we have heard about is that we have had one test that has gone through an FDA clearance process. We know that there are hundreds, if not thousands of tests that are being used in the clinical arena today, which would seem to suggest that we have a pretty big hole that people are going through where, for a variety of reasons that are well articulated in the report, we have gaps in oversight.

Establishing a registry does nothing to deal with this. I think the critical issue here relates to the ownership of who in fact has the authority to say we look at this or we don't look at that.

As I have looked at Recommendation 4-A, the purpose that I saw of putting the consortium together is to try and see who is going to step up to the plate. Maybe that won't do it. Maybe that would just end up with more talk. But I don't see a registry doing that, either.

I think that ultimately, if we don't come down with some tangible recommendations to the Secretary that say somebody has to take ownership of this -- and maybe we can't define who it is but these are three suspects,

get them in a room, and figure out who is going to do it -- it will be just another footnote on the lengthy trail towards reasonable oversight of genetic tests. I just think we are completely lost at the present time.

DR. FERREIRA-GONZALEZ: Any other comments?

MS. ASPINALL: In answer to the question Matthew raised, today CLIA owns oversight of LDTs? Would CLIA not say that?

DR. WILLIAMS: No, CLIA wouldn't say that. Or, they have said it, but in terms of actually realizing what they have said, it hasn't been done. That is the gap. That is the elephant in the room that we are not addressing.

MS. ASPINALL: You may go either way, but --

DR. WILLIAMS: That is what is in the report. Two hundred pages explaining exactly why we have this. The first rule in quality improvement is systems are perfectly designed to give you the result that you have. Our system is perfectly designed to give us the results of an essentially unregulated market for genetic tests.

MS. ASPINALL: What does CLIA regulate today if not LDTs? I guess that is the piece that I'm confused

about.

DR. WILLIAMS: They are looking at the analytic validity of it.

DR. FERREIRA-GONZALEZ: But I think we also have to look at the reality. Like Reed said, what is their idea. What can we actually do to make sure we don't stifle innovation.

DR. WILLIAMS: Right. I am perfectly cognizant of that point. That is why I think the recommendations that we have come to to say let's at least get the players that we think are important in a room together and say, here is the problem you need to address. We need to have a tangible solution come out of the room.

We as a Committee certainly don't have any right answers that we can impose, but I think we can at least say here are the players that we think are important and we think that the Secretary should ask them to say what is the system that you would propose to fix this gap which currently exists.

DR. FERREIRA-GONZALEZ: So, do away with the current recommendation and say these are the issues that we have identified in the report, these are the three

agencies that have some kind of overlap or not, they need to get together and figure out how or who is going to go about obtaining that.

DR. WILLIAMS: I wouldn't say it is getting away from the recommendations. I think that we have articulated that within the recommendations. I think it is in there. We can tweak it, but we have suddenly become focused on something that is in the recommendations but is only a part of the whole picture. If we just focus on that solely, we are going to lose what is really important, I think.

DR. FERREIRA-GONZALEZ: I think what we have focused on is very important to the entire recommendation, too, because the devil is also in the details of how we are actually going to do this.

DR. TUCKSON: Let's try to bring it on home.

DR. FERREIRA-GONZALEZ: Kevin, you have a comment?

DR. TUCKSON: No, no, no. I always defer to my colleague Kevin. It is never too late in the day.

DR. FITZGERALD: Sure. At the end.

[Laughter.]

DR. FITZGERALD: I agree very much with what Marc is saying here. Agreed, the registry is going to be key, but this other part is also key. When you started to say let's just total No. 3, I thought what we tried to do in 4-A was to make sure that in order not to stifle innovation, in order not to leave anybody out from around the table, everybody is supposed to be there. That is 4-A. When we have this discussion, we want to make sure those voices are there at the table so nobody later on can come back and say "You didn't listen to us. We weren't in on it."

DR. FERREIRA-GONZALEZ: But you are still assuming that FDA will be the body to regulate all these LDTs.

DR. FITZGERALD: I believe what we have here is HHS convenes these agencies. I don't think we claim necessarily in that 4-A, right?

DR. FERREIRA-GONZALEZ: In the preamble we do. That is the issue. In the preamble we do. Mara.

MS. ASPINALL: Kevin and Mark, I guess I have a question. I appreciate what you have said, but if we have a lot of different agencies listed, what worries me

is that that will make it less likely that one would step up because it then becomes a very large committee and it takes a longer period of time to come to clarity with having a longer list of people rather than a shorter list of just CMS and FDA.

DR. WILLIAMS: It depends to some degree on the direction that they receive from the Secretary. If the Secretary says "Sit in a room and in a month I want an answer from you," they are going to do that. That is why I think we have to say this is really important. We can't create a solution as an advisory committee, but here are the people that can.

Again, whether it will be acted on, whether it will just again fade away, at least I think we can say we didn't pass the buck, and I feel like we are passing the buck.

DR. TUCKSON: Let's try to get to some consensus here and play this thing out. What we may have to do is have Marc, who has a good grasp of this, try to draft something.

So here's the deal. Let me try this and just see where we get. We say in our preamble something to

the effect that, Dear Mr. Secretary, it is clear that there is a major gap in the oversight of genetic tests when it comes to the assignment and evaluation of clinical validity. That is a major, huge problem that has a truck that can drive through that hole all the way through to the end.

Therefore, we find that to be unacceptable. Our recommendation is that that reality is clearly identified and determined to be unacceptable. It needs to be fixed.

The solution to that involves a combination of approaches: risk-based assessment that goes through an FDA-like process that is used for blah, blah, blah, and potentially a separate process for less risky things that still meet the hurdle of protection of the public with legitimate oversight. We define "risky" as attributes such as, and we have a few attributes in here as to what is high risk.

To accomplish this, we urge you to fix this urgently through a process of convening the appropriate agencies, blah, blah, blah, and in an expeditious way assign this accountability for this issue.

In making this recommendation, we are cognizant of the concern around innovation and not stifling it. We are also cognizant of the differential data requirements between different kinds of product manufacturers, the IVDTs and the LDTs and all that. However, with that cognizance in mind, we still cannot avoid the recommendation that every test has to pass some scrutiny.

Lastly, Mr. Secretary, a companion recommendation is, to facilitate this process there should be a registry. That registry needs to have the following attributes: blah, blah, blah. That registry will then make it much easier for the FDA review, the FDA-like review, and the alternative pathway review, as well as serve other public purposes.

MS. CARR: Reed, what is the "FDA-like"?

DR. TUCKSON: "FDA-like" is whatever that thing is that he is doing now.

[Laughter.]

DR. TUCKSON: She is challenging me because I was afraid to assign the FDA to be the grand poombah of this because you all made me nervous. I will be happy to have more courage. So I have more courage and say the

FDA ought to be the thing. There it is.

DR. AMOS: I'm going to be a broken record. You have to have the evidence of harm to make such a strong statement. You have to have the data.

DR. TUCKSON: We have 10 minutes. I have thrown out a strawman recommendation. Now what I want to get are people who disagree, and be specific. They have already changed it. My weak, scaredy, fraidy "FDA-like" word has now been changed to "FDA." Now, what other modifications to this knucklehead proposal of mine do you want to make?

DR. FERREIRA-GONZALEZ: I think we have to write it down and come back tomorrow with it.

DR. KHOURY: Why don't you repeat what you just said?

[Laughter.]

MS. ASPINALL: I just have one clarification. I agree with the comments that say we shouldn't pass the buck. So what I was concerned about was that the first paragraph of 4-A was passing the buck back to HHS to make the decision.

MS. CARR: No, about risk. About the risk.

MS. ASPINALL: Just about the relative risk?

MS. CARR: Yes. FDA, bless its heart, did not get it completely right with its first attempt at regulating LDTS, which is the IVDMIA guidance. That is what the preamble says.

So the taskforce is presenting this recommendation that we agree that FDA is the agency that has the authority and has the right mechanisms to review laboratory-developed tests to get at the clinical validity issue. But we also say that they didn't quite get it right the first time they did it, which is with the IVDMIA guidance.

So 4-A says, convene a group of all the agencies and stakeholders to help FDA get it right. The reason they didn't get it right was because they, in our understanding, did not rely on what they say they always do, which is risk, but rather they relied on the technology. That is what we, the taskforce, found. So we want to provide some further input, although, as you said, FDA got a lot of input from the public on the guidance.

MS. ASPINALL: That helps me. I withdraw my

comment because I was confused about having the multiple agencies. Now I understand.

DR. TUCKSON: What we are going to do is this. Poor Andrea and Reed and Sarah are going to redo this now, tonight, right now. Lucky Marc is off the hook with his one neuron dangling like a participle.

[Laughter.]

DR. TUCKSON: We are going to write this, and you will have it as soon as you walk in the door tomorrow. You will decide, hopefully, that it is close to what you want, you'll tweak it a little bit, but we are not going to fool around with it much because we have to move to the next issue.

Muin gets the last word.

DR. KHOURY: While you are doing Recommendation 4, take a look at Recommendation 3 because that [refers to] the registry. Maybe you can work on improvements simultaneously.

DR. TUCKSON: Thanks, Muin. I really appreciate that.

[Whereupon, at 5:28 p.m., the meeting was recessed to reconvene the following day at 8:30 a.m.]

CERTIFICATION

This is to certify that the attached proceedings

BEFORE THE: **Secretary's Advisory Committee on Genetics, Health, and Society**

HELD: **February 12, 2008**

were convened as herein appears, and that this is the official transcript thereof for the file of the Department or Commission.

SONIA GONZALEZ, Court Reporter