SECRETARY'S ADVISORY COMMITTEE
ON GENETICS, HEALTH AND SOCIETY

Twenty-third Meeting

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EBERLIN REPORTING SERVICE
576 Hooker Drive
Gettysburg, Pennsylvania 17325
(717) 334-8200

Committee Members

Steven Teutsch, M.D., M.P.H, Committee Chair
Chief Science Officer
Los Angeles County Department of Health

Janice V. Bach, M.S.
State Genetics Coordinator and Manager
Michigan Department of Community Health
Genomic and Genetic Disorders Section

Paul Billings, M.D., Ph.D., FACP, FACMG
Acting Director and Chief Scientific Officer
Genomic Medicine Institute at El Camino Hospital

David Dale, M.D.
Professor of Medicine
University of Washington

Gwen Darien
Executive Director
Samuel Waxman Cancer Research Foundation

Charis Eng, M.D., Ph.D.
Chair and Founding Director
Genomic Medicine Institute Cleveland Clinic Foundation

James P. Evans, M.D., Ph.D.
Professor of Genetics and medicine
Director of Clinical Cancer Genetics and the Bryson Program in Human Genetics
Departments of medicine and Genetics
University of North Carolina at Chapel Hill

Andrea Ferreira-Gonzalez, Ph.D.
Professor of pathology and Director of Molecular Diagnostics Laboratory
Virginia Commonwealth University

Barbara Burns McGrath, R.N., Ph.D.
Research Associate Professor
University of Washington School of Nursing

Committee Members (continued)

Samuel Nussbaum, M.D.
Executive Vice President
Clinical Health Policy and Chief Medical Officer
Wellpoint, Inc.

Charmaine D. M. Royal, Ph.D.
Associate Research Professor
Institute for Genome Sciences and Policy (IGSP)
Duke University

Sheila Walcoff, J.D.
Partner
McDermott, Will & Emery, LLP

Marc S. Williams, M.D., FAAP, FACMG
Director Intermountain Healthcare
Clinical Genetics Institute

Ex Officios

Department of Defense
Adam B. Kanis, M.D., Ph.D.
Lieutenant Colonel, Medical Corps, U.S. Army
Chief, Medical Genetics
Tripler Army Medical Center
Department of Pediatrics

Department of Health and Human Services
Denise Geolot, Ph.D., R.N.
Director
Center for Quality
Health Resources and Services Administration

Jennifer Weisman
Health Information Privacy Specialist
Office for Civil Rights

Department of Veterans Affairs
Douglas Olsen, R.N., Ph.D.
Nurse Ethicist

SACGHS Staff

Sarah Carr, Executive Secretary
NIH Office of Biotechnology Activities

Cathy Fomous, Ph.D.
Senior Health Policy Analyst
NIH Office of Biotechnology Activities

Symma Finn, Ph.D.
AAS Science and Policy Fellow
NIH Office of Biotechnology Activities

Allison Lea
Program Assistant
NIH Office of Biotechnology Activities

Andrea B. Collins
Deputy Committee Management Officer
NIH National Cancer Institute

I N D E X

P R O C E E D I N G S

OPENING REMARKS

STEVEN TEUTSCH, M.D., M.P.H., SACGHS CHAIR

CHAIRMAN TEUTSCH: Good morning, everyone.

Welcome to the 23rd and now final meeting of the Secretary's Advisory Committee on Genetics, Health and Society.

As always, the public was made aware of the meeting through notices in the *Federal Register*, as well as announcements on the SACGHS website and the LISTSERV.

I want to welcome all the public members who are in attendance, as well as viewers who are tuned in via our webcast, and thanks to everyone for your interest in our work.

We have public comment session scheduled for today at 9:15 and tomorrow at 11:45. We have a couple of people lined up. If there are others who wish to speak, please let us know at the desk so we can get you on the schedule.

As most of you are probably aware, this will be the committee's last meeting and there will be no more committee work after this meeting is

adjourned. All of our task forces are going to be ceasing operations and what remains to be done over the period of time that our charter has been extended, which is through February, is just the completion of administrative tasks such as transmitting our final correspondence to the Secretary and fulfilling the recordkeeping requirements.

The work of this committee, agendas, transcripts, minutes, all of our work products will be available on the NIH website that will remain publicly available.

So this is our time to finalize our work and complete whatever we wish to say to the Secretary so we will have a busy couple of days.

The timing of the decision to sunset SACGHS was based on the expiration date of our charter, which was September 23rd of last month--that is last month.

And the charters of advisory committees are time-limited for a reason. It gives the opportunity for the government to assess whether committees have fulfilled their mandates. And in review of the charter, the NIH Director and the Secretary recognized that the five major topics that

we've been charged to address that were related to genetic and genomic technologies had been addressed by the committee through a series of comprehensive reports and other recommendations that we've generated.

Just as a reminder of the topics that we were asked to talk about or to weigh in on were:

The integration of genetic and genomic technologies into health care and public health; and their clinical, public health, ethical, economic, legal and societal implications of genetic and genomic technologies and applications; gaps in research and data collection; the impact of patent policy and licensing practices on the accessibility and availability of genetic and genomic technologies; and how these technologies were being used in other settings such as education, employment, insurance and law.

So looking at this the HHS decided that a six month period extension would permit us to wrap up our work and allow us to have this meeting to wrap up our work on education and training, and to come to closure on some of the work that we had begun exploring in earnest earlier this year.

Clearly I think all of us believe that

while we made great strides the work is not completed and it behooves us to weigh in on where we think those needs continue to be so that the government--we can encourage the government to seek external advice on these issues, if not from us, from other advisory committees or other sources.

What I wanted to do this morning was to run through many of the accomplishments of this committee. None of us were here when this committee, except for staff of course, was formed and it's an impressive body of work so we have a lot to be proud of but before I get into that I want to really take the time to thank all of the committee members and all of the ex officio members who have really made this an extraordinarily productive committee.

You've all devoted an incredible amount of time. We've had interesting discussions. We've had stimulating discussions. We've had differences of opinion which we need to have on these committees and it has been under--we've had those discussions with civility and I think we've brought harmony to most of these things, and it's really due to all of you. So thanks for all of your work over all these years.

And I'd be remiss if I didn't recognize who actually makes this committee works and that's, of course, Sarah and her staff who do an incredible amount that's not always so visible to the outside world but is very visible to those of us on the committee. They not only keep us functioning but they do an enormous amount of the background work and an enormous amount of the writing, and rewriting and rewriting, as some of us know, that really allow us to produce the work that we do.

So many thanks to all of them.

(Applause.)

So let me start by going through some of the accomplishments.

Do I need to do something to get the slide up? Do I just press forward and it goes? And it goes away. I was afraid of that.

So let me begin.

The committee was first chartered back in September of 2002 and its first meeting was in June of 2003. The first chair was Ed McCabe, who has come back, and we welcome him and we'll hear from Ed a little bit.

DR. : Never left really.

(Laughter.)

CHAIRMAN TEUTSCH: I don't know. I've actually never met Ed.

So this is a treat for me.

Anyway just so you know Ed was the first chair of this committee and Reed Tuckson was the second chair, and both of them, as you can see, had done an awful lot of work during their tenure.

So, as I said, the first meeting was in June of 2003 and the committee's first letter to the Secretary urged support for federal protections against genetic discrimination. And this has been one of the major activities of the committee over the years.

At its second meeting of that year the committee was briefed by FDA and CMS on the status of the oversight of genetic testing and it began preliminary work on genetics education and training. At that time they began a strategic framing process and on the slide that will appear you'll begin to see the topics that they identified.

(Slide.)

At the third meeting in March of 2004 the committee outlined a roadmap for integration of genetics and genomics and health and society that identified the topics that you see here. I'm going

to walk you through each of them a little bit.

The committee played an important role in the enactment of the 2008 Genetic Information Nondiscrimination Act known to all of us as GINA. From its first meeting, concern about the potential misuse of genetic information in health and insurance and employment and passage of the federal legislation protecting against genetic discrimination was one of the committee's highest priorities. And between 2003 and 2005 the committee submitted three letters to the Secretary that urged HHS to support GINA and provided evidence of the need for federal action by documenting the impact of public fears and discrimination on medical decision making, as well as gaps in the law.

On May 21, 2008, GINA was signed, which was an enormous accomplishment, and the committee continued to monitor the rulemaking and the implementation process. We'll hear actually more about that later on in our meeting.

In 2004 the committee issued a resolution on genetics education and training that provided actions the Secretary should take to ensure adequate genetics and genomics education and training of all health care and public health professionals and, in

particular, promoted culturally appropriate public education to equip consumers with the knowledge and skills they need to participate effectively in health care decisions that are informed by genetics. This topic, too, has not ended and we'll be hearing from the committee working on that and we'll have some recommendations, hopefully, to move forward to the Secretary as we complete that report.

In 2006 SACGHS completed a report that provided nine recommendations to alleviate barriers and improve current mechanisms for coverage and reimbursement of genetic tests and services.

Between 2004 and 2006 the committee wrote two letters to the Secretary recommending enhanced collaboration between FDA and FTC in monitoring DTC advertising for genetic tests.

In July of 2006 the FTC, Federal Trade Commission, FDA and CDC issued a joint consumer alert that warned consumers that direct-to-consumer tests may lack scientific validity and provide results that are meaningful only in the context of a full medical evaluation (more on that later as well).

In 2007 the committee completed a report on policy issues associated with undertaking a large

population cohort study of genes, environment and disease, and provided 18 recommendations to address policy gaps and evaluate public opinion about such a study to inform study planning and implementation.

In 2008 the committee finished its report on pharmacogenomics which provided 14 recommendations to enhance the development of pharmacogenomic applications and their integration into clinical practice and public health.

Now as we move forward here you'll see things that some of us were actually heavily involved with.

In 2008 the committee completed a report on the oversight of genetic testing and made 15 recommendations to maximize the benefits of genetic testing and minimize harms.

Finally on this list, the SACGHS began its analysis of the impact of gene patents and licensing practices on patient access to genetic tests in 2006 and that report was completed in 2010.

Patient access to genetic services and technologies was one of the committee's three overarching issues when it identified priorities in 2004 and public awareness of genetics and consideration of genetic exceptionalism were the

overarching issues.

The Patent report's six recommendations identify steps that HHS could take to help address existing harms and help eliminate potential barriers to the development of promising new technologies.

(Slide.)

As many of you know, having worked through that initial set of priorities, Paul Wise, who unfortunately couldn't be with us today, led us through a priority setting process and the list of our priorities since 2008 is on this list. In addition to what you see here we were reminded that we needed to pay particular attention to health disparities across all of these topic areas.

In 2010 we completed a report on DTC testing that identified gaps that limit the ability for consumers to make informed decisions about testing results and how DTC test results can be applied to guide health decisions. To address these gaps the report identified five action steps based on prior recommendations. In addition, the report identified issues that need further study by appropriate federal agencies.

Since the committee's 2004 resolution advances in genetics and genomics have provided and

continue to provide better insights into disease process and improved applications of genetic testing to inform public health or health decisions. The health care community, however, as well as the general public are challenged to keep up with the pace of these advances. Adequate and appropriate education is needed to ensure that everyone has the knowledge and tools necessary to aid decision making regarding genetic testing and screening.

Today we will consider six recommendations for genetics education and training, and we'll bring the report on this topic to closure. I hope. I am confident.

Over the past year the committee, with the assistance from expert speakers, has explored issues related to genomic data sharing. Today we'll hear from a final panel of speakers and identify the salient issues that should be conveyed to the Secretary.

Clinical utility and comparative effectiveness determinations help guide clinical care, establish clinical guidelines and inform coverage decisions. Given the growing role that genetic testing is expected to play in the future of health care assessing the clinical utility and

comparative effectiveness of various genetic tests will be a constructive way to ensure high quality health care and potentially control future health care costs.

Over the past year the committee followed and analyzed federal activities related to comparative effectiveness research in the formation of the Patient-Centered Outcomes Research Institute, PCORI. To come to closure on this topic later today we will identify the salient issues that we should convey to the Secretary. To come to closure on this topic later today we will identify the salient issues that we should convey to the Secretary.

In 2009 SACGHS held two sessions to hear the perspectives of various stakeholders in health care reform to identify key issues that can enhance and challenge the effective integration of genetic and genomic technologies and services into health care.

In 2010 the committee decided to focus on implications of affordable whole genome sequencing. At the June meeting we heard from speakers who provided insights on the quality and management of whole genome sequence data, ethical, legal and social issues related to whole genome sequencing,

and the impact of whole genome sequencing on clinical practice, and the economics of health care. Today we'll hear from the two final speakers and then identify the issues that we need to convey to the Secretary.

Problems with coverage and reimbursement limit the accessibility of genetic tests and services and their integration in the health care system. The committee continued to pursue these issues that were originally identified in the 2006 report but remained unresolved, as well as new issues that have emerged since that report was completed. In a 2009 letter to the Secretary, coverage and reimbursement of genetic tests and services was one of the four areas identified as a priority as HHS considered health care reform.

Finally, on this list, public health genomics was identified as a multi--which many of you know is a multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technology to improve population health.

In 2009 we sent a letter to the Director of the HHS Office of Disease Prevention and Health Promotion in support of the incorporation of

genomics into Healthy People 2020, the nation's health objectives. However, the committee did not have an opportunity to explore this important area.

During the meeting we will discuss the salient issues in public health genomics that we may wish to transmit to the Secretary.

(Slide.)

So over its ten years the committee completed six reports and the last one, which is blank, we will do today, which is on education and training.

I was terrified when I saw this slide.

(Laughter.)

Talk about tabula rasa.

(Slide.)

We also sent ten letters to the Secretary on coverage and reimbursement, direct-to-consumer genetic testing; the Surgeon General's Family History Initiative, genetic discrimination, health information and infrastructure; and the oversight of genetic technologies.

(Slide.)

In addition to the letters to the Secretary we have sent correspondence and other federal activities and published two articles. The

additional letters were sent to the IOM Committee on Comparative Effectiveness Research. We provided input to the Meaningful Use Workgroup of the Office of the National Coordinator of Health Information Technology Policy Committee, ONCHIT. We have sent letters to the Centers for Medicare and Medicaid regarding a proposed rule on its Electronic Health Record Incentive Program and ONCHIT's interim final rule on the initial set of standards, implementation specifications and certification criteria for electronic health records.

As I indicated, we also sent a letter to the Office of Disease Prevention and Health Promotion regarding Healthy People 2020 and the need to have objectives on genomics.

We also have two publications in the *New England Journal.* Perspective highlighted a subset of our recommendations that would help ensure the promise of genomic medicine, which hopefully all of you have seen. It was just published in September and it's in your table folders. And an overview of the Oversight Report was published in 2008.

(Slide.)

We've made over 60 recommendations and, in fact, we didn't just make recommendations and

generate reports. The good news is that many of these activities have led to actions on the part of the Federal Government and we believe have influenced others as well.

(Slide.)

I just want to highlight a few of the recent ones. In fact, they go back many years and I mentioned a couple such as GINA which are clearly landmark events.

The FDA is moving forward with regulation of laboratory development--laboratory developed tests.

CMS is planning to update the requirements for proficiency testing of non-waived laboratory tests. They are developing standards for evaluation of genetic tests as part of their work.

NIH has ongoing work to develop a genetic testing registry.

(Slide.)

Through the MEDCAC CMS has begun to evaluate coverage of genetic testing for diagnosis, screening and to guide cancer treatment.

CDC has implemented GAPPNET, the Genomic Applications in Practice and Prevention Network, to help translate genetic and genomic research into

evidence-based clinical guidelines.

NIH has responded to the recommendation to assess the public's willingness to participate in a large population cohort study by funding a research study to assess public opinion and the expectations for such a study.

And, of course, our letter has played an important role in the enactment of GINA and the FTC/FDA/CDC joint response on DTC genetic testing.

So much of our work provided a roadmap to these agencies and at least this illustrates a number of the really concrete steps the government has taken in regard to the recommendations that we made.

So, hopefully, all of you take pride in all of this work as I do and particularly for the work of others and our predecessors. It really is an impressive amount of work and a tribute to the committee and certainly to staff.

Even though the committees will sunset we know that HHS believes that our body of work provides a solid foundation of knowledge and advice to guide them going forward in the integration of genetics into clinical practice and public health. We have an opportunity to build on the foundation

that we've already laid and I would like us to accomplish at least two things at this our last meeting.

First, we will be coming to closure on the Genetics Education and Training Report but, second, I think it would be ideal if we could develop a final letter to the Secretary that sums up not only our prior work but also captures our concluding thoughts about the issues we have just begun to explore, namely the implications of the "affordable genome" and "genome data sharing" and "comparative effectiveness research and utility."

We've organized the agenda with both of these goals in mind and our taskforce chairs have been giving a great deal of thought to these topics over the past two weeks as we've quickly re-crafted the agenda for this meeting. We've asked them each to think about the recommendations that we can make based on our progress to date and you'll be hearing about those later

But before we go further with that approach and in addition to coming to closure on the Education Report I want to make sure that we have consensus that we should be writing a letter to the Secretary to bring these things to closure just to

make sure that we're all in agreement so that we can proceed on that over the next two days.

I see a lot of heads nodding.

Do I see any heads shaking?

No shaking.

(Laughter.)

Just me trembling.

(Laughter.)

How are we going to come to recommendations in two days on things that we have only begun? Okay.

So taking that as a consensus, over the course of the meeting today and tomorrow staff will help draft text for the letter and we'll devote tomorrow afternoon to the discussion of the letter itself and we'll talk about potential recommendations as part of each of the sessions as we go through.

Paul?

DR. BILLINGS: Have there been particularly effective last letters from committees like ours? You know, I wonder if there's any experience that we can draw upon for this. We're lame ducks so that gives us some advantages and some disadvantages that maybe people in Congress will

learn very soon but--so I wonder about that.

CHAIRMAN TEUTSCH: Well, I wonder--particularly successful, I guess, is always relative so--you know, I can't cite chapter and verse and I'll be interested if anybody else has any thoughts. One of the things I did ask our taskforce chairs to do as part of this is to not just think about what we want to recommend to the Secretary but what organizations we want to step forward on some of these issues as well because one of the things we've done over the course of this committee is to revisit our recommendations, talk to the agencies about what they're doing, got updates and at times sent queries back about progress to date and our ex officious have played a really important role in maintaining that pipeline for us. Obviously we're not here to do that but other organizations that have keen interest in these topics and the stakeholders may be able to play that role. So I've asked folks to do that but if any of you have particular insights into how we can make our final letter more impactful or as impactful as possible I'd love to hear it.

Sheila, having probably received a number of these letters over her tenure--

(Laughter.)

DR. WALCOTT: I knew you were just waiting for me to start.

CHAIRMAN TEUTSCH: I figured we could count on you.

DR. WALCOTT: I guess it kind of reminds me of my husband's words at Passover that brevity is always his key to a successful Seder unlike his grandfather who didn't actually follow that but, anyway, I think to the extent that we have all these great ex officio members and folks are going to be continuing their work and the recommendations and hopefully not just having our great blue books sit on shelves in their offices but I think, you know, really keying in so that folks--there's a lot of turnover as we all know, you know, each couple of years in the leadership. And so I think having it not be too long and having really the key points upfront so that when somebody new or even, for example, Dora (sic) coming back from maternity leave, you know, she can really take a look at that and say, you know, here's where we need to kind of go with this and know who to reach out to, to do that. I think that's helpful.

CHAIRMAN TEUTSCH: Thanks, Sheila.

And on my way here from Dulles last night

I got a call from Reed and so I can't channel Reed all that well but his advice was similar to have a few really key points that we want to make. He was more specific. He said three. So, you know, I think we have probably three key things we want to talk about, the whole genome sequence issues, the data sharing and the clinical utility that we need to move forward on and that it reflects the work that we're actually currently doing.

So staff has prepared a draft, whether you think its brief enough we'll see but we--what they've not put in the draft is what we actually want to say in terms of recommendations and I think you'll see that draft tomorrow but that's sort of where we're going.

David?

DR. DALE: Well, on that short list I'd like to add "translation to practice" because there's a huge amount of information but how does it affect the American public.

DR. EVANS: That could be able to perhaps be folded into clinical utility.

CHAIRMAN TEUTSCH: Were you going to say something else, David?

DR. DALE: I think that's feasible. I

just didn't want it to be neglected.

CHAIRMAN TEUTSCH: I think that's absolutely right. I think in many ways what this committee has been most about is about the translation into practice as opposed to the research. We want to make sure that there's a firm grounding that allows the research enterprise to go forward but part of our main job is to make sure that that information gets out and used and used appropriately to take advantage of all the new learning.

Mac, if you could add that to your agenda that would be great.

DR. WILLIAMS: It's on there.

CHAIRMAN TEUTSCH: It's on there. It's in there, all right.

So let me just run through the agenda so you know where we are headed. This morning we'll first hear an update from the FDA and following a public comment period the committee will discuss the final draft recommendations for the Genetics Education and Training Report. And, as I've said now three times, our goal there is to come to agreement on the recommendations so we can approve the final report for transmittal to the Secretary.

After lunch we will have a session on the implications of the affordable whole-genome sequencing and GINA. We had hoped to schedule time for the EEO Commission to present the final regs implementing the employment provisions of GINA, however those regs have not yet been issued so instead we'll be hearing about the initial findings from a study on public awareness of GINA.

To close out the day Marc will be providing an update on policy and funding developments related to comparative effectiveness research and he has also drafted proposed text for a letter to the Secretary and we'll need to discuss whether to decide whether to adopt those.

While we're talking about comparative effectiveness, for those of you who are unaware, ECRI, NIH and AHRQ are sponsoring a conference on comparative effectiveness and personalized medicine on October 19th and 20th here on the NIH campus. That conference will also be available via webcast and a copy of the agenda is in your table folders and we've provided information for the public at the registration desk. So for those of you who are interested in that, and hopefully many of you are, that should be a good event.

Tomorrow morning we will focus on genomic data sharing. Four speakers will provide their perspectives on group risks and benefits related to genomic data sharing and then we'll try to come to some concluding thoughts on this topic for our letter to the Secretary.

Finally, and certainly not least, tomorrow afternoon Dr. Collins will be here on behalf of the Secretary to present certificates of appreciation and I'm sure provide some reflections on the committee's work.

So before we move to the first topic this morning we have just a few announcements. At our last meeting some of our members and ex officios volunteered to serve on the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children Working Group for Carrier Screening. Although our committee is coming to closure the other committee has invited our members to continue their participation in that working group. The working group met once by teleconference in August and decided to do a Delphi analysis to help identify the key issues and will be holding a second teleconference in November so thanks to those of you who are willing to continue in that capacity.

Also at our last meeting we provided comments on the SACHDNC draft report on the retention and use of residual dried blood spot specimens after newborn screening. And that report has been revised based on comments that they received from many groups and individuals, and will be sent to the Secretary this week.

And I assume--do you know when that's going to be available for us to--people to see, Sarah?

DR. : I don't.

CHAIRMAN TEUTSCH: Yes. So, hopefully, that will be then available shortly thereafter. It's usually within a span of two to three weeks.

DR. : Yes.

CHAIRMAN TEUTSCH: Over the summer we had some attrition of the SACGHS staff. Both Darren Greninger and Kathy Camp moved on to other positions.

Some of you have also expressed concerns about what happens to our extraordinary staff with the sunset of our committee. Sarah has assured me and reassured me because we've asked on several occasions that the staff is fine. They have more work than they know what to do with. She didn't say

that she was happy to see us go but all the staff will be able to continue and so it's good to know they'll continue productive work in OBA.

So, Sarah, you have an opportunity to again talk to us about the ethics rules.

MS. CARR: One last time, right?

CHAIRMAN TEUTSCH: Yes, with feeling.

(Laughter.)

MS. CARR: I know you'll miss this especially but I'm going to be very brief today.

Before every meeting you provide us with information about your personal, professional and financial interests, information that we use to determine whether you have any real, potential or apparent conflict of interest that could compromise your ability to be objective in giving advice during committee meetings. While we waive conflicts of interest for general matters because we believe your ability to be objective will not be affected by your interests in such matters, we also rely to a great degree on you to be attentive during our meetings to the possibility that an issue will arise that could affect or appear to affect your interests in a specific way. 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 our discussions. And if this happens we ask you to recuse yourself from the discussion and leave the room.

And I want to say thank you especially on this day to how attentive to the rules you have always been as committee members.

Thank you.

CHAIRMAN TEUTSCH: Thanks, Sarah.

So before we get into the body of the meeting just one more note. There is a group dinner tonight. As custom, logistical information is in your folders and if you're planning to join us, and hopefully all of you are, please let Allison know by the end of lunch today. We'll meet in the lobby of the hotel at 6:30 and walk over.

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: We have our per diem.

(Laughter.)

And maybe that's the reason we're sun-setting. There has been too big a budget on our per diems. Okay.

So let's get into the meat of the meeting.

The first presentation is from Liz

Mansfield who we always welcome. She is with the Office of In Vitro Diagnostic Device Development at FDA. As most of you know, she has been a valued member of this committee for many years and she's going to provide us an update on the recent activity at the agency.

Welcome, Liz.

UPDATES FROM THE FOOD AND DRUG ADMINISTRATION (FDA)

ELIZABETH MANSFIELD, PH.D., OFFICE OF IN VITRO DIAGNOSTIC

DEVICE EVALUATION AND SAFETY CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FDA

DR. MANSFIELD: Thank you.

(Slide.)

So approximately three months ago I stood before you telling you of FDA's newly hatched plans. I think, if any of you want to come get me, I actually told you what was going on approximately 15 minutes before the *Federal Register* officially published so you heard it first here. I also understand that I was one of the most Twittered people that day.

I'm here to give you an update on what we've accomplished since that time and where we think we might be going. Somebody mentioned to me

before the meeting started that it has been awfully quiet from FDA and I think it's because we have had so much work to do we haven't been able to open our mouths with the revision of the 510(k) paradigm, oversight of laboratory developed tests, direct-to-consumer testing, and many other things.

(Slide.)

So this is actually--some of you may have seen this presentation before. It's a retread of what I've been talking about to a lot of people recently but I want to say for the record to take caution with anything I say. It's all provisional and we're still working on this. Anything that I say here doesn't represent a final decision by FDA and I'm trying to provide you insight but this doesn't constitute any guidance.

(Slide.)

So I think this committee is probably acutely aware of the long running discussion on the need for oversight of laboratory developed test. I remember when I started at FDA in 2001 the first Secretary's Advisory Committee on Genetic Testing was going on in which they were talking about exactly the same thing. So it has been ten years that at least this body or its predecessor has been

talking about it. We've gotten a number of other recommendations from other groups over the last couple of years and, of course, the oversight report published by the committee was a very strong motivator.

As I mentioned at the last SACGHS meeting we were going to hold a public meeting, which we did, on July 19th and 20th. It was very well attended. We started off with a venue that I think could hold 240 people and the registration filled up within two days and we got tons of angry phone calls. We moved it to a larger venue that held over 700 people and it was full so there was a tremendous amount of interest, and I think the meeting actually was quite interesting and went rather well. The Federal Register notice that announced that meeting was held open until September 15th upon request of certain of our stakeholders and we have received--I haven't looked lately but I think we've received over 90 comments from various stakeholders on our plans for oversight. We are analyzing the comments and should be done soon. And while we're doing that we're starting to put together a framework document of how we think we might approach oversight of laboratory-developed tests.

(Slide.)

So I will just go through this briefly. I think you've heard all of this from Steve Guttman or Alberto Gutierrez or me over time that laboratory-developed tests are medical devices under the definition in the Act, as well as the regulations in 21 CFR, labeling regulations--not labeling regulations but 809.3.

And, of course, there are history lessons. We scramble around and see when we talked about what. We have public commentary regarding our authority over laboratory-developed tests since at least 1992. Before that there were very few electronic records so sometimes it's hard to find things and to remind people that's not very pertinent here--that we're seeking to regulate the devices that are manufactured and not the laboratories. We believe that CLIA still remains the appropriate body to regulate the laboratories.

(Slide.)

Medical device amendments preceded the Secretary's Advisory Committee by a few years. They went active in 1976 and at that time most of the laboratory-developed tests that we were aware of that were on the market were those tests that used

regulated components like stains, dyes, microscopes, centrifuges, general laboratory reagents and used the subjective interpretation of the results made by a pathologist or other skilled person.

(Slide.)

In the ‘80s genetic testing began to appear as laboratory-developed tests, probably coinciding with some technology such as PCR and the ability to do Southern blotting and so on well.

As a result of that and sort of in the early ‘90s there was a recognition of some safety and effectiveness issues because a lot of laboratories had begun to use unregulated components--we call them RUO--in these genetic tests and the Secretary’s Advisory Committee on Genetic Testing was, in fact, quite worried about this genetic testing and went around and around for a number of sessions. Later on but before that we implemented the ASR rule to provide regulated components so that genetic testing and other new types of testing could go forward and that was an application of a light control.

(Slide.)

So as all of you are acutely aware and as we will be talking about, I think, through the rest

of this meeting the technology has advanced tremendously over the last five years but reaching back even further than that microarrays became available, certain types of highly complex PCR became available. Now whole genome sequencing is on the threshold of entering clinical practice. In some places it actually has entered clinical practice.

Certainly the completion of the Human Genome was very important for many of these because now we knew where to look for what we were interested in and we could put different pieces of the genome on arrays and so on. As this happened, we saw a tiny explosion of even more new tests using even more unregulated devices that came on the market as laboratory-developed tests, including microarrays and the PCRs and so on that had come out of the research arena. They had started out doing research, basic fundamental things which was fine, and had entered into the diagnostic space without any regulation which was concerning to us. In addition, the introduction of complex analysis methods, as well as the ability to do informatics expanded rapidly and we began to see a large number of laboratory-developed or so-called laboratory-

developed tests, I guess I would say, of very much increasing complexity depending on instrument function that for instruments that may or may not have been produced in a standardized quality systems guided way. Many of these laboratory-developed tests were using prefabricated reagents and kits which in our mind took them out of the true spirit of the laboratory-developed test enforcement discretion area.

(Slide.)

I think you agreed as a committee that the enforcement discretion that we had initially applied which seemed reasonable at the time became a loophole and many of the laboratory-developed tests that were coming on the market were dependent on components that were assembled and marketed by others but not regulated by FDA so there’s a significant gap there and, in addition, business models arose that leveraged our practice of enforcement discretion to get to the market rapidly and to avoid FDA oversight.

We realized a lot of this was driven by opportunity as well as funding. We’ve heard from numerous venture capitalists and other people who might fund that a return on their investment is

quite important to them in order to provide money for innovation but we still find that the business model is not really problematic. The lack of oversight is really problematic.

And, in addition, as this laboratory-developed test complex mechanism started to go forward it really began to parallel the traditional IVD manufacturing industry and looked quite a lot like it and it seemed rather unwise, at least in my mind, to have two very similar industries, one regulated and one not.

(Slide.)

So we did try to put our tail in the water in 2006 and again in 2007 to enter into oversight of laboratory-developed tests of a kind that we had not seen before about 2003 which we called IVDMIAs, and that’s IVD Multivariate Index Assays in which the algorithm used to generate the test result is completely dependent on the test set used to derive it and if you change that test set and re-derive the algorithm you’d probably get a different algorithm.

So not only were these tests highly dependent on the developers’ understanding extremely complex validation issues and if you followed the Duke University story and don’t worry about the

Rhodes Scholar part you'll that the real issue is that the tests weren't properly validated. And not only that, they are dependent on--again on uncontrolled complex components that laboratories simply buy and have to trust were manufactured in a way that makes them stable, reproducible and so on. This approach, the IVDMIA oversight approach, was widely criticized from many areas. One of our biggest problems was to be able to define these tests so that people could recognize I'm either making one or I'm not.

We were also criticized for taking a piecemeal approach that is not looking at the entire universe of laboratory-developed tests but rather trying to pick them off one at a time. We actually kind of agreed with that. We wanted to go for things that concerned us a lot but we would actually rather sort of take all the LDTs in a larger more holistic framework, and that's what we're doing now.

(Slide.)

So our current approach is that the IVDMIA is kind of off the table as a standalone kind of oversight and our plan is to look broadly at all laboratory-developed tests or so-called laboratory tests. We don't even know at this point how many

there are, what's being tested and the risks of the tests that are out there. We will be attempting to find this out. As I have told other people I heard a criticism that FDA is trying to regulate laboratory-developed tests and they don't even know how many there and I said, "Do you? Is anybody at risk, because we'd love to have that number?" We've been able to estimate it but we actually don't know and so we're going to have to use a way to get at that.

Our framework so far to implement oversight has included the public meeting to initiate stakeholder input and we've had a wide variety of stakeholder input. We left the docket open for I think 90 days which is a good long time for comments. We have received a large number of comments and we've been meeting since then with quite a few industry groups and so on who have concerns, who have ideas and are trying to help us as we move along, and we continue to meet with these groups because we think that input into this area from a group who have never been regulated before is critically important to put our framework together.

(Slide.)

Here is where I get into don't quote me

and don't believe that this is exactly what FDA is going to do. The elements of our framework--I think it's pretty certain that we'll do a risk-based oversight because that's what we're good at and it has stood the test of time over the last 30 some years since the medical device amendments were enacted. And our plan would be to address the highest risk first because that simply makes sense. It also puts the most work on us because the highest risk tests are also the most difficult to review. So we don't take this lightly because we know that it will give us a lot more work than we necessarily would love to have. We think we're going to start because of what I mentioned before. We don't even know what's out there. We're not sure who is offering what. We will probably have to do some type of registration and listing. Whether that goes through our established registration and listing portal or whether that comes through the Genetic Test Registry, which unfortunately--well, I shouldn't say unfortunately--which does not exist yet (that's the unfortunate part; not that it's voluntary) or something. We need to know who is offering what so that we know, first of all, what we're dealing with; and, second of all, at some

point we're going to need probably to go find the people who aren't complying and say why are you not complying.

Our idea at the moment is we expect that many, many, many of the tests that are offered as laboratory-developed tests now do not have intended uses that we've seen before, that they are unique and have never been regulated. Therefore, we're considering how to classify these ahead of time to give people predictability and to give ourselves predictability in what we're dealing with. We're thinking of using classification panels as we did when we first classified medical devices. We would like to avoid numerous de novo down classifications. That's a lot of work for everybody. So at some point we may be having public classification panels that some of you might be interested in attending and we might even try to draft some of you to be on them.

(Slide.)

Our operational plan at the moment, how we're working internally and why we're not talking very much outside is because this is really hard, we are developing the oversight plan and trying to decide what our options are for moving forward. We

do believe that we will communicate this through publication of guidance describing both general requirements and information on complying. It's still a work in progress so again don't take anything that I'm saying here as a done deal and certainly we want to continue stakeholder interaction.

(Slide.)

I wanted to touch momentarily on direct-to-consumer oversight. We had decided at some point in thinking about this as the direct-to-consumer model began to grow, we did a lot of deliberations, we thought that this model wasn't appropriate for enforcement discretion even if the tests fit the model of laboratory-developed tests due to the way that the tests are offered and the way that the results are received without having the intervention of a health care provider. I think the same week as we had our laboratory-developed test oversight meeting there was, as most of you know, a congressional hearing (the star witness is sitting here among us) in which the GAO reported on issues they had encountered in investigations of direct-to-consumer testing companies. We gave testimony--the FDA gave testimony and were more or less directed by

that committee to consider moving forward with some kind of activity. We had already sent and continue to send letters to the direct-to-consumer test offerers (sic) that we could identify and we've had meetings with many of them so far.

The interesting part is they all use very different models for offering their information. They use different testing platforms. They test different SNPs or whatever they are testing. They analyze them in different ways. They report them in different ways so this is--we're working on a one-by-one basis right now. We've not been able to come up with a single framework that would fit direct-to-consumer testing but we are beginning interactions with these companies to define timelines for when they can make submissions to us and what would be required in those submissions. I think it's interesting to note that upon receiving our letters there have been several companies--I can't even tell you exactly how many--who have chosen rather than to deal with us to leave the direct-to-consumer market and so we've put them aside for the moment and are focusing on the people who want to stay in this market. I think our interactions with the stakeholders are going well. That's the feedback

that we've heard.

(Slide.)

I thought I avoided that but anyway.

(Slide.)

So that's where we are now and where we think we're going. I would love to take any questions or comments if you like.

CHAIRMAN TEUTSCH: Why don't you take a couple of questions?

Questions or comments for Liz?

David?

DR. DALE: Would you comment about a timeline for some of these new engagements or can you?

DR. MANSFIELD: We don't have an exact timeline right now. We think the whole process of getting to the end of the ones that we want to actually see something from could be 15 to 20 years away. One slide--and I wonder if I did skip it or if I accidentally left it out. I guess I left it out--is that I think what will be very important for this group is in our deliberations we have determined that tests for rare diseases, tests for biothreats and possibly for emerging infectious diseases will be an area that we'll want to define

and have a plan for minimal regulatory oversight. Something like maybe registration and listing and reporting adverse events. We have no interest in scaring sole offerers off the market for rare disease testing, biothreats and so on. So we would like to reassure everyone that we're not going to go in--we're working very hard to try to avoid disrupting availability and access to all kinds of tests but especially to these. And so we would like to get something out sort of saying that to give those people--you know, they can breathe a sigh of relief and carry on, probably within the next six months and probably try to describe our framework in a draft for comment in probably the next six months but we don't get to control exactly how quickly things come out.

CHAIRMAN TEUTSCH: Other questions?

If not, thank you, Liz, for moving this forward.

DR. MANSFIELD: Thank you.

CHAIRMAN TEUTSCH: Obviously faster is always better from our perspective but we're glad to see that it's moving forward.

As always, we have a time for public comment and we appreciate the views of our

commenters. They provide not only thoughtful comments on our work but provide us some guidance on where we've gone in the past. That won't be the case this time of course but we still welcome our commenters and the issues that they raise. Copies of speakers' full statements are part of the meeting record for the ones that I know are speaking are in your table folders.

So our first speaker is Ed McCabe, who I mentioned briefly before, who was the first chair of this committee.

So you've seen the sunrise, Ed, and you've seen the sunset but I think you're here to talk to us primarily about some of your concerns where you are now because you have moved since you were the chair.

Ed is the executive director of the Linda Crnic Institute for Down Syndrome.

It's great to see you here. Welcome back.

PUBLIC COMMENT

ED McCABE, M.D., Ph.D.

DR. McCABE: Well, thank you.

Thank you for allowing me to speak to the committee this morning. As a former chair of the committee I have followed your work and have been

gratified by what you have accomplished.

I had asked to give public comment before I learned that this would be the last meeting of the SACGHS. I'm pleased to have been a part of this committee at its beginning and to be here now at your conclusion.

Congratulations on completing your charter.

As was mentioned, I appear before you today as the Executive Director of the Linda Crnic Institute for Down Syndrome at the University of Colorado. Our vision is that the LCI will be a beacon of hope clinically for individuals with Down Syndrome and their families around the world. Our research mission is to eradicate the medical and cognitive ill-effects of Down Syndrome. I come to you to make you aware of a concerning practice that we consider discriminatory against children with Down Syndrome by insurers, specifically Medicaid in Mississippi and Aetna in Colorado. We feel this is a violation of the civil rights of individuals with Down Syndrome.

Children with Down Syndrome in Mississippi have begun to be removed from the state Medicaid rolls leaving the parents to pay out of pocket for

expensive speech, physical and occupational therapy.

We know of at least one letter sent by Aetna Insurance to the father of a child with Down Syndrome in Colorado denying payment for occupational therapy, and that letter with his permission is appended to my comments. Basically they are saying that since these disorders are developmental and/or chronic they are, therefore, intractable and children affected with these disorders will not benefit from these therapies. The services being denied (speech, physical and occupational therapy) are habilitative (sic) services and are considered “essential health benefits” under the Patient Protection and Affordable Care Act.

We challenge the concept that Down Syndrome is an intractable disorder based on simple observation and a recent epidemiologic study. The observation is that I’ve been at this for 49 years. I did get an early start but if we look back at the nearly 50 years with individuals with Down Syndrome they have improved dramatically in terms of quality of life, cognitive function and life expectancy and one must consider that these improvements are due at least in part to access to the very services being

denied by Medicaid and Aetna.

There was a recent epidemiologic study published in 2002 but based on data from 1997 that talked about life expectancy of individuals with Down Syndrome and they categorized white people and showed that they had a life expectancy of approximately 50, black people approximately 25 years, and other races approximately 12 years. Speculation includes access to services is responsible at least in part for these impressive and unacceptable survival disparities.

There is expert opinion from the Down Syndrome Medical Interest Group in the American Academy of Pediatrics that children with Down Syndrome benefit from these services and the guidelines from these committees recommends specific services from birth through adolescence at 18 to 21 years and even into adulthood.

Maryanne Bruni who is an expert in occupational therapy for children with Down Syndrome shows data that support her recommendations, and I quote, “An occupational therapist is one member of a team that can provide professional assistance throughout the growth and development of our children.”

So why have the state of Mississippi's Medicaid and Colorado's Aetna Insurance Programs and perhaps others decided to deny services to children at this point in time? We speculate that there may be coercive intentions in these actions and the speculation is based on precedence from state programs and corporate insurers that I referenced in my written comments.

The concern is that Mississippi Medicaid and Colorado Aetna could be sending a message to their communities that if children with Down Syndrome are born then these insurers will not pay for physical, occupational or speech therapies, and the families will be responsible for payment for these services. These coercive actions have been considered very concerning by a number of authors, including Dr. Linda McCabe and myself in our writings about our fear that we are on the verge of a resurgence of eugenics only with a different name.

In summary, thank you for allowing me to bring this issue to your attention, specifically discrimination against children with Down Syndrome by restricting habilitative (sic) services and what we feel is a violation of their civil right of equal

access.

Congratulations on achieving the milestones set forth in the SACGHS charter and thank you for your outstanding work.

Thank you.

CHAIRMAN TEUTSCH: Thanks, Ed.

Since this is our last meeting and we obviously aren't going to be able to set up a time to talk about this subsequently but reimbursement coverage and discrimination is clearly a fundamental part of what we do.

Maybe if you have--if we have a comment or two or a question for Ed that would be good.

Yes, Mark, why don't you start?

DR. WILLIAMS: So thank you for bringing this to our attention. I certainly would concur with the comments that you've made and would also speculation that, you know, this may just be the tip of the iceberg since the arguments that are being made in relation to Down Syndrome could effectively be extended to just about any developmental condition that we deal with and I think that it's quite important that we address this.

However, wearing my hat of the Clinical Utility and Comparative Effectiveness Research Task

Force I think--and this is not the first time that I've sort of called us out as a specialty--we have not done as good a job as we should to develop data around the effectiveness of the interventions that we put forward. And, while Down Syndrome arguably has more data than many others, I think it does put us on the spot to be very thoughtful about how we actually develop data about the effectiveness of the interventions that we do offer to children and not accept them at face value as always being good and to try and study them. It raises some challenging methodologic issues particularly for rare disorders but I think it's time that we as a genetics profession try to step up to the plate and bring ourselves into the evidence-based medicine world.

DR. McCABE: W e agree completely with you and one of our missions in the Linda Crnic Institute for Down Syndrome is to develop evidence-based best practices because, in fact, the professional guidelines frequently, as you comment, do not have an evidence base. I think for these there actually is some evidence-based that are referenced in my written comments but I agree that it's important for us to step up to this.

And you're also correct, in the Aetna

letter which you have, they talk about these chronic and developmental disorders which include autism and some other disorders. So, you know, my focus is laser-like since August 1st on Down Syndrome but I think this is just the tip of the iceberg.

CHAIRMAN TEUTSCH: David, and then we'll move on.

DR. DALE: Do you have--

CHAIRMAN TEUTSCH: You just turned yourself off.

DR. DALE: Do you have an active program for monitoring state regulation in this area? You singled out two states. Does that mean the others are all okay?

DR. McCABE: We don't know the answer to that. We only know who sent us letters. The Global Down Syndrome Foundation, which supports the Linda Crnic Institute for Down Syndrome, they received three letters from Mississippi but it has also been in the news in Mississippi. Part of my reason to come here is to make it clear because I think it has been somewhat of a local story. And then the Aetna letter, which was used with the permission of Mr. Lloyd Lewis, who happens to be the head of ARC Thrift, A-R-C Thrift, for the State of

Colorado and has a child with Down Syndrome. So he is very public about this issue and very concerned but we don't know how many other letters and whether this is a common decision that's being made. Part of my reason for being here knowing that CMS was represented is to bring it to their attention in case they were unaware of this.

CHAIRMAN TEUTSCH: Thank you. It certainly becomes part of the record and we hope gets addressed and, regrettably, we won't be able to do that as a committee but at least as individuals.

DR. McCABE: Thank you.

CHAIRMAN TEUTSCH: Thank you so much, Ed, and thanks again for coming.

Our next speaker is Mary Steele Williams who is the Chief Operating Officer and Director of Scientific Programs at the Association for Molecular Pathology. We have had folks from AMP here on multiple occasions and always appreciate what you have to say.

So welcome.

MARY STEELE WILLIAMS

MS. WILLIAMS: Dr. Teutsch, thank you for the opportunity to address he committee.

AMP commends the SACGHS for continuing

their consideration of challenges and promises of whole genome sequencing.

AMP recognizes that this is the last public meeting and, as such, we would like to take the opportunity to also express our gratitude and appreciation for you and your colleagues' great work on exploring complex policy issues emerging from advances in genomics from gene patents all the way back to GINA. We thank you.

While we are saddened to lose this valuable public forum and regret that AMP and other stakeholders will not have the opportunity to work with SACGHS on the drafting of a full report on whole genome sequencing, we thank you for your dedication and partnership over the past decade.

As we stated last June, AMP's concerns focus on the clinical applications of whole genome sequencing and not on the advent or adoption of the technology. The wealth of data revealed by whole genome sequencing creates new practice questions that molecular pathologists will have to address. Sharing data among laboratories will promote faster interpretation and scientific understanding of advances and such.

AMP recommends the creation of a central

repository for all sequencing data and corresponding phenotypic information. The submission of clinical and analytical validity information to such a repository would further inform interpretations and the clinical utility of the results.

AMP also views whole genome sequencing to be at times analogous to a fishing expedition and dissimilar to conventional targeted genetic testing. Next generation sequencing can also be used to sequence the entire genome and to perform gene panels for a specific disease. The latter is more in line with the type of testing clinical laboratories have done in the past. However, even with the gene panels using this new technology will require a significant amount of work from the molecular laboratory professionals. Whole genome sequencing will have a significant professional component to the test interpretation and reporting. Understanding the clinical significance of the data generated by these tests will require more cognitive work than usual. The molecular pathologist will be even more instrumental in reporting results than with targeted genetic testing and will take on new challenges such as being the gatekeeper and deciding which information to report and when to update the

interpretation as our understanding advances.

AMP believes that many of these issues and challenges will be best addressed through professional practice guidelines developed by thought leaders in the profession. While molecular pathologists evolve their practices to best implement whole genome sequencing into their clinical laboratories, ordering physicians will also need training and education in genomics to understand and act on the results. AMP believes that medical school curriculum and residency training programs need to devote more time to applications in genomics and integrating complex genetic testing into the clinic.

As hospitals adopt electronic medical record systems their health information technology infrastructure will need to be upgraded to handle the large volume of data generated from whole genome sequencing. A major factor in the rate of adoption of this technology into the clinic will be an institution’s bioinformatics capabilities. AMP encourages advisory committees, agencies and stakeholders working on health information technology to consider the challenges of whole genome sequencing data. As we mentioned in our June

comments, AMP has formed a working group on whole genome analysis and will address these issues in an ongoing fashion.

Thank you very much for your attention and consideration of our remarks on whole genome sequences, and best wishes as you conclude your work over the next few months.

CHAIRMAN TEUTSCH: Thank you very much.

Any comments or questions for Mary?

(No response.)

Thank you for your kind words and we certainly agree about the need to move the field forward so we can take advantage of these new technologies.

So we come to the time for our break. I think we're actually pretty close to on schedule so why don't we take a 15 minute break and then when we come back we will begin the review of our report on education and training.

We'll see you back at 10:00.

(Whereupon, at 9:43 a.m., a break was taken.)

GENETICS EDUCATION AND TRAINING REVIEW OF REVISED DRAFT REPORT ON GENETICS EDUCATION AND TRAINING AND DISCUSSION OF REVISED DRAFT RECOMMENDATIONS

CHAIRMAN TEUTSCH: So welcome back, everyone.

We now turn to the Genetics Education and Training Report, which has been ably led by Barbara Burns McGrath. As you know, we've been through an extensive process to get to this point and we are at the stage where we need to finalize this report and approve the recommendations so we can transmit the final report to the Secretary.

So Barbara is going to lead us through the discussion of the recommendations and she has got the remainder of the morning to do that.

So Barbara?

DR. McGRATH: Thank you.

CHAIRMAN TEUTSCH: It's all yours and thank you for all your work on this. It is great to see it coming to fruition.

SUMMARY OF PUBLIC COMMENTS ON DRAFT REPORT AND OVERVIEW OF REVISIONS

BARBARA BURNS MCGRATH, *R.N., PH.D.* SACGHS MEMBER

DR. McGRATH: Great. Here we go.

(Slide.)

So what we'll do in the next couple of hours is fill in that last little blank box on Steve's slide, that little seventh report that was empty. We can doodle on that and, hopefully, we'll fill it in.

(Slide.)

I would like to start with acknowledging who worked on this report. If you look at this task force roster you can see it's quite a large group of people. I'm not going to say unwieldy but just large and it represented a lot of diverse areas of knowledge and practice so we had quite a wide ranging group of people.

Why you're looking at this is everyone on this list really contributed in a very meaningful way to this report. It was an absolute joy to work with everybody on it.

I'd like to make a little comment about the staff at the bottom. You're hearing a lot of accolades about the staff and I'm going to just keep on that a little bit. We started the report with Cathy Fomous and then she handed it off to Kathy Camp, who then at one point Kathy Hanna helped in the writing of it so we had a richness of Kathies (ph) throughout this whole report. As you know,

Kathy Camp retired at the end of summer and she handed it off to Symma who has really stepped up to the plate and helped a lot at the very last minute. And all of this, as always with all the reports, was led by the steady hand of Sarah. So I just want to acknowledge the staff on this report.

(Slide.)

For the next couple of hours--we have two hours allotted for this--we'll go over the draft report and that includes the summary comments that we've gotten from the public, and then we'll discuss the final recommendations, and that's the main goal.

(Slide.)

Before we do that I wanted to give a very brief history of this report. We weren't the first ones to recognize that education is a key so we weren't the first ones to have this notion of how important it is. We followed the 2004 previous SAC group and their meeting and resolution that had a number of recommendations for the Secretary.

In 2007 we revisited that in this committee. We started off by having a panel discussion of a series of experts talking about the educational needs. At that point after that a task force was formed and we were charged by this

committee to look at three areas. One was point of care health professionals. Another one is public health providers and consumers and patients. This was a very broad scope and we talked about this a lot, about whether it would be better to focus just on one out of the three, but we came to the decision that health care in general was a very integrative thing and people don't see just one provider. These groups don't operate in isolation. So we decided to try and with this report show the integration that's necessary and show that health care happens in a holistic manner. So we'll see if that was successful.

In 2009 we worked on a literature review and conducted our own research. That was the heavy lifting.

And in 2010 we completed a draft report that went out for public comments.

(Slide.)

Because of that larger scope we established three work groups to sort of focus on each one. Let me talk about these.

The Health care Professional Work Group started with Greg Feero and he was the one who established the data collection activities and

decided what information was needed in that report. He then headed up to Maine and David Dale came on to the committee and was able to very seamlessly pick up where Greg left off and was key in the interpretation of the data that Greg was responsible for collecting.

The Public Health Provider Group was led by Joseph Telfair. He was a committee member here when we formed and was involved for a couple of years, and he rotated off the committee but very generously stayed involved. He has really deep knowledge of public health issues and so was valuable and we appreciate the fact that he stayed involved even though he wasn't formally on the committee any longer.

The Consumer and Patient Group was led by Vince Bonham and you'll hear more from him tomorrow, and you'll understand why he is just the perfect person to lead the issues looking at consumers and patients. And he was assisted by Sara Harding and I'd like to acknowledge her as well on this.

So these groups were very autonomous. They each had their own goals, their own activities. They had their own conference calls that were led by the work group chairs. Staff and I were involved

in as many of these as we could be. I think most of them. We were there to provide continuity but the work groups were the real heavy lifters of setting out the goals as well as collecting the data and analyzing it. So I think these individuals deserve a little extra acknowledgement.

(Slide.)

The draft report that's in your book under Tab--I can't remember what tab it's under--3. Thank you. And 3 is organized in the following fashion: The final report will start with an executive summary and recommendation which obviously haven't been written yet but that will be at the very beginning. The first section that you see is the introduction and in there we have tried to discuss the importance of genetics and genomics in health care, particular examples of technologic advances, the complexity of genomic information. We describe the purpose and the scope of the report and summarize the training needs, and particularly calling attention to gaps. We continued to pull in a thread of the intersection of emerging genetics technologies with health disparities and hope that we did that throughout the report.

The background covers a very extensive

literature review for all groups emphasizing needs and gaps. I just had a comment in the hallway about how heavily referenced that was and what a rich resource that will be for people using this in the future.

The survey chapter describes the original data that we collected and it's an update on activities of selected federal agencies.

The discussion section synthesizes the findings of the report, describes trends in education and training, and the role of the federal government and the private sector.

When you read these sections, if you haven't read them yet, if you're reading these either in the meeting or on the way home on the plane and you've got comments, please email those to Symma or myself and we will integrate that into the final-final version of it so we welcome any comments if you think there's any editing changes or information you think that we really need to add. Not tons, we're not going to get new data but any comments, please feel free to send those.

The report concludes with a summary and six recommendations.

When I was looking at this slide I

remembered that--you've seen me come up here a number of times talking about this report over the last couple of years and I'm remembering that I often used metaphors perhaps too much. The first one I remember using was "it felt like a hydra" to sort of describe the chaos of trying to figure out all of these stakeholders and how were we going to pull that together in a single report. I think I then moved into developmental metaphors and talked about "an unruly teenager" at one point or something like that. I know, whether I said it or not, the last report that was sent out for public comment was--I envisioned that as sort of a "late adolescent" that was heading out into the world full of optimism and looking forward to great exposure out there in a great world, perhaps a little chubby. When that report came back after public comment and we looked at it and some editing happening with a lot of help of staff as you can imagine, it's now looking more like a "a young adult" coming back. A little trimmer and perhaps a little more realistic but I hope a particularly interesting person that you'd want to sit down and talk with.

I don't have a good metaphor for what happens next. The one that--the idea I have, the

hope I have is that the--

DR. : (Not at microphone.)

DR. McGRATH: No, and I'm not going developmentally because that would get into "wizened old men or old women," and that's not pretty either. So I'm stopping with that. There's no continuity here.

The only image I come up with is my own personal hope that it ends up being like those books we read in high school like maybe *Moby Dick* or maybe even *Sometimes a Great Notion* where you read it and it's assigned reading and you kind of slide your way through it and maybe you kind of get why it's important but it doesn't really hit you but then later you go back and you find a handful of gems in there. So I sort of hope this report ends up being like that that as it gets distributed, and as we say the blue notebooks get put on people's shelves, that every once in a while people pull it out and there are some gems in there that get followed up; anyway, enough of the poetry.

(Slide.)

So on to the finding. The key finding is that "the times are a changing" and we sort of know that. That's getting to be an old notion because

this is the idea of the new normal. Change is everywhere so we found that to be the case as well here.

We certainly all are familiar with the idea that genetic technologies keep changing so the content that people need is a moving target. We need to be able to be able to deal with that. The service--the areas where genetic services are provided changes, maybe not so much in specialty areas but more in primary care settings or maybe with laboratorians (ph) doing more as we just heard with the last speaker.

We certainly know that the way individuals access health related information has changed dramatically in the last decade and is going to continue so there are always undercurrents that kind of give a sense that whatever recommendations we make or whatever suggestions we make must take this into account that it is a moving target. So we did find in the literature as well as our data generally a widespread appreciation of the increased integration of genomics into health care, especially for common complex diseases. Everyone gets that that’s going to be an incredibly important area for continuing education for everybody. The

appreciation for the role of population-based applications of genomics, that was something that--maybe people didn't realize that five years ago but now are recognizing that there's an emerging role there, and the need for consumer genetics literacy and access to accurate information.

We were told time and time again that health professionals are key to translation. We learned that consumers prefer to learn about genetic test providers even though they are accessing information other places as well. And we are aware that the decreasing cost of whole genome sequencing may increase demand. All of these last three things indicate the continuing need for genetics education for all three sectors.

(Slide.)

Some of the gaps or barriers that we summarized were noted before but some new ones were identified. Continuing gaps in genetic knowledge across all of the three groups were looked at. There is limited genetics education both in the basic levels, the undergraduate as well as K-12, and continuing education for practicing persons due to competing priorities. You'll hear more about that in a bit. We were told that education does not link

to accreditation, certification and licensure, and that has implications. We continue to--or everyone confirms the notion of the lack of evidence of clinical utility is seen as a barrier to providers implementing it in their practice. We learned that the public health workforce is very diverse with different backgrounds, educational backgrounds, different jobs and so that their educational needs really vary widely. And similarly consumers and patients have a wide range of knowledge and needs depending on what their reason is for looking for information.

(Slide.)

So, in general, in sort of broad strokes, educational needs should move beyond traditional models and include innovative approaches. There are a number of examples of them throughout the report. A couple of them are using emerging technologies such as just-in-time resources and medical records, the whole notion of competency-based learning, and information dissemination using a variety of formats for diverse populations so not to get too hung up just on internet information even though that is widely used.

It also is clear that success in terms of

education and training requires a more comprehensive, more holistic look and coordinated efforts involving multiple stakeholders. So there needs to be more people at the table than maybe have traditionally been when looking at educational issues.

(Slide.)

The report went out for public comment last year. We got 35 of them and, as I recall, this slide looks pretty similar to the public comment slides we get on a lot of reports, a chunk from academia, state public health departments, testing labs and equipment companies, medical and nonprofit associations, a health insurance association, some private citizens, and one federal advisory committee.

(Slide.)

What we did with these is they were all grouped thematically and then the task force had a conference call a couple of months ago to talk about them. We divided them up by individuals and we looked at these areas. They are kind of clustered into people commenting about clinical utility and the need for evidence-base, of course reimbursement for genetic services, consumer issues, as well as

the need for more integrated and forward thinking K-12 education, issues and comments about public health practice and different places that genomics can be implemented. People called out existing resources and models and wanted to be sure that we know that there are some successes out there. And there was a number of comments about the larger pool of genetics health professionals, meaning we should remember that more and more people will be involved and have a need for understanding genetic technologies. We looked at all of these comments, every single one of them, talked about them and changed text in places to take in additions or make any corrections that were noted.

(Slide.)

Okay. The big gun stuff: There are six recommendations and they start on page 59, and here I have it under tab 3 so I'll read them aloud or you can read them in there, whatever is easiest for you. And I think what I'll do since it's a lot of words is I'll read through all of them and then we'll go back and go over each one individually because there may be comments that come up early on that are addressed later on.

This is my literacy lesson here to see if

I can read aloud this long.

(Slide.)

Draft Number 1: The first one should show that this is background information. So the way we've organized these recommendations is that there's a little bit of a prelude or a background and then the actual recommendation comes next. So this text here is that prelude part. This is not the actual recommendation. "Evidence from the United States and abroad suggests inadequate genetics education of health care professionals as a significant factor limiting the integration of genetics into clinical care. Significant specific inadequacies include the amount and type of genetics content included in undergraduate medical school curricula and a small amount of genetics related knowledge and skills of physicians, nurses and other health professionals once they enter clinical practice. Modifications in medical, dental, nursing, public health and pharmacy school curricula and in medical residency training programs are needed to ensure that health care professionals entering the workforce are well trained in genetics. Innovative approaches that coordinate the efforts of entities controlling health professional

education and training are needed."

This is the actual recommendation number one, and the text of the actual recommendation is: "HHS should convene a workshop to identify innovative education and training approaches that will promote integration of genetics into clinical care. The workshop would build upon the findings of the June 2009 Blueprint for Genomics Education meeting hosted by NIH, SACHDNC and HRSA, and other organizations, and newly established programs at HRSA, and would include representatives of HHS agencies and other federal departments with established programs in genetics professional education, representatives of health professional organizations engaged in accreditation, certification and continuing education efforts, and private sector entities that provide genetics education."

So just to preface discussion on this, there is discussion between having a workshop versus a panel, whether it's ongoing or one time, and the main point that we thought in this slide--in this recommendation is to include new players at the table to take a forward looking view towards education and training and that all professional

needs are represented.

(Slide.)

There's a couple of finer points under this recommendation to explain what we meant and they are six of these or--no, at least--well, we'll see. There are three on this one. "The workshop goals are to identify successful education and training guidelines and models that are outcome based; (B) to identify potential and current funding streams for developing and promoting genetics education for all relevant health care professionals; (C) recommend mechanisms for expanding and enhancing the content needed to prepare all health care professionals for personalized genomics health care."

(Slide.)

There is more. "(D) recommend mechanisms for evolving standards, certification, accreditation and continuing education activities to incorporate genetic content; (E) determine the need and, if appropriate, appoint an advisory panel representing a range of educational and health care stakeholders to facilitate implementation of the approaches identified during the workshop and to reevaluate educational needs on an ongoing basis; and (F)

publish findings and recommendations and develop a plan to monitor the outcome of these efforts."

That's Recommendation 1.

(Slide.)

Moving on to 2: This is the background for 2. "The inherent diversity of the public health workforce makes it difficult to target educational efforts that are relevant across groups. A systematic effort is needed to evaluate the composition of the public health workforce with current job responsibilities related to genetics and genomics, and to identify future priorities such as the potential impact of affordable genomic analysis."

(Slide.)

And this is the wording of the recommendation: "Tapping the expertise of its agencies with relevant missions in public health, for example the agencies listed, HHS should assess the workforce to determine the number of public health providers with responsibilities in genetics and genomics to ascertain certain trends and future needs to identify education and training needs and to promote leadership development in the field."

(Slide.)

And then we have some comments from that, "two should(s)."

"Based on this assessment HHS should (A) support and encourage the incorporation of basic genetic and genomic core competencies and public health training programs and in the knowledge base of federal and nonfederal public health providers and specific competencies for those whose responsibilities require specialized genetic knowledge such as environmental interactions and risk assessment for population-based genomics; and (B) based on these competencies fund development and implementation of accessible educational programs and continuing education in genetics and genomics for the public health workforce and explore incentives for the end user and for organizations that provide these programs." Clearly this recommendation is very competency based.

(Slide.)

Number 3: This is the background for it. "Findings in the literature and SACGHS surveys indicate that health care professionals and public health providers serving underserved and underrepresented groups and populations face significant challenges. HHS should promote the

development and implementation of targeted genetic and genomic education and training models for health care professionals and public health providers serving underserved and underrepresented groups and populations."

(Slide.)

Specifically, "HHS should (A) direct research funding to identify effective educational models for health care professionals and public health providers in underserved communities; and (B) identify and support programs to increase the diversity of health care workforce in general and the genetics specific workforce, and explore use of incentives such as CEUs to encourage health care professionals to practice in underserved areas."

I'll point out a comment has already been received about why CEUs would encourage professionals to practice in these areas and one of the intents there was to talk about other programs such as loan repayment so we might want to revisit that.

(Slide.)

Under the same recommendation: "(C) incentivize organizations to increase the development of targeted genetics and genomic

educational models (for example, provide support for meetings where curricula are drafted); and (D) ensure that consumers and representatives of rural minority and underserved communities participate in the process of developing education and training models to assure that they are culturally and linguistically appropriate and tailored to the unique needs of these diverse communities."

(Slide.)

Number 4: This is the background for four. "A significant amount of genetic related information directed to consumers and patients exists in a variety of formats and from a number of sources but the quality of the content is variable. Consumers have consistently expressed the desire for accessible web-based genetic information that they can trust and consider provision of these resources as a role of the federal government."

(Slide.)

There are three "should(s)" on this one. I'm sorry. This is the actual recommendation for number 4: "HHS should endorse and fund the development of and maintain an internet portal to a vetted collection of comprehensive, accessible and trustworthy web-based genetic information and

resources for consumers. This portal should utilize existing governmental resources such as those developed by NIH, CDC, HRSA and the National Newborn Screening Clearing House."

(Slide.)

And there are three "should(s)" that follow: "HHS should assure that (A) these resources include scientifically validated information and/or links to credible information regarding topics such as genetic contributions to health and disease, gene environmental interactions, genetic testing and legal protections against genetic discrimination; (B) these resources should include references to identify other types of information that are not web-based such as television and radio programs and print materials; and (C) the availability of this portal be promoted using a wide range of strategies from collaborating with developers of internet search engines to working with community leaders at the local level, mechanisms to alert interested persons to updates and new information should be developed."

(Slide.)

Okay. Number five: This is the background for it. "With the vast increases in

scientific knowledge stemming from genetics research, the development of new technologies and the increase in direct-to-consumer genetic services, educational efforts are needed to translate this information to reach consumers of all literacy levels. HHS should support research and public…“ Okay, sorry.

This next paragraph is the recommendation itself, number five. “HHS should support research and public-private collaborations to identify methods that are effective for translating genetics knowledge into information that consumers and patients can use to make health decisions. Specifically, HHS should…” And there’s four should(s) for this one.

“(A) support research that identifies effective methods of patient and consumer communications specifically by increasing availability of funding opportunities that call for collaboration among various disciplines (for example, increase the number of requests for proposals for patient and consumer education by year 2015); (B) based on this research and to reach diverse people in communities HHS should develop educational programs that use a wide array of media

(for example, radio, television, print and mobile phone) and community-based learning, and provide for translation of materials into locally predominate languages."

(Slide.)

"And (C) support the dissemination of these educational programs and materials into science and/or health education initiatives through collaboration with other relevant departments and agencies such as Department of Education, NSF, and who can explore issues surrounding K-12 learning; and (D) increase the availability of funding opportunities that call for collaboration among various disciplines to research."

(Slide.)

The last recommendation, Recommendation 6: This is the background for it. "Family history tools are a potentially powerful asset for consumers and health care professionals to use in risk assessment and health promotion."

The actual recommendation is this text here: "HHS should support continued efforts to educate health care professionals, public health providers and consumers about the importance of family health history and to support efforts to

validate family history tools for risk assessment and health promotion."

(Slide.)

We next outlined how this might work for each group. So "(A) for health professionals HHS should in collaboration with private sector stakeholders support the use of family history in clinical care through development of clinical decision support tools and mechanisms to integrate pedigrees into electronic health records; (B) for public health providers HHS should promote research identifying the role of family history and population health."

(Slide.)

And then "For consumers HHS should (1) promote research on how consumers use family history to make health care decisions; (2) assess the effects of gathering family histories with diverse cultures and communities and among individuals where family histories are unavailable; (3) expand public health awareness of programs and patient information materials on the importance of sharing family history information with primary care providers and promote the embedding of educational materials and family history collection tools directed to

consumers and ensure access for all by providing these tools in various formats."

(Slide.)

Okay. The last slide is in response to the fact that there probably won't be a follow up SACGHS education task force in five years like we were able to follow the previous one, when we started this task force we thought there would be and so that was one of our motivations to try and make our recommendations measurable so that the next group could come through and see if there were any metrics to show that they were either achieved or not achieved. So in lieu of being able to do that the staff has talked about, and I'm presenting it now to the whole group, whether it makes sense to include something in the cover letter that goes with this report asking that there be some sort of follow up on this since it won't necessarily be us. This is some language that is out there for us to discuss. So this would be in the cover letter. It's not a recommendation.

"The committee recommends that the Secretary consider involving or charging other federal agencies such as those listed with (1) tracking the implementation of the recommendations

in the report; (2) establishing metrics to measure the success of genetics in genomics education and training programs instituted or funded as a result of the report; and (3) reassess the state of genetics education and training within five years to ensure that federal efforts continue to reflect the diverse and unique needs of health care and public health professionals and consumers."

I'll just make a comment about that last one, and that is calling up the federal efforts because it may be tempting for the federal agencies to feel that a lot of these responsibilities come under academic institutions or professional organizations so we'd like to call out that some of this might be picked up by the federal government.

Okay. I'm done reading aloud. Did I pass my third grade reading aloud test? It's like I put everybody to sleep.

This is the time for discussion and I'd like to go over the recommendations, and this is the time we always say we're not going to wordsmith. Well this is the time for wordsmithing particularly on the recommendation itself but, if you're interested, some of the background as well. So I think the most logical thing is to go linear and

start with number one so if you have thoughts on late ones hang on to those. And Symma is coming up here and will be taking down notes and we'll be able to modify them so you'll see them as a final version. I think that's the goal. So going back to one:

(Slide.)

There, that's the language of it.

So does it make sense? It's awfully wordy and that is always a concern in recommendations. Do you get the punch line?

Do you think workshops accomplish things? Or is it--you know, making a recommendation for somebody else to make a recommendation--is there enough measurable in here?

DISCUSSION OF FINAL DRAFT RECOMMENDATIONS

FACILITATORS: STEVEN TEUTSCH, M.D., M.P.H. AND BARBARA BURNS MCGRATH, R.N., PH.D.

DR. NUSSBAUM: It strikes me this is an absolutely wonderful and comprehensive report but it strikes me as you read through this that there's a lot of process in here. For example, workshop and all the invited constituencies are process as opposed to recommendations that could be much more focused on policy and output.

DR. McGRATH: Mm-hum.

DR. NUSSBAUM: And again it's always a challenge when you're developing this but, you know, as I look at these you could have mentioned--also as you go through these, this is an example, a lot of federal agency--convening of federal agencies, and I think there may be also opportunity to advance initiatives by convening, you know--and you have them there but AMC, various professional nursing and medical associations so one could take that task too. I think the overarching statement is as we go through these how much of this is process-driven to get to a result versus a recommendation of why it's needed and then let others drive the specifics.

DR. McGRATH: I think that's a great comment. So that--particularly in number one that kind of language might be in the preamble a little bit because this is the process to get to an outcome or something like that.

DR. NUSSBAUM: Something like that that we assume that there are many constituencies here and we wish federal agencies to take the absolute lead because, you know, looking at the last decade those other organizations have not met their charter or their success so I think it could be sort of

powerfully stated in the preamble then therefore we recommend.

DR. McGRATH: Great.

DR. NUSSBAUM: Again I don't want to wordsmith. You've done so much good work on this.

DR. McGRATH: Now this is the wordsmithing time but I actually like that in the preamble because it just sort of summarizes. I mean that's the beginning and then the cover letter will say that again.

DR. NUSSBAUM: I mean if everyone had worked well and effectively on genetics education we probably wouldn't be making these very strong recommendations to re-educate or newly educate.

DR. McGRATH: Right, but I think your point is that the idea of working in silos has not worked so we need some more oversight.

David?

DR. DALE: A suggestion in that regard to follow on what Sam said is you could divide the recommendations into policy recommendations in action and if you highlighted action, like the workshop idea, you could make that very directed and also it would be assessable a year or two or three in terms--a little more specific. Anyway you could

divide it and satisfy that need but maintain the content.

DR. McGRATH: One way I've seen on another report is in the executive summary that really--we were taught early on in this committee that that's the most important piece of paper, that executive summary, that maybe that's the place we can call out which recommendations are policy and which are actionable rather than reorganizing them that way. I think that's a good suggestion.

Gwen?

CHAIRMAN TEUTSCH: What I hear them saying, though, is that items (A) through (F) could be what the "should(s)" should be.

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: And the workshop is the action.

DR. : Right.

CHAIRMAN TEUTSCH: So that it's a matter of reversing the recommendation.

Isn't that what you're saying?

DR. DALE: Right.

DR. NUSSBAUM: Yes.

DR. McGRATH: Gwen?

MS. DARIEN: That was basically what I was

going to suggest as well is that the outcomes are in the workshop goals and if you just put right upfront what the expected--what the goal of the workshop is then I think that answers that question without having to totally redo.

DR. McGRATH: Okay, great.

Any other comments on number one?

(Slide.)

Okay. Number two is about the public health workforce. So the main action verb in this one is HHS should assess the workforce, do an assessment of it and that underlying idea is that we really don't know--the survey made it clear that the public health workforce is immense and it's quite diverse, and some people do a little--do some services and some it's their total job but we don't have a real handle on what that is so the first recommendation is just to do an overall assessment of it. Clearly after that the needs follow and I think there is some language there later about facilitating leadership in this area. That was another identified gap.

So what comments about--is this the most important thing we want to say about the public health workforce and the growing need for an

educated workforce dealing with population-based genomics?

DR. MANSFIELD: It looks vaguely like you're trying to hide a bunch of different recommendations under one recommendation here.

DR. McGRATH: You mean with the "should?"

DR. MANSFIELD: Well, you start off recommending that there be a survey of the workforce and then you go on to (A) and (B) that with separations that aren't completely related to surveying the workforce so I think these are actually different recommendations (A) and (B) that are separable from your overarching recommendations.

DR. McGRATH: Okay. I think the reason they were put in there--but I get your point because they do have a different tone to them--that this was an example of how the educational training--after the assessment is done--how it might be and there's a notion that it be very much competency based.

DR. WILLIAMS: I would--yes, I guess I would support that. As I read this I think that these-that (A) and (B), you know, follow directly from that assessment but the assessment of personnel and also what is being done in the public health area and what are the identified gaps would lead

then to the creation of the things that are articulated in (A) and (B), and so I see them as being integrated and logically follow. Now we may be able to tweak the wording to make that more obvious but to me if (A) and (B) don't follow directly from the result of the survey then we've kind of missed the boat.

DR. McGRATH: So maybe just--rather than support and encourage there would be a line that educational programs--you know, just make it start off with that?

DR. WILLIAMS: Well, you know, in the previous slide you end that--the last sentence is "Based on this assessment HHS should…" So I think you do set it up that, you know, (A) and (B) are going to be the result of what this assessment shows or at least should be directly related to what the assessment shows. And I don't know if there's a way to be clearer than that or whether we're too granular in (A) and (B) so that we're presupposing what the assessment might find. I don't know but I guess--I think that they do go together and I don't think that conceptually there are problems. I think it's just a matter of if there's wording that's not clear we can clarify it.

DR. McGRATH: I can see that.

Steve?

CHAIRMAN TEUTSCH: I think what we found out from the survey is that people don't know why they need to know this stuff. It's not clear outside of the area of sort of the newborn screening arena what it is that public health professionals should do with this and so they're not paying attention but somehow that still remains to be articulated in a clear fashion. So I think part of the problem is if you just go out and assess community health workers and public health nurses and public health professionals in practice most of them won't know what to answer. They will say they don't have the competency but they don't know--they still don't know why they need those competencies beyond--I mean other than, yes, it's good to know it so they see it coming. So I think we probably need something here that basically is going to call on the leadership of the agencies to help articulate the needs clearly so that we can manifest the specific needs of folks because otherwise--you know, we saw this a little bit with the primary care practitioners, you know, why do I need to know this now. Although it's a little bit clearer, I think

it's a lot clearer in the clinical arena that's what's coming down the pike than it is in the public health sphere.

So, you know, the important thing that we'd be talking about here, and you mentioned the environmental-genetic interactions, the social determinates and their interactions, they are really very important but public health professionals really have no idea how that really fits together. They are just beginning to even deal with the environmental and social determinates overall. I think we need something in the preamble that basically--this is pretty nascent in the public health arena and some of that we're going to need the agencies or someone to articulate otherwise we're left with where you are here with, yes, we have a series of competencies; yes, that need to be--where the training is needed. So we may want to articulate that more clearly.

DR. McGRATH: I think your analogy with primary acre is great.

Marc?

DR. WILLIAMS: So I think that Steve is on to something here in that I assumed that the survey would--sort of implicit in the survey would be

taking a look at what I might call exemplar programs. In other words, we have examples within public health of people that are, you know, going beyond just newborn screening to explore how this can be useful but maybe we need to be explicit about that to say that part of this survey would be to identify those exemplar public health services that are involving genetics and genomics and engage the leaders of those programs to help to inform this gap analysis because I think Steve is absolute right. If we just go out in a general survey we'll get what we don't know what we need to know and we don't know what we don't know. Whereas, here we can have people that are actually beginning to explore the boundaries and tell us what we should be learning.

DR. McGRATH: I agree.

Gwen?

MS. DARIEN: And just to wordsmith a little bit and follow on these comments I think that in comment (A) rather than, as you said, assuming that there is basic knowledge that is needed say support the incorporation of genetic and genomic competencies that have been shown to be--or I'm not articulating it very clearly but the point is it's to address the gaps, not to assume that the core

competencies are missing. So whatever the gaps are that were pointed out in the survey that's where the educational--

DR. McGRATH: Right.

MS. DARIEN: --development of the--

DR. McGRATH: Right.

MS. DARIEN: --educational materials should go.

DR. McGRATH: Right. Good.

I would like to throw out an idea that, Katy, you and I were talking before the meeting that particularly the first--we're only on the second recommendation but the first recommendation is written for health care providers like primary care doctors, nurses, PAs, et cetera, but it didn't include public health professionals in that one and I wonder if, you know, this issue that we're talking about that we need an expert body to help identify what some of the potential roles in public health are, just like we did with primary care a number of years ago, it wasn't necessarily the primary care providers, it was outsiders helping with that. I wonder if we want to include in that recommendation for the panel or workshop that we include a public health presence in that and look at the educational

needs for all. At that group you could imagine it would be a pretty interesting idea to have primary care providers talking with public health providers to think about what are the educational needs of all they might articulate. So I wonder if that's another way to get other people involved in identifying what the potential roles might be.

Marc?

DR. WILLIAMS: I think the other thing that needs to be explored here relates to--you know, I appreciate the fact that we are sort of independent with the health care providers and with public health but in some ways we may have influenced the process in a negative way because I think as we've been thinking more about aspects of screening for genetics and genomics it's clear to me that some of the screening is going to be very important to do within the public health setting and other screening that could be considered to be public health really takes place in the health care practitioner's office. So if you take the United States Preventive Services Task Force recommendations relating to BRCA testing, for example, it's not something that I would ever see falling within the purview of a state public health

department but it's a public health function. In some ways I think what we really need to put in here as well is a definition of under what setting the different public health genomic efforts really need to be held and how we can coordinate between traditional government-based public health and public health that takes place in health care delivery settings.

DR. McGRATH: That makes me nervous because what we say today may not be true two years from now because things may shift. The public health sector may pick up more of those things with health care reform so I worry about stating what we think--where we think all those boxes should lie at this point versus maybe a language in there that that would be part of some assessment or something. Does that cover it?

DR. WILLIAMS: That was my intent and if I wasn't clear--

DR. McGRATH: Oh, okay.

DR. WILLIAMS: --then I apologize.

DR. McGRATH: Okay.

DR. WILLIAMS: No, I don't think we can a priori define which boxes are--

DR. McGRATH: Okay, great.

DR. WILLIAMS: --appropriate but I think we need to say this has to be part of the assessment--

DR. McGRATH: Great, great.

DR. WILLIAMS: --that setting for delivery is an important part of the assessment.

DR. McGRATH: Thank you. I'm sorry I misunderstood.

So, Katy, do you have any--although I'm going to put you on the spot since we talked about that--would you--this is one that's heavily with--and you're representing--a lot of other public health things--and Janice as well--do you think that we should add some language in number one to include public health in that? Would that be helpful or do you think we should strengthen number two to have more of a larger pool of people involved in that?

DR. KOLOR: Thank you, Barbara.

My understanding from reading number one is that public health is listed among a variety of groups that will contribute to the health provider education but our conversation this morning was more focused on recommendation number two and expanding the conversation of innovative approaches to education and training of the public health

workforce in general so I was talking more the latter I think.

DR. McGRATH: Okay. So we'll expand number two to include that kind of language, great.

MS. BACH: But public health would definitely be included in the workshop?

DR. McGRATH: Of number one, yes. It would pick that up. I just didn't know if we wanted to highlight it more in number one or make number two a little stronger with some of the new language, which I think we're going with the latter.

CHAIRMAN TEUTSCH: And some of this may go into--just to be clear in the text that precedes all of this that we're talking about the health system. It's not medical care and public health and that, in fact, we have a health system and there are individual level services and there are population level activities, and they've got to be integrated in a way that contributes to the overall health. So I think we have got to be careful of creating artificial distinctions but we probably need to say that earlier on in the report.

To my earlier comment I think in the sort of preamble to this statement you can indicate that they tap the expertise of agencies and other public

health organizations and professionals to define the role of population health interventions more clearly so they can then inform those curricular and other kinds of developments so that it looks like it's at least a two step kind of process.

DR. McGRATH: Good. That was the intent.

Great, all right.

Number three.

(Slide.)

The recommendation is the lower text. Okay. So this one--this is the notion of trying to increase access to care in different underserved areas, and then there is a couple of should(s) after it.

So let's look at the next one. So let's look at the should(s) because here is one that we had a comment on (A) and (B). (B) is the one that has the CEU as examples in there. You probably have that in front of you.

(Slide.)

Here we are.

So the hope of this one is to increase providers that--increase services to underserved areas, appropriate services.

DR. WILLIAMS: So I don't know. It just strikes me and maybe it wouldn't have if you hadn't highlighted it but it does sort of strike me that this is a bit of a non sequitur in the sense that, yes, this is an issue across all domains. This is not one where I think genetic exceptionalism is relevant. So in some sense if in our second recommendation we are--in the first and second recommendations that we're going to be developing strategies to better educate the workforce, in general, about genetics and genomics then in some sense do we need something specific in a genetics education document about improving the workforce in underserved areas. I would think that unless there is something that we can identify that's specific to genetics or genomics that is an additional barrier to bringing this into underserved populations that this may not have a place in the document.

DR. McGRATH: Other thoughts?

Vince?

DR. BONHAM: I guess the only question I would have is that one of the charges to the work groups was the issue of health disparities and issues of inequities with regards to access and services. That's just my question.

DR. WILLIAMS: Well, it is a charge without a doubt and again there may well be something that, you know, comes out of the survey in assessment in recommendation two that would say, hey, there is something specific to genetics and genomics that is impacting health disparities and maybe it does relate to issues of cultural competencies, which I think are addressed in (A) in particular and (D) in recommendation three.

I guess the point I was making was that we don't have any evidence to my knowledge from all the work that was done that would indicate that there is something specific about competency and genetics and genomics that's contributing to difficulties getting people working in underserved areas.

CHAIRMAN TEUTSCH: Just as a process, I think, because this is our one chance to get these things worded right, we should go back to the beginning to recommendation one and let's--

DR. McGRATH: Finalize it?

CHAIRMAN TEUTSCH: --get it as close to final.

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: If we need some final tweaks overnight we can do that but let's--

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: Some of the changes that are being suggested are substantive.

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: And we need to get those words right because we're not going to be able to do anything once we leave here tomorrow except little editorial things.

DR. McGRATH: Okay. A good point.

CHAIRMAN TEUTSCH: So why don't we go back to one?

DR. McGRATH: Get in the weeds.

CHAIRMAN TEUTSCH: And I don't--yes, we need to get a little bit down and dirty here.

DR. McGRATH: All right.

CHAIRMAN TEUTSCH: And I don't know--Symma, I haven't been watching what you've been doing--how much of this you've captured already.

So why don't we go through? And I'm not worried about the preamble so much, but we can look through that, as we are with the recommendation statements themselves.

We have a couple of hours now or an hour-and-a-half to do this so let's make sure we get it done.

DR. McGRATH: All right.

CHAIRMAN TEUTSCH: So we talked here about moving the six statements at the bottom that follow this.

DR. McGRATH: I don't understand how that would read but let's look at it.

CHAIRMAN TEUTSCH: Well, you would say HHS should identify successful educational and training guidance, identify potential and current funding--

DR. McGRATH: All right.

CHAIRMAN TEUTSCH: I mean that's--

DR. McGRATH: Do they all work?

CHAIRMAN TEUTSCH: I mean I--that's sort of how I visualize it. You can probably be a little bit--but that's why we need to go through and make sure we're clear on what we're saying.

DR. McGRATH: Okay. So maybe we should look at the (A), (B), (C) and see if there is a--so it will just start like this: "HHS should identify successful guidelines and models, identify potential and current streams…

CHAIRMAN TEUTSCH: I mean we've got to be clear if that's what we mean but if--that's what it would say, right?

DR. McGRATH: I don't know where the

workshop part will go.

CHAIRMAN TEUTSCH: The workshop then would follow all of that which is after we say what it should do we should say, “HHS should convene a workshop to…” or this could be accomplished through a workshop. I mean that’s what we have to figure out, what we really want to say.

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: But that’s what--we’ve got to get to some agreement here.

DR. McGRATH: Okay, great.

CHAIRMAN TEUTSCH: So, David, and then Paul?

DR. DALE: Well, if we’re wordsmithing I would--instead of having letters--so I would begin by saying “Actions recommended:” and then I would list these as one through six. And then at the end I would say “A workshop or other forum for accomplishing these goals will be necessary” or something to that effect. The goal--

CHAIRMAN TEUTSCH: So we--

DR. DALE: The actions recommended are to conduct these one through six.

DR. McGRATH: We need some language before actions.

CHAIRMAN TEUTSCH: Yes. So the question really is which is the action; the workshop. Where is the action, which would be the identification and that sort of thing. I think we have to be clear which is the objective and which is the thing that we think HHS should do, and it could be done either way but that's what we need to get some agreement about.

DR. McGRATH: And that's exactly right because when we wrote it the action was the workshop and this is what would be the product of it.

CHAIRMAN TEUTSCH: Right.

DR. McGRATH: But it doesn't matter.

CHAIRMAN TEUTSCH: Paul, and then Jim?

DR. BILLINGS: Yes. So I vaguely remember discussing this in other reports but the recommendation is that you want a "successful" education and training guideline that is outcomes based. Those are terms of art in my view what "successful" is and what "outcomes" are that, you know, I have trouble without--are we endorsing a particular set of outcomes based training or, you know, what's our model for that? Did you discuss it at all? If everyone is comfortable leaving that kind of language in there--it's kind of vanilla and

sometimes it looks kind of good and sometimes bad.

CHAIRMAN TEUTSCH: Right. So, Sam, you have sort of raised this issue. What are we really trying to accomplish? So those things one through six are basically gaps. They are needs that need to be filled, right? So we may not even have to have quite so much verbiage. What we need is to have developed guidelines and models for evidence-based education and training. That might be the statement of that first item as to what's needed, right, which gets you a little bit out of what's sort of fluffy--old fluffy language. I need the sense of what you all think.

Jim?

DR. EVANS: So I would agree with Paul's recommendation to kind of trim some of the adjectives but I also think that inverting this makes sense because, after all, having as your major goal a workshop seems kind of crazy. What you should--what I think we should say is we should do these things. One way of beginning to address this would be to convene a workshop.

CHAIRMAN TEUTSCH: So would you help us with what the first line would be for this recommendation? What is it we want to say?

DR. McGRATH: Maybe we can go back to the--what--yes, maybe there's something in here. No, sorry. That's all about the workshop. I thought there might be something or something in the background.

CHAIRMAN TEUTSCH: I mean it's also apparent to me that some of the things that we have under number six are really objectives. We need good curriculum and that sort of thing and other things like monitoring and things like that are part of the action steps that you need to take once you sort of know what those are.

DR. McGRATH: Well, the last sentence of the preamble was innovative approaches that coordinate the efforts of entities controlling health professional education and training are needed.

DR. EVANS: Yes, I mean I think that the words are here. I think we can say something like "innovative approaches to coordinate the efforts are required, therefore we would advocate (a) identify education and training guidelines that are outcomes based; (b)…" et cetera.

DR. McGRATH: Yes.

DR. EVANS: And then at the end say that

one way to begin this process is by convening a workshop.

DR. DALE: So that moves what's on tab or page 14 shown here to the end after these specific goals, doesn't it?

DR. McGRATH: Right.

DR. DALE: It says who should be at the table and it says all the players.

DR. McGRATH: Right. And so with the language like one way to accomplish this or the recommended way to accomplish this is through the convening of a workshop.

DR. EVANS: I wouldn't say accomplish. One way to begin to address this.

DR. McGRATH: Okay, all right.

DR. EVANS: Because I mean I don't think a single workshop is going to--

DR. McGRATH: Yes. No, you're right. Okay.

CHAIRMAN TEUTSCH: Janice?

MS. BACH: I am not sure where this fits but I was wondering if the group talked at all about the need to educate health plans?

DR. McGRATH: What--

MS. BACH: Health plans.

DR. McGRATH: Health plans.

MS. BACH: I'm not finding them referenced in here.

DR. McGRATH: Right. It's not in the recommendation and there is some stuff in the text talking about groups we didn't talk about--we didn't address in here. And health administrators, insurance plans, all of that were listed, and the groups that should be addressed in future reports basically.

MS. BACH: So you're basically just waiting until later to address those?

DR. McGRATH: Right. They are in that group of people who are not addressed in this report.

CHAIRMAN TEUTSCH: So if I can be really concrete here it seems that what we have under now (A) to (D) are the things that we need to have happen and there are three things that we think actions could be taken to help us get there. One is the workshop. One is (E), which if needed, appoint an advisory committee to carry on. And the third is (F) which is to publish the findings but the (A) through (D) are the core of this recommendation.

DR. McGRATH: Yes, absolutely.

CHAIRMAN TEUTSCH: And so if we--I don't know what we want to call it. If it says actions recommended or if HHS should identify the education and training guidelines, should identify appropriate funding streams and that sort of thing. How do we want to say that?

MS. DARIEN: I think HHS "should" because otherwise the action--it's not clear who should be taking the action.

CHAIRMAN TEUTSCH: Exactly.

MS. DARIEN: After all of these changes are incorporated in order to make it more concrete and come to consensus maybe it would be helpful to just read them out loud again or somebody else can read out loud.

DR. McGRATH: I don't know if there--are we planning on that tomorrow?

CHAIRMAN TEUTSCH: Well, we will have only a little bit of time.

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: I think we may need some final wordsmithing overnight but we've got to--but I agree with Gwen. It would be helpful to at least verbalize as best you can what you think it's going to say so we can get agreement on how this is

going to be framed.

MS. DARIEN: Right. We don't need to know what every word is but we need to know how it's--

CHAIRMAN TEUTSCH: What it's going to look like.

MS. DARIEN: Yes.

DR. McGRATH: So (A), (B), (C) and then (D) are the "should(s)" and then there's language about a way to begin to accomplish this is through…and then these--and that's one of the three. There's three ways that it might be accomplished.

CHAIRMAN TEUTSCH: So let me ask you, Barbara, is the first thing--this is what--we think HHS--are we in agreement that HHS should do this, HHS in collaboration with partners should do this? One is the who. I mean what is--

DR. DALE: To be effective I think it should be with partners.

DR. : Right, because it's--

CHAIRMAN TEUTSCH: HHS can certainly convene by itself but I think we want to accomplish these objectives with other stakeholders; right, whoever they are, the AAMC, AFPH, whomever.

DR. McGRATH: And then those three are three kind of freestanding things, the (E), (F) and

now the (G).

CHAIRMAN TEUTSCH: The first would be to convene a workshop.

DR. McGRATH: The first--

CHAIRMAN TEUTSCH: The first would be--

DR. McGRATH: It looks like the first is advisory panel so this may be redundant if we say workshop. What's the difference between an advisory panel and a workshop? So this first one is saying "advisory panel" and the second one is--well, it would be the third--published but then the last one is the whole notion of the workshop.

CHAIRMAN TEUTSCH: Yes, Sam?

DR. NUSSBAUM: It strikes me again that we're maybe several steps removed. Why not just, you know, as you say "workshop" and then determine the need and, if appropriate, advisory panel, why not just ask for--again there will be a need for an advisory panel maybe with stakeholders and that might be your action step on this.

DR. McGRATH: Yes.

DR. NUSSBAUM: And then, you know, that also gives it sort of a process going forward, a life going forward where that advisory panel can be the ones that maybe glean information from the

workshop, make further recommendations, and take on the task of continuing to advance the area.

CHAIRMAN TEUTSCH: So workshop first, advisory board second, and then disseminate the findings, is that what you're saying, and monitor the implementation or you would put it the other way? I just wasn't clear which way you meant.

DR. NUSSBAUM: One way is--and I know this--we're sun-setting but to create an advisory board on this topic then the advisory board could say whether it's a workshop or not. Here are your goals. We want an advisory board that's broadly constituted by these groups and that advisory board then meets and determines the way to achieve these goals. In a way it's perpetuating a solution here as opposed to only coming up with the idea of a workshop which in and of itself may begin to achieve the goals but it would require more work. And I don't mean necessarily that it's another, you know, extensive advisory committee but that this is critical enough, the field is advancing continuously, that an advisory board of key stakeholders, you know, educators and public agencies and public health, whatever those are. It could even be the private sectors that Janice was

pointing out were not addressed in this first round. You know, then that provides ongoing activity with goals.

CHAIRMAN TEUTSCH: Gwen?

MS. DARIEN: Okay. So I have a little--I understand what you're saying, Sam, but I'm wondering if it's something other than just in the language and the workshop is really more of a task force because it's a workshop of experts, not a "think" (sic). So maybe just changing it to task force accomplishes both incorporating the committee and the workshop idea which I think might be more appropriate because I'm thinking about some of the works of task force forces that have been convened of experts before.

DR. NUSSBAUM: I sure like that idea because again given that we're an advisory board that's not there, task force makes it much more focused, directed and action oriented.

CHAIRMAN TEUTSCH: But a task force in this case would be at least somewhat ongoing, right?

DR. NUSSBAUM: Yes.

CHAIRMAN TEUTSCH: It's not just a task force for this workshop. It's to convene a task force to do long term educational--

MS. DARIEN: To identify innovative educational programs, to monitor it, to do--does that make sense, Barbara?

DR. McGRATH: Yes, it does if I'm hearing it correctly that we would combine the two, the one that had the advisory board panel and the workshop, that's just now one. Kind of work the language so it's one and it's called a "task force."

MS. DARIEN: Yes.

DR. McGRATH: Does task force--is that a common enough term that it means ongoing because that was the deliberation because advisory panel conveys ongoing, whereas workshop does--

CHAIRMAN TEUTSCH: You can say ongoing task force.

DR. McGRATH: Yes, I was wondering about that.

DR. WILLIAMS: Well, in some ways I don't know that we necessarily need to presume. I mean, I think we all have the sense that it would be good to have something that is ongoing but, I mean, in some ways the purpose of the task force would be to determine, you know, the subsequent steps as opposed to our defining it upfront.

DR. McGRATH: Right. That's a good

point. Okay. So that cleaned it up so we only have two issues after the break.

CHAIRMAN TEUTSCH: So let me be clear now. So are we saying HHS should convene a task force to do these things that we've said in what were formerly (A) through (D)? Is that what we're--is that the recommendation? So that's the way it's going to read. It's not going to say HHS should do those things by… It's going to say that it should do this.

DR. McGRATH: Did we just flip it again?

CHAIRMAN TEUTSCH: That's what I'm asking. I'm--that's sort of what I heard but I wasn't positive. So--

DR. : We need to see some language.

CHAIRMAN TEUTSCH: Right. I mean it's hard to do that much--

DR. : Say what you just said again.

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: All right. So the recommend--what I think I heard--I'm looking for confirmation here--is that HHS should convene a task force of appropriate stakeholders to basically do

these--and potentially hold workshops or whatever, identify successful intervention and training guidelines, potential and current funding streams, those sorts of things. That's what its job is supposed to do and we'll get rid of (E) because we've said that's the task force; right? And (F) is "publish findings and recommendations." We could say that could be part of the initial piece, right? So the guts of this are to convene a task force to accomplish--however it's going to do that. If it has the expertise it can do some of it itself and if it needs to convene a workshop it can in (A) through (D) with some tightened language of (A) through (D). Is that what we heard?

MS. DARIEN: And then subsequently publish findings and recommendations and develop a plan to monitor.

CHAIRMAN TEUTSCH: Right. So that's a lot to write here in committee. What I would suggest we do is if--that's clear enough to all of you?

DR. McGRATH: I'm sorry. I was just talking. Are we starting with the "HHS should convene a workshop…" and then--

CHAIRMAN TEUTSCH: No. Convene a task force.

DR. McGRATH: Task force, sorry. Convene a task force.

CHAIRMAN TEUTSCH: With the--

DR. McGRATH: And then those four things.

CHAIRMAN TEUTSCH: Four points.

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: Right. And they can do that through the workshop or through--

DR. McGRATH: I understand.

CHAIRMAN TEUTSCH: --and we want them to publish their findings and monitor the implementation.

DR. EVANS: And I think another way to tighten this up is things like publish their findings. In past reports I know what we've often done is here are the bullets, right, and they are hopefully crisp and concise, and then there's a paragraph either justifying that which we probably don't need to do as much here or maybe elaborating a little on it following the bullets. And things like disseminating and publishing that probably doesn't need to rise to the level of the recommendation.

DR. McGRATH: I was thinking that because it doesn't flow any longer anyway so we're going to drop that one. Okay.

CHAIRMAN TEUTSCH: Right. And even the workshop if that's the way they think they can get the job done best. If these experts know the answers to these questions then they don't have to do that either or they can have much more focal discussion.

DR. FERREIRA-GONZALEZ: Are we going to get to see these again?

CHAIRMAN TEUTSCH: I would hope. If we can get the folks to draft these overnight so we can see them and make a final look-see (sic), which doesn't mean we can't do some extremely minor editing afterwards but we need to make sure we're in assent. I think this is really--this has been pretty constructive. Do we have agreement on this recommendation? Let me just take a quick straw vote. Everybody in favor of it the way we just sort of framed it signify by raising your hands.

(Show of hands.)

Any dissenters?

Okay. So you'll have a final chance to see it.

Yes, David?

DR. DALE: Can I make one comment sort of being on the ground in this area. There is the

material side. That is, what are the materials that help you to accomplish this because any sort of educational strategy leans on materials that have been developed by experts in some way?

Barbara, where is that in the other recommendations? It doesn't have to be here but do you understand what I'm saying?

DR. McGRATH: Yes, I do and I think this would be the only place. Maybe there is--when we look at this we can make a note to add some language and evaluate educational materials, something like that.

DR. DALE: Or somewhere the educational guidelines and materials needed to--somehow the--what I think you'll immediately get back from health care professional education groups is what are our resources.

DR. McGRATH: It looks--it seems like it would fit under (A).

DR. DALE: Yes.

CHAIRMAN TEUTSCH: (A) or (C) here.

DR. DALE: I'll volunteer to work with Barbara.

CHAIRMAN TEUTSCH: Please do. I think that we would take that as a friendly amendment.

DR. DALE: Yes.

CHAIRMAN TEUTSCH: Okay. Do you want to move on to two?

DR. WILLIAMS: I have some very specific language on two to propose.

DR. McGRATH: Okay. Good.

DR. WILLIAMS: So slide 18.

(Slide.)

Yes, that one.

So what I would propose here is on the third line "HHS should: (A)…" and then you would read those as needed and I would add one additional clause somewhere in that to say "to assess the most appropriate setting to deliver public health genomics." That's not separate. It's part of (A). So in other words you've got "should assess the workforce to ascertain current trends and future needs; to identify education and training needs," and then I would say "to assess the most appropriate setting to deliver public health genomics and promote leadership in the field." That is already there so in other words we've just got some new--the formatting introduced stuff because "to identify educational and training needs" is part of that--is part of (A).

Can you--I suppose you can't undo everything.

DR. McGRATH: So you'd use a colon and semicolon for the three clauses?

DR. WILLIAMS: Yes.

DR. McGRATH: Yes.

DR. WILLIAMS: Yes, okay. And then--okay.

CHAIRMAN TEUTSCH: What do you mean by setting?

DR. WILLIAMS: I mean is it traditional statewide public health. Is it in a health care delivery setting? I mean it's what we talked about before or what I talked about before with the idea that we don't have a good definition of where the different public health roles are best being delivered.

CHAIRMAN TEUTSCH: Janice?

MS. BACH: I think maybe you just said it, Mark, but I was just going to ask you to clarify. Are you trying to get at what exactly is the role of public health in genomics education in the different settings that could be construed as public health?

DR. WILLIAMS: I think what I'm trying to say is that public health takes place in--when we've

used the word “public health” I think a lot of people think of health departments and I think that the reality is that public health is delivered across all delivery settings. And what we have not done a good job of in my opinion is to really define under what circumstances are certain public health programs relating to genomics that are delivered in a health care setting, like BRCA for example, as opposed to in a public health department which would be best served say in newborn screening.

MS. BACH: But also it’s what type of education is public health trying to deliver? In other words, there’s--you know, there may be a role for public health in a statewide family history campaign which is much less specific.

DR. WILLIAMS: Right.

MS. BACH: But obviously the counseling for BRCA is done in a clinical setting.

DR. WILLIAMS: Right. So I see that as part--I see that one and two are actually going to be complementary because I think a lot of the education things are going to be subsumed under the task force in recommendation one but in this assessment I think that one of the things that needs to be assessed is appropriateness of the delivery

setting for various types of interventions. That's what I'm trying to articulate under (A).

DR. McGRATH: Well, if there's only one it can't be--

DR. WILLIAMS: No, there's not one. That's why--that's--because I'm not done yet so I still want (A) there.

DR. McGRATH: Okay, sorry.

DR. WILLIAMS: Okay, so alright. And then--so after the period there would be a (B) which is "identify and engage exemplar public health genomic programs to identify critical information not captured in the workforce assessment." And that addresses the point that we raised earlier about the--that a general survey is not going to have as much utility because people don't know what they don't know.

DR. McGRATH: The one thing I wanted to say about that was the survey in our minds wasn't asking people like we did in the report do you feel competent. It was more to assess what they're doing so to try to get the landscape of who is doing what out there.

DR. WILLIAMS: Right. And I understand that but I think that this (B) suggests to me an

active role of identifying those that are definitely--rather than just sending general information out, we know from doing that before that the people that are returning the information may not be aware that there is, in fact, a small group within their organization that is actually focused on this issue.

DR. McGRATH: Okay.

DR. WILLIAMS: So this is an active engagement as opposed to what might be characterized as a more passive collection of information.

DR. McGRATH: So does that cover, Katy, the issue of trying to get more diverse players looking at this, your nontraditional people and agencies to look more creatively at public health workforce?

DR. KOLOR: I think a struggle with this recommendation from the beginning has been reaching beyond the traditional genetics and genomics public health professionals to the broader public health sphere. I'm not sure that we're doing that yet here.

DR. WILLIAMS: But that would be more (A) than (B) then.

So maybe what I can do since it sounds

like some people want to revisit what is now the proposed (A) just to kind of go on and finish this piece out--so now if you go to the next slide.

(Slide.)

So I would like to replace “based on this assessment” with “using the results of these assessments,” which is a little bit more directive. And then we would need to either--we now have two (A)s and two (B)s, and so whether this would be (C) and (D) or whether this would be (1) and (2) or whatever, that’s more formatting and I don’t really matter so much about that but that’s what I was proposing to capture the points that I raised in our previous discussion.

DR. McGRATH: So there is “…address the gap. Using results of this assessment…”

DR. WILLIAMS: And actually it probably should technically be “these assessments” given that there are--we now have two.

DR. McGRATH: And then would we want to add language “…and addressing identified gaps.” Does that cover that or is that so obvious that that’s what you would do?

DR. WILLIAMS: So you could say using the results of these assessments and--

DR. McGRATH: Say “based on identified gaps.”

DR. WILLIAMS: And “using the results of these assessments and the identified gaps HHS should...”

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: Now we have sort of created different problems. One is we are trying to identify a mission-driven set of skills that people need. I think that’s the first part. The second part, which is what’s up here now, is a competency-driven thing, which is I think where we got to because we didn’t know what the mission really was and that’s probably why there has been such resistance in public health to getting this kind of training because nobody was quite sure what they were going to do with it. So I sort of agree with Marc. We’ve got to get this identification upfront and then I would probably simplify the second part and talk about based on the specific needs that are identified for population health interventions--because I would frankly put the things like newborn screening and things like that at the individual level and part of clinical management because it’s individual oriented in large part but the population

part here is what we actually need as a complement to it. And just make it pretty simple, “based on those needs develop the appropriate curriculum and training.”

DR. McGRATH: Would you not even talk about core competencies?

CHAIRMAN TEUTSCH: Well, I think we have to decide is this competency-based or is it need-based and I know public health likes all the competencies, god knows that there are enough of them, but I’m just concerned that people are going to shrug if they don’t know why they need them and it will be pretty nonspecific.

DR. McGRATH: Well, except your point was--what you had just said was that if the first becomes “identifying the need” then the competencies come after that.

CHAIRMAN TEUTSCH: Right, if you can link the competencies to those needs that’s fine.

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: But if you look at sort of the competencies they are pretty much all over the map.

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: As they are now. At

least that's how I read them.

DR. McGRATH: I know that--Joseph is not here of course and I can't quite channel him but we did talk a long time about why competencies because I'm not used to that in my world but he said that's the language of public health.

CHAIRMAN TEUTSCH: It is but it is hard for people to understand.

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: The competencies need to be based on the need.

DR. McGRATH: Right.

CHAIRMAN TEUTSCH: And right now they are based on sort of an abstract set of wouldn't it be good for people to know and, therefore, they are pretty generic.

DR. WILLIAMS: So you could really--if you go to the next slide--to address Steve's point, you know, (A) could be--so if we have "using the results of these assessments and the identified gaps HHS should support development of competencies in genetics and genomics that specifically address the identified needs and gaps."

CHAIRMAN TEUTSCH: That would be better.

DR. McGRATH: Yes. And I don't think we

need the rest of that.

DR. WILLIAMS: And not have the rest of that.

DR. McGRATH: Right.

DR. WILLIAMS: And then “based on these competencies” that then flows I think.

MS. DARIEN: I also think that--just to--I was just thinking back to Steve’s point and Joseph’s point. We can’t--we have to have language that everybody--somebody that’s reading the report understands. So even though “competencies” may be a public health term if the wider world doesn’t understand it, it can’t--we can’t have each section have jargon for the group to which it’s trying to fulfill the needs.

DR. : Capabilities would be--

DR. McGRATH: Capabilities.

CHAIRMAN TEUTSCH: I mean I don’t have--capabilities is just another--

DR. McGRATH: Okay. I mean, I--

DR. EVANS: I take your point but I also think part of the whole reason to do this is we’re talking to the public health community here and we do want to speak their language and--I don’t know. I think it has become general and I don’t think it

is--

(Simultaneous discussion.)

DR. : It's a general educational- kind of approach, right?

DR. McGRATH: Well, we could do both. You know, a compromise, so "skills and competencies" or something like that.

MS. DARIEN: I would just do both, yes. I would just use both so that it gave somebody a sense of what it was.

DR. McGRATH: Because they have skills. Okay.

CHAIRMAN TEUTSCH: So I think you're probably close enough here. Why don't we just get a sense of other people and then some of the wordsmithing can go on offline and we'll have a chance to see it again tomorrow.

DR. McGRATH: Right.

CHAIRMAN TEUTSCH: So again let's take a quick straw poll. Folks who are comfortable with this raise your hands.

(Show of hands.)

Some are half raised.

Any other opposed?

Okay, so all right.

Why don't you move on to three?

(Slide.)

DR. McGRATH: So the recommendation itself is at the bottom. "HHS should promote…"

DR. WILLIAMS: And I would propose based on previous discussion to delete (B).

DR. McGRATH: Okay. Well, we were right in the middle of that discussion and Vince responded. Are there other opinions about that? There seemed to be two things on the table. One is, is this really an issue of genetic exceptionalism? Is there anything unique about genetics that requires a more diverse workforce than the general health care world? Or the other opposite side, if I'm summarizing it right, is the committee is charged with really looking heavily at diversity and rather than having a separate task force on diversity the idea was that it would be infused in all reports so whenever you can have a chance to highlight the fact that services are not accessible--that health disparities exist in the health care system--we should use an opportunity to add language about that to bring it to the forefront.

DR. BONHAM: Well, if we're going to keep something in here then I think what we would need

to--how I would recommend modifying (B) would be to say something to the effect of “assess whether genetic or genomic factors are impacting the practice in underserved communities and, if so, develop strategies to address this to encourage health care professionals to practice in underserved communities.”

DR. : I’m not sure what that means. Don’t we know that these are underserved?

DR. WILLIAMS: Well, we know they are underserved but the point I was trying to make--obviously unsuccessfully earlier--was that we have no evidence to suggest that there’s anything in the realm of genetics or genomics education that is preventing health care professionals from wanting to work in underserved areas and so this is a genetics document. If there are issues relating to genetics education or genomics education that is somehow impacting willingness to serve in underserved communities then it’s appropriate to address it here. My contention is the factors that impact people not going to work in underserved communities have nothing to do with genetics and genomics.

DR. EVANS: I think your point may be well taken but I hate that wording. It says “whether

genetic and genomic factors are impacting the practice." I mean that sounds bizarre.

DR. WILLIAMS: I'm open, Mr. Editor, to suggestions.

DR. : Do you want to speak to this?

DR. BONHAM: Yes, I guess the only comment I want to make is that this is both about education and training and part of this is kind of really getting to the training issue of diversity of the workforce that's providing the genetics and genomic services.

CHAIRMAN TEUTSCH: So when you--can I get some clarity on this because it says "using incentives such as CEUs." It wasn't clear to me whether we give CEUs for people to go to serve underserved areas or whether we need to have more CEUs associated with the issues of genetics in underserved communities. I couldn't understand what that was about.

DR. BONHAM: I don't know. Barbara? I wasn't on this--

CHAIRMAN TEUTSCH: Oh, okay.

DR. McGRATH: I don't remember--I think maybe it got thrown in--you know, a cut and paste

deal but the point we're missing with this is that phrase "the diversity of the health care workforce." One of the issues here was that--we know this from literature, we don't need more research--that when people have access to practitioners that are similar to them health care ends up being better accepted. So the notion is that the health care workforce is not very diverse and so this is also speaking to the issue of not just getting more people to work in underserved areas but to get a more diverse workforce. So that's the issue of--it wouldn't be captured by just are there needs for more services but a different workforce, too.

And the CEU thing, I think we can just drop that. And I think we talked about some more--more other programs like loan repayment programs which is nothing unique to genetics.

CHAIRMAN TEUTSCH: So what I'm hearing you say is that--and partly to do with Marc's concern--it's not we have unique problems in genetics.

DR. McGRATH: No.

CHAIRMAN TEUTSCH: As in other areas--as another aspect of the care system we need to create incentives for more--I don't know what the right word is here--a more diverse--for development of a

diverse workforce and to enable them to practice or to provide incentives for them to practice in these communities.

DR. EVANS: And we might be able to do that just with some parentheses. I mean maybe--and I agree with Marc. It seems to stand out as a little bit of a non sequitur but if we said "identify and support programs to increase the diversity of the genetic specific health care workforce…" and maybe in parentheses "…(and indeed the entire health care workforce)…" something like that "…because of our overarching mission" t hen it might be more--do you think it would be less of a non sequitur?

DR. WILLIAMS: Yes, I mean I think that the issue for me is just, you know, we're talking about how to get people in underserved communities as it is currently stated and that's not the point. I think the point is if the point is, in fact, about diversity of the workforce and there's an educational role for genetics and genomics in workforce diversity then absolutely that's what we need to frame in this recommendation.

MS. DARIEN: But I think--I mean just to reflect something that I was hearing, we have been

focusing a lot on education but it is education and training so I think that that's a really important point to not--you know, that we don't lose that point because, you know, we all go to meetings and the makeup of the meetings is the workforce. So I think that education and training is a really important issue. So that's all.

CHAIRMAN TEUTSCH: David?

Dr. DALE: Well, I think the language "genetic specific workforce" is confusing. I don't like it.

DR. WILLIAMS: It's really more from my perspective are there different educational and training strategies that need to be applied to enhance the diversity of the workforce? I mean it's not that--you know, there may be some people that are--when we think about things like genetic counseling and that where clearly there are some issues that are ongoing relating to the diversity of that workforce but that's really more the issue as I see it. And we're--the language as it is--I would agree with you, David. I think it's not a genetic specific workforce. It's really about how--

DR. EVANS: A genetically competent workforce.

DR. WILILAMS: Yes.

DR. EVANS: Right? We can say that.

DR. WILLIAMS: And it is really--for me in these recommendations it's really are there different educational and training modalities that are going to be needed to enhance the genetic competency of a diverse workforce as opposed to our current workforce? I mean that, I think, is what we're trying to get at here. Maybe I'm completely missing the boat.

DR. McGRATH: No, I think that last phrasing was good. "To identify the need for different modalities to encourage…" something like that.

DR. WILLIAMS: Yes. I mean that to me seems to be what we're talking around here and I'm not sure I could recapitulate what I just said. That usually never happens.

DR. McGRATH: It's all on tape.

DR. DALE: I would suggest that what we want is access to genetic services for underserved communities where it's hard to imagine someone going and practicing in Whitefish or smaller communities where you live and I live. There's just not the work but what they need is services.

DR. WILLIAMS: Yes, but I don't think we should conflate an education and training document with previous reports that the committee has produced specifically relating to access to services where we have specifically addressed the issues of underserved populations. I don't think we need to-- I think this is trying to get at something different, I guess, is what I'm saying.

CHAIRMAN TEUTSCH: Can we keep it really simple by just saying "identify and support programs to increase the diversity and genetic competency of the health care workforce serving underserved communities."

DR. : Yes.

DR. : Yes.

DR. EVANS: That's exactly right.

DR. : Excellent.

DR. EVANS: Yes, and get rid of that early verbiage there. Get rid of "assess whether genetic…"

DR. McGRATH: Yes. It's gone.

CHAIRMAN TEUTSCH: So it would read "identify and support programs to increase the diversity and genetic competency of the health care workforce serving underserved communities."

DR. : “In underserved.”

CHAIRMAN TEUTSCH: “In.” Yes. Well, “…in serving,” whatever the right word is. “Serving in underserved” is sort of redundant.

DR. : Yes.

CHAIRMAN TEUTSCH: Anything else with this recommendation?

All right, so let’s see again. Do we have a consensus that this is now what we want to say?

(Show of hands.)

Okay. Anyone feel this is not appropriate?

Okay. Barbara, now we can go on to the new stuff, right?

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: Number four.

DR. McGRATH: Sorry, there was two more two more on three. A couple more should(s).

CHAIRMAN TEUTSCH: I didn’t hear anybody disagreeing with these.

DR. McGRATH: We hadn’t gotten this far though so let’s just make sure.

CHAIRMAN TEUTSCH: Okay. Well, go ahead.

DR. McGRATH: So these are two more should(s) under the workforce issue. Okay.

DR. WILLIAMS: So to reflect David's comment earlier I would just suggest "educational material" or "models and materials."

DR. McGRATH: Great.

DR. WILLIAMS: In (C) "educational models and materials."

DR. McGRATH: Yes, great. I don't know if we need that "e.g.", do you think?

DR. WILLIAMS: No.

DR. McGRATH: Okay. We can edit down a little bit too. Okay.

DR. WILLIAMS: The same thing in (D) "models and materials." Then it would be consistent.

DR. McGRATH: Okay, moving on to four.

(Slide.)

Okay. This is the portal. This came out of the idea that we really--the literature showed and in our interviews it came out pretty consistently that people would like the federal--they trust the federal government as a source to vet information they have on the internet and they don't see that the existing ones--I mean there are other models.

CHAIRMAN TEUTSCH: Sam?

DR. NUSSBAUM: I think this is an example where we can make this really pithy. It's basically if you endorse and fund and maintain you're doing one. There should be an HHS portal that incorporates the most comprehensive up-to-date information and tools, period.

DR. McGRATH: Okay. So just get rid of "endorse."

DR. NUSSBAUM: I mean just rather than tell people how the portal should be developed and what's on it, I mean the most--using the term "contemporary, up-to-date, sophisticated," whatever it needs to be but I think basically there is--there needs to be a portal.

DR. McGRATH: So do you mean HHS should develop? What's the verb? What verb do we want?

DR. NUSSBAUM: "Create."

DR. McGRATH: "Create." Okay. God-like.

DR. NUSSBAUM: Yes.

DR. McGRATH: And maybe we don't--and what you're saying in that spirit "this portal should utilize…" do we not have to tell them what should be in it or do you think it's useful to--

DR. NUSSBAUM: State-of-the-art portal, scientifically valid, incorporating the newest tools

of consumer and professional engagement, whatever.

DR. McGRATH: Yes.

DR. NUSSBAUM: Just a state-of --

DR. McGRATH: And then take out that last sentence?

DR. WILLIAMS: Yes, and what I would probably also include in addition to what Sam just said is, you know, there are a couple of things about, you know, how to trust genetic information that have come out of Genetic Alliance and that, and you may have referenced those in the body and, if so, I would just make it very specific that they should also incorporate what has been learned from efforts about evaluation and trust of genetics resources.

DR. McGRATH: So then we should maybe keep that sentence “this portal should utilize resources…”

CHAIRMAN TEUTSCH: No.

DR. WILLIAMS: No.

DR. McGRATH: I mean because it--

DR. : That’s part of the trust.

DR. McGRATH: Take it out, all right. So then where would the trust part be?

CHAIRMAN TEUTSCH: It’s under

"trustworthy." It says "web-based."

DR. McGRATH: Oh, okay. All right, that's the main part.

CHAIRMAN TEUTSCH: So it reads "HHS should create and maintain a state-of-the-art internet portal…" I'm not sure I like the word "to a vetted collection of "…to scientifically accurate, comprehensive, accessible and trustworthy…" something like that.

DR. McGRATH: Well, I think the word "vetted" actually is redundant. So maybe that can go out because we're wanting it to be trustworthy and comprehensive so that means they have to vet it to do those things, right?

CHAIRMAN TEUTSCH: Right, and there doesn't need to be a collection of--"Two: Comprehensive, accessible and trustworthy web-based genetics information and resources for consumers."

(Simultaneous discussion.)

DR. McGRATH: Okay. Good enough with a little tweaking.

CHAIRMAN TEUTSCH: And then we don't--do we need the sub-bullets under this one?

DR. McGRATH: There's a couple--well, there are a couple. Let's just look at them. This

is describing the portal.

(Slide.)

CHAIRMAN TEUTSCH: It seems to me this can all go in text.

DR. McGRATH: Yes, I'm looking at it. I agree.

DR. WILLIAMS: Do we want to include anything to just add reasonably accommodations for individuals not able to access internet materials should be developed or something like that, should be considered? I mean I think we have--I remember in the document that that was discussed and I seem to recall in one of these iterations that we talked about that. I think we probably do need to not put all of our eggs in the internet basket.

DR. McGRATH: Well, I think it comes up in another--

DR. : It comes up in the other--

DR. WILLIAMS: It's in (B) but then (B) kind of went away and that's--I didn't want--I guess I didn't want (B) to go away but we could incorporate that somehow under the new--

DR. McGRATH: Saying "widely accessible," is that too--that's not specific enough? You know, the first--the new first language.

DR. WILLIAMS: Well, but if--but the new first language says “internet-based,” doesn’t it? Doesn’t that specifically say that?

DR. McGRATH: I see, yes. This is all about the portal. There is other--another recommendation deals with communication and education.

DR. WILLIAMS: Okay. So I just--but we were just talking about--okay. So maybe I was misinterpreting what I heard.

DR. McGRATH: Let’s make sure we do.

DR. FERREIRA-GONZALEZ: So what you’re trying to say is there has to be other sources other than web-based for those individuals that don’t have access to the internet?

DR. WILLIAMS: Correct, right.

DR. FERREIRA-GONZALEZ: Because the portal is going to be web-accessible so then the idea would be having another recommendation a part of that--

DR. McGRATH: I think--

DR. FERREIRA-GONZALEZ: --non-web-based.

DR. McGRATH: Do you think number five covers that because this really is a web-based portal? So five now--

DR. WILLIAMS: Okay. So five would be--

DR. McGRATH: Non-web, you know, multiple venues. Okay. If it doesn't, let's go back and change this because it's an important point.

DR. WILLIAMS: So in some ways then maybe we should consider flipping four and five. Five is a more broad recommendation to create a panoply of different ways to educate but that we are, in fact, making a specific recommendation that a web-based portal be created and maintained.

DR. McGRATH: Change this one to five and we'll just move them. We'll do that later. Okay.

DR. FERREIRA-GONZALEZ: Number five is more--not just to consumers because number four is for the consumers so there has to be different language specific for, you know, the general public. In number five we're talking about education at different levels of genetic information.

DR. WILLIAMS: But the preamble to five talks about consumers and patients so I thought five was consumer-patient directed as well.

CHAIRMAN TEUTSCH: So one of the other suggestions is in text because there are so many people getting access to the internet except for the libraries going out of business. You can go to the libraries and other places. At least in text "to

meet the needs of those without internet access the government should assure that these same materials are available in other forms or through other media," something like that so that you can just deal with it in text.

DR. McGRATH: So I think all of this is gone now.

CHAIRMAN TEUTSCH: Right. But you're going to put some of it in text, right, in other places.

DR. McGRATH: Right.

CHAIRMAN TEUTSCH: So you'll still have radio and other media.

DR. McGRATH: All right. So with that addition of the preface about make it available other ways in the background, we're okay on that?

CHAIRMAN TEUTSCH: Everybody okay with that one?

DR. McGRATH: Okay. I like the idea of flipping them. So this would actually--the new--this next one would go in front. I think that's the background and the recommendation at the bottom, yes. There are four bullets under it.

CHAIRMAN TEUTSCH: I am sorry. I'm a little confused. So you have combined four and five

now?

DR. McGRATH: No, just switched the order.

CHAIRMAN TEUTSCH: Just the order of them.

DR. McGRATH: So this is number four. The portal would come after. Marc's point is this is more general and broad and then the next one is a very focused portal. So they are separate recommendations. It's just this comes before. So in your text we're looking at number five.

DR. WILLIAMS: Again in (A) I'm not sure we need the parenthetical.

DR. : Yes, I don't think we need any parentheticals in here.

DR. McGRATH: Okay.

DR. : And you can just put some of them in text.

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: I think people do know about what other media are.

DR. McGRATH: Yes, okay, so all print.

CHAIRMAN TEUTSCH: Yes, radio.

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: Tweeting your whole genome but by the time we publish this there will be new media.

DR. WILLIAMS: By the time any of us of our age figure out what currently is going on they are two steps ahead already.

DR. McGRATH: What about (C) and (D)? Do you want to take out the “such as the department” and then is (D) necessary?

DR. WILLIAMS: I actually foresee--I think that we should be more directive to the Secretary to engage with Department of Education and National Science Foundation because what we’re really trying to do here is to develop the idea of a continuity of information about genetics and genomics really all the way through the educational curriculum.

DR. McGRATH: So maybe put that phrase at the beginning of it. “In collaboration with the Department of Education and NSF…” That will call it--

DR. WILLIAMS: Yes. Something to that effect, yes.

DR. McGRATH: --a little higher. And then do we want (D) still or is that a little--

CHAIRMAN TEUTSCH: (D) is already in (A).

DR. McGRATH: Yes.

(Simultaneous discussion.)

DR. McGRATH: Right, that’s what I was

just wondering. Okay.

CHAIRMAN TEUTSCH: I wonder if (C) you can't streamline further, too: "In collaboration with the DOE and the National Science Foundation incorporate genetic training into the K-12 curriculum."

DR. McGRATH: What did you just say?

CHAIRMAN TEUTSCH: You've got it basically. "In collaboration with the DOE and NSF support the incorporation of effective genetics education into K-12 curriculum."

DR. McGRATH: "Incorporation of genetics."

CHAIRMAN TEUTSCH: I'm just suggesting just a way to streamline it again.

DR. McGRATH: I think all that goes in.

DR. : This goes out?

DR. McGRATH: I think so. Does that do it? And then get rid of the--

CHAIRMAN TEUTSCH: And get rid of the rest.

DR. McGRATH: Does that do it?

Gwen?

MS. DARIEN: So (D), it ends with "call for collaboration among various disciplines to research." Research what?

DR. McGRATH: We just thought we'd take it out.

CHAIRMAN TEUTSCH: We took it out.

DR. WILLIAMS: (D) is gone.

MS. DARIEN: Oh, okay. Sorry.

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: What was (B) again?

DR. McGRATH: That's diverse media.

CHAIRMAN TEUTSCH: You had something about health literacy somewhere. Where did that go?

DR. McGRATH: Maybe it was in the background in the preface.

CHAIRMAN TEUTSCH: Oh, we said "at all literacy levels." Okay.

DR. McGRATH: Yes, in the preface.

CHAIRMAN TEUTSCH: Okay.

DR. McGRATH: Okay. How do we feel about this one in your text five but the new four?

CHAIRMAN TEUTSCH: Just as a point--I think you want more than "translation of materials into locally predominate languages." It has got to be--it's about culturally appropriate, culturally and linguistically appropriate--

DR. McGRATH: Right. Okay.

CHAIRMAN TEUTSCH: We see a lot of

translations that don't translate.

DR. WILLIAMS: So really what you're saying is it would be "…and provide culturally and linguistically appropriate materials," and that's the end of it.

CHAIRMAN TEUTSCH: Yes.

DR. WILLIAMS: That's all you need.

CHAIRMAN TEUTSCH: That's all you need.

DR. McGRATH: So you are getting rid of the translation but "should develop…"

CHAIRMAN TEUTSCH: That is linguistically.

DR. WILLIAMS: Right. "Provide culturally…"

CHAIRMAN TEUTSCH: Material.

DR. WILLIAMS: "…and linguistically appropriate materials."

(Simultaneous discussion.)

DR. McGRATH: But you're getting rid of "develop educational programs that use…"

DR. WILLIAMS: No.

CHAIRMAN TEUTSCH: No.

DR. WILLIAMS: This is after.

DR. McGRATH: All right, okay.

DR. WILLIAMS: So this is after.

DR. McGRATH: Right.

DR. WILLIAMS: "A wide array of media and culturally and linguistically appropriate materials."

CHAIRMAN TEUTSCH: Okay, anything else on this one? Do I see nods or shakes?

We're good?

DR. : Yes.

CHAIRMAN TEUTSCH: All right.

DR. McGRATH: Okay. Number six.

CHAIRMAN TEUTSCH: Bring it home.

(Slide.)

DR. McGRATH: Yes. This one I kind of smiled when I was reading this on the plane. It kind of--you could call it--it's a time capsule because we are writing family history as it was just like the buzz (sic). So, who knows, in five years they'll wonder why we had a specific one on family history in 2010.

So the actual recommendation is that "HHS should…"

DR. EVANS: So I have been--in going through all of this the one thing that I felt was missing, I think, that could fit well in here and that is that I think we need to work something in about incorporating our educational records or

integrating it with the electronic medical record. In other words, we need to highlight in some way the fact that education is about much more than just passively having portals, feeding people information in medical school that they'll forget, and I think we could insert that into here because it's discussed, right, in the--

DR. McGRATH: Yes, I'm trying to remember where.

DR. EVANS: --report and say something about educational or--I mean educational technologies that can be integrated into the electronic medical record and, therefore, serve the needs of practicing physicians will be critical, something like that.

DR. McGRATH: Practicing health professionals.

DR. EVANS: And that kind of gets us also the added plug of the whole EMR and genomic issue.

DR. WILLIAMS: So actually let me maybe take a crack at this in (A) because I think I might be able to get at what Jim is saying and fix some of the issues in (A). So what I would propose in (A) is through the development of--

DR. McGRATH: Oh, there it is.

DR. WILLIAMS: --so add after “of”--do you see where I am? Yes.

DR. McGRATH: Yes, okay.

DR. WILLIAMS: “Point of care educational materials and clinical decision support tools.” Now take “and electronic health records that utilize coded and computable family history information.”

DR. EVANS: The only thing I wonder--I think that sounds great. The only thing I wonder about is I don’t think we should focus exclusively on family history information. What we’re going to see is this deluge of genomic information that goes beyond family history.

DR. WILLIAMS: Okay.

DR. EVANS: So I think we need to--

DR. WILLIAMS: So we can make that “coded and computable family history, genetic and genomic information.” And we’ll forget the other ‘omics for now that will surely emerge but this is completely consistent with all of the communication that we’ve done in the last two years relating to the need for an electronic health record that will be able to actually code this type of information so it can be utilized. I specifically eliminated the use of the term “pedigree” because that is really something

that most practitioners are not interested in dealing with so we need to put that information in there in a way that it can be used and not define it as being pedigree information. So I think that captures the point that Jim was making into the recommendation and is supportive of comments that we have made for meaningful use in other things.

DR. DALE: Steve, in this area I worry about HIPAA. That is the privacy part of one person telling about another person's medical information. As you go deeper into that you get into privacy issues.

DR. WILLIAMS: According to HIPAA which actually issued a clarification on family history, any information that you obtain from your patient about family medical information, including names, birthdates, social security, whatever, is acceptable and is covered under HIPAA. So those are not exclusions. You are not excluded from collecting that information under HIPAA.

CHAIRMAN TEUTSCH: But how you use it is what you're worried about.

DR. DALE: Yes.

CHAIRMAN TEUTSCH: You're worried about how it gets used because once you have it from one

source you can use it for something else, right. Is that what you're getting at?

DR. FERREIRA-GONZALEZ: Discovery and the use cannot be disclosed unless they have permission.

CHAIRMAN TEUTSCH: True but you often--primary care practitioners often take care of families and as you start--

DR. EVANS: Yes, but I think that that's actually a much--it's a completely separate issue. I think that--I don't even think we should go there because like Marc says this is entirely legitimate under HIPAA and important information to obtain, and we don't want to call that into question in people's minds because it isn't a question.

CHAIRMAN TEUTSCH: I am just looking at (B) and (C), and they look a little bushy and nonspecific to me--to use a technical term.

(Laughter.)

I wonder--particularly (C). (B) is a little vague.

DR. McGRATH: Well, we just--we wanted to call out to all three groups family history--I mean one reason it has a separate--its own recommendation is it was one of those exemplars that cross all boundaries--cross all boundaries I guess is what I

want to say, so all three groups are using it in slightly different ways. So we would like to be able to have some parity. If we say something about health care professionals, primary care--

DR. EVANS: Does that belong in the--since it specifically designates public health providers, does that belong in the other recommendation that addresses public health?

DR. McGRATH: You mean in the public health recommendation?

DR. EVANS: Yes, I'm looking at the--

DR. McGRATH: Like the second one.

DR. WILLIAMS: See I don't see that as sitting in the public health recommendation because that one is really not--this one specifically articulates research around family history which I think is not--it doesn't really fit with the other.

DR. EVANS: That's fair enough. Do we want to confine it again to family history?

DR. McGRATH: For this recommendation?

DR. EVANS: For this one, too.

CHAIRMAN TEUTSCH: I think this is really confusing partly because the public health providers would contract the individual care in (A), with population care in (B), and population care isn't

about family history per se unless we have something we want to say about how understanding the family history of your community is going to influence this because I think what you'd want to say is for health care professionals who could be practicing within the public health context or within a more traditional medical care.

DR. McGRATH: Except I think the examples we had were that the public health workforce has a lot of experience with surveillance and research and patient education, and so they would be involved separately from providers, hands-on providers, in dealing with family history.

CHAIRMAN TEUTSCH: And what is it we want them to do? It says we want them to do research. I guess I'm not clear what--we want them to do surveillance of family history? I think we either need to give this more flesh or get rid of it.

DR. McGRATH: If we get rid of it we're sending a message perhaps that we don't think there's a role in public health workforce for dealing with family history. Is that true? I mean I'm happy with it but I think that's what we're saying.

CHAIRMAN TEUTSCH: Well, I think you can--

I'll leave it to others but I--yes, Sam?

DR. NUSSBAUM: It strikes me that the educational tools and models that will get developed could encompass family history. Nowhere else--well, I guess that's not true. We're talking about internet sites but I think this is being very focused and it may be good but why not just in the others sort of put in, you know, as a sentence in one of the other recommendations, you know, including in the education the strong commitment and use of family history tools in the educational process or something where it's not its own recommendation.

It just strikes me that it's standing out too paramount away considering it's important but it's one of several methodologies.

DR. WILLIAMS: Yes, I have some affinity for that. I think one of the reasons that this was included is because obviously parts of DHHS, specifically the Surgeon General and the NIH, are actually actively investigating and supporting collection of family history and promoting that to the public as a way to take control of their health and so I can understand the reason for wanting to include that.

So the question would be is whether this would somehow fit into a recommendation in one of these that would be support and expand ongoing efforts in the collection and use of family history by current DHHS and other governmental agencies or whether this would be something that would be more appropriately reflected in the text to say, you know, this is primarily an education document and we recognize that family history is a way to engage people around educating themselves about the role of genetics.

CHAIRMAN TEUTSCH: Here is another fix for you. Delete (B) and in (A) just talk about health professionals.

MS. DARIEN: Well, I think the one--the only issue with that is that this is a parallel construction. So we say, you know, its health care professionals there's (A); public health professionals there's (B); consumers there's (C). So maybe then in the--over the six it should say "health professionals" and combine rather than saying health care and public health.

CHAIRMAN TEUTSCH: I agree, in the preamble.

MS. DARIEN: Yes, in the preamble.

DR. McGRATH: Though (A) really--I don't--public health providers don't necessarily get too involved in clinical care through development of point of care education. That doesn't really work. That's not what, as I understand, public health workforce is involved in with family history. It has other areas. I think you're right. It stands alone and I think it's just as I was saying. It's the testimony of the context within which it was written. There was a lot of buzz about family history in the last three years.

CHAIRMAN TEUTSCH: But this is about education. I think you can think about family history as a risk factor that you can study, you can do all kinds of things with it. That's not to say it's not important to public health but it's not clear to me that you--what this is going to do that's related directly to the education agenda.

DR. WILLIAMS: Yes, in some sense as we think about the previous recommendation around the assessment in public health, you know, family history would be part--you know, the collection and use of family history in the public health setting would be part of that assessment and, in fact, one of the exemplar programs that could be targeted

would be the use of the Surgeon General's tool to inform the competence--the need-based competencies.

DR. McGRATH: That's what I was getting at. So I could see that this could be integrated into the previous slide with a little bit of careful language and I can see that, and I was just explaining--I mean it does stand out and it stands out because it was written in 2010 right after the State-of-the-Science and all kinds of things. So it may look really dated in five years because why did it rise up when GWAS didn't or something. So I wouldn't be opposed to integrating it with the other.

Vince?

DR. BONHAM: So should it be integrated into the text and not be a specific separate recommendation?

DR. McGRATH: Well, I was thinking we could integrate some of this in the text of the previous recommendations like, you know, we're trying to get away from parentheses but somehow insert the word "family history" and various things, including in the consumer one because the next slide is all about consumers.

Do we--it's going to lose its "oomph" if

we do that. Right now it's kind of saying there is this great--just as you were saying family history is a group portal for all kinds of things, patient education, health promotion so we kind of lose that little "oomph" by integrating it.

DR. WILLIAMS: I would not want to lose in our articulated recommendations the call from this committee to continually present the idea that we need to have electronic health records that can consume and use this information, family history, genetic, genomic, whatever we want. You know, I think that needs to be a continual message from this committee, at least continual up until the end of tomorrow, from this committee to the Secretary to say this is really important stuff and our electronic health records don't do this right now.

I'm also--

DR. McGRATH: We have to tie it into educational because the report is on education.

DR. WILLIAMS: Well, and that's why point of care education--which is by the way in my opinion going to be the only way we're ever going to fix this. You've heard me say that any number of times. All of our traditional educational things will not scale for this. It's just not going to happen. So

if we somehow miss the opportunity to build it into electronic health records going forward we're never going to get anywhere. Again that's my personal opinion on this issue.

The other thing that I would like to somehow salvage--and I don't know if this becomes a recommendation that's more focused around electronic and personal health records but the whole idea that we can actually embed education within personal health records and things that people are using to enter their own information, whether it's around family history or tests or whatever, you know, to teach them at the point that they're interested in entering information about what it is that they're entering that's--those are the things that I would like to somehow salvage out of this into a recommendation.

CHAIRMAN TEUTSCH: You've actually got public health in the (C)(3).

DR. McGRATH: There you go.

CHAIRMAN TEUTSCH: So I guess my suggestion would be to keep this clean in (A) just get rid of "for health care professionals" and then it's just HHS should deal with all those issues. And then you don't have to say "for consumers." You

can say it should also do those other things.

DR. McGRATH: Okay. So get rid of that and you get rid of the whole bullet (B). Yes, get rid of (B)? Okay.

So look at four, Marc. Are you--do you want to add any strength to that one?

DR. WILLIAMS: So maybe just to say "promote embedding educational materials in family history collection tools and personal health records."

DR. McGRATH: This is a sorry looking bunch of looking faces I've got to tell you. You guys need lunch.

(Laughter.)

Okay. How are we feeling about that? So we're going to leave in family history and they will say, 'Oh! That was back in the day, 2010.'

I'll take your vote.

CHAIRMAN TEUTSCH: Are we good with this one?

DR. : Yes.

CHAIRMAN TEUTSCH: Yes, yes, yes.

DR. McGRATH: All right, cool.

CHAIRMAN TEUTSCH: Okay.

DR. McGRATH: So let's--do we even need to

talk about this last thing?

CHAIRMAN TEUTSCH: Well, I think we should at least go--why don't you quickly go through that and this is going in the preamble, right, or in the cover letter?

DR. McGRATH: Oh, no, the cover letter, "Dear Secretary."

CHAIRMAN TEUTSCH: Okay. Why don't you walk us through this?

DR. McGRATH: So this would be--when you convey the report--and I don't know if it would be repeated again, Sarah, in the executive summary. These are the finer points I don't know.

CHAIRMAN TEUTSCH: Well, does the letter have the Secretary appear in the report? So it would--

DR. McGRATH: Okay. So the entire--

DR. McGRATH: Okay. But we can refer to the sun-setting of the committee.

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: Well, but we could say since, you know, the committee will--you know, it normally takes a great deal of interest in monitoring, since we're not here--

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: We have to say it nicely.

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: In the letter.

DR. McGRATH: So the three points are track the implementation of the recommendation, establish--maybe the order might be--it might be we're changing the order. Anyway the second one is establishing metrics to measure the success of training programs that are--that came out of this report. And a third one is to do a five year look back.

David?

DR. DALE: I would suggest a little stronger language in the first phrase. "Consider involving." I think it's work with other federal agencies.

DR. McGRATH: Oh, I see on the very top.

DR. DALE: Yes.

DR. McGRATH: Work with other federal agencies or collaborate with or--

DR. DALE: Well--

DR. McGRATH: --you want work?

DR. DALE: I don't like the word "consider." I'd be more directive.

DR. McGRATH: Doe the order make sense or do you think one and two should flow?

DR. DALE: I would use the word--not to track the implementation but to “implement the recommendations.”

DR. McGRATH: Well, except some of them it’s not HHS to implement--

DR. DALE: Well--

DR. McGRATH: Well, I guess they all do say “HHS should.”

DR. DALE: They all have--

DR. McGRATH: Yes, all right.

DR. FERREIRA-GONZALEZ: We are saying that “the committee recommends that the Secretary work with other federal agencies” but some of those are under the purview of the Secretary like CDC, NIH.

DR. DALE: Right.

CHAIRMAN TEUTSCH: With HHS and the agencies, right? The only one that isn’t I think is the one that refers to DOE and Education and NSF.

DR. McGRATH: They went with “HHS and other agencies.”

Well, is it “work with HHS agencies” or “federal agencies?”

CHAIRMAN TEUTSCH: We can work on the wordsmithing because this will be in the cover letter.

DR. McGRATH: All right. Yes, okay.

CHAIRMAN TEUTSCH: The question I have on the first one, the one that says “implement,” that’s what the recommendations actually say, right? The recommendations are to implement. One seems a little redundant that we’re going to ask her to sort of monitor the implementation, right, which is the metric--

DR. McGRATH: That’s right.

CHAIRMAN TEUTSCH: --that we want to get at. So my inclination is to get rid of the first one because that’s just reiterating the recommendation, right?

DR. McGRATH: But then it’s not just establish metrics but then the first--the original language had something and “monitor.”

CHAIRMAN TEUTSCH: Right. I think--

DR. McGRATH: So we need that in there, not just--

CHAIRMAN TEUTSCH: “Monitor the implementation to establish metrics--“

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: "--to assess the success of the…"

DR. McGRATH: That's it. "Monitor the implementation."

MS. DARIEN: Then if you change it to "works with" then it would have to say "to" as opposed to "with." If you consider involving--so "the Secretary will work with" to "track" to "establish to reassess." I mean there has to be more direct language, you know gerunds.

DR. McGRATH: Okay.

CHAIRMAN TEUTSCH: Okay.

DR. DALE: Could you combine one and two?

DR. McGRATH: Yes, we just did. We just have to get rid of that number.

DR. : Oh, okay.

DR. DALE: Not quite.

CHAIRMAN TEUTSCH: So anything else on this in the cover letter? I'm less worried about getting the words exactly right there than I am on the--

DR. McGRATH: We'll fix the grammar. The grammar is off a bit. Okay.

CHAIRMAN TEUTSCH: So everybody okay with this? All right.

So, Barbara, this is great and a lot of work. I think we have tightened things up substantially--

DR. McGRATH: Yes, very good.

CHAIRMAN TEUTSCH: --which is always a good thing. Complexity is not one of the things I deal with very well.

But if you and Symma and whoever else you can round up on the task force could take care of this and give us not necessarily this particular one but--so we can see a recommendation--a set of recommendations with all the changes incorporated and then we can take a final vote on it tomorrow.

I didn't see any dissent from anyone on any of these recommendations so I assume once we get the language right we're good.

Does anybody have any other issues or thinks we're missing something?

Taking that as a measure of hunger!

Thank you, Barbara. I know this process is always surprising in terms of what we come up with but I do think this is leading to a tighter set of recommendations so congratulations.

Thank you and the task force for a lot of work. This will be our final formal report.

Jim is going to say something.

DR. EVANS: I was just going to say that my hat is off to you, Barbara, because this was a really difficult specific committee or subcommittee because not that it was controversial as some have been but because it was so broad, right?

DR. McGRATH: Yes.

DR. EVANS: So my hat is off to you.

DR. McGRATH: Thank you very much.

Thanks, Symma, for helping with this. I never could have done that.

I like the recommendations much better so thank you all for helping me.

CHAIRMAN TEUTSCH: Great.

So thanks again, Barbara, to you and your entire task force.

So we have earned our lunch and we have until 1:30 so we get an extra five minutes for which I expect you'll be eternally grateful.

Lunch can be obtained in the cafeteria which, I understand, is on the first floor in the A Wing. Is it going to be obvious?

MS. CARR: It is all the way down.

CHAIRMAN TEUTSCH: Can someone going to-- can someone walk a group down and lead us?

DR. : Yes.

CHAIRMAN TEUTSCH: It's pretty obvious. Okay. Those who have been there more recently than I have can say.

We'll reconvene at 1:30.

Thank you all.

(Whereupon, at 12:23 p.m., a lunch break was taken.)

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

IMPLICATIONS OF AFFORDABLE WHOLE-GENOME SEQUENCING

SESSION ON THE IMPLICATIONS OF AFFORDABLE WHOLE-GENOME SEQUENCING (WGS)

CHAIRMAN TEUTSCH: Tomorrow afternoon is reserved for us to try and get our letter finalized for the Secretary. In order to do that we need a quorum and I understand that not everybody will be here the full time so I need to find out who will be here.

It is our last chance to make things happen. If we don't do it tomorrow it isn't going to happen so we have to compress things in a very different way.

Can people--how many people are going to be here until the end tomorrow?

(Show of hands.)

One, two, three, four, five, six, seven, eight, nine.

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: What? Oh, I'm sorry. Of the committee members, how many? Sorry, one more time.

(Show of hands.)

One, two, three, four, five, six, seven. Oh, eight.

Sheila, you're here, right?

DR. : Yes.

CHAIRMAN TEUTSCH: Sheila is here.

We'll check with David and if he's going to be here.

Janice, are you going to be here until the end tomorrow?

DR. : Yes.

CHAIRMAN TEUTSCH: Good. Okay. So we'll have about eight. Anymore? Nine. So that's nine, right? We've got--one more time. We are not being able to get all the way up to ten.

One, two, three, four, five, six, seven, eight, nine, okay. So my understanding is a quorum is nine people. So I regret for those of you who can't stay that you probably won't have a chance to

vote on these things because we won't be taking votes. We will just be doing wordsmith kinds of corrections after tomorrow.

So thanks for everybody who can stay. I guess we'll find out from Jim and David if they are going to be here, too.

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: Jim is not but David will be I hope.

So, David? David, that's you. Are you planning to be here all day tomorrow?

DR. DALE: Yes.

CHAIRMAN TEUTSCH: Wonderful. Okay.

DR. DALE: And tomorrow night, too.

CHAIRMAN TEUTSCH: And tomorrow night. I can't promise you a very good night but I can promise you that we need you tomorrow afternoon.

So thanks, everyone. That's great so at least we can get our business accomplished.

So this afternoon we have a challenge and that is not only to do a lot of absorbing of more of the information on the whole genome sequencing topic but we've asked Charis and Paul also to help us figure out what we want to say to the Secretary on this topic. So, as always, I think we had a

tremendous session last time with lots of good discussion and learning, and look forward to more of the same.

So, Charis and Paul, you're on.

DR. ENG: Thank you, Steve.

May I suggest cloning to reach a quorum?

CHAIRMAN TEUTSCH: We can't hear you, Charis. Is your mike on?

DR. ENG: Yes.

CHAIRMAN TEUTSCH: Try again.

DR. ENG: All right.

Is that all right for volume now?

CHAIRMAN TEUTSCH: We don't want to miss a single word. Charis, it may be better to use one of the table mikes and you can use the--they're going to try it.

DR. ENG: Should I use both because sometimes it will echo off each other.

CHAIRMAN TEUTSCH: It's better now.

DR. ENG: It's not echoing. Okay. All right.

Here we go. I'm sure you'll give a yell. You're not very shy.

(Slide.)

OVERVIEW OF SESSION

CHARIS ENG, M.D., PH.D., SACGHS

PAUL BILLINGS, M.D., PH.D., SACGHS

DR. ENG: So just by way of background for everyone in December of ’08 during the priority setting process implications of affordable whole genome sequencing was included in the priority area for genetics and the future of our health care system.

In February of this year, moving very quickly, SACGHS identified topics for an exploratory session on the implications of WGS.

In June, three months ago, we had an initial exploratory workshop that examined the quality and management of WGS data, ELSI issues, and the impact of WGS data on clinical practice and the economics of health care; the committee therefore decided to form a task force.

And here we are in the last month, very quickly, the task force assisted in identifying topics and speakers for the October SACGHS meeting, which is now.

(Slide.)

So since this is our second and last time meeting in person, acknowledge the quite a bit that

our little taskforce has accomplished. My friend Paul and I, of course, co-chair this; Janice, Gwen, Jim, Andrea, Sam, and Charmaine; our ex officios are Muin and Jonathan; and our ad hoc members were Ellen, Emily, Martin and Cliff. Of course, we couldn't do this without Cathy and, in fact, we were quite delighted that she came back to help us in this process.

(Slide.)

So the current session goals to date are to learn about the practical, and I mean practical, implications of WGS from the laboratory and clinical perspective; what do we need done. And the two speakers we'll hear will address these.

We will then identify the issues and needs in this topic area that should be brought to the Secretary's attention and come to a consensus on any guidance or recommendations that would address these needs.

(Slide.)

So the speakers were asked to speak for 15 minutes each and there will be a five minute question and answer for each speaker, and then a committee discussion of 75 minutes to probe the practical implications of WGS in the lab and clinic,

and finally--hopefully finally--come to a consensus on guidance and/or our recommendations for the Secretary.

(Slide.)

So without further ado my friend Paul will introduce Karl.

DR. BILLINGS: So our first speaker is--it's a great pleasure to introduce Paul Voelkerding.

Karl is the--leads--is the medical director of the Advanced Technologies Group at ARUP Laboratories and is the past-president of the Association for Molecular Pathology. He is certified as a pathologist in clinical pathology and also as a molecular genetics pathologist from the American Board of Medical Genetics. His current research interests include the development of accessible new technologies in molecular diagnostics for the medical community and our binders have a very nice paper from him on some of the aspects related to whole genome sequencing and genome sequencing.

So, Karl, you're on.

WGS FROM THE LABORATORY PERSPECTIVE

KARL VOELKERDING, M.D., MEDICAL DIRECTOR, ADVANCED TECHNOLOGY AND BIOINFORMATICS

DR. VOELKERDING: Okay. Can everyone hear me, hopefully, in the back? I'll stand near this microphone.

(Slide.)

Well, first, it's certainly an honor to be here and present. I was challenged by trying to present in 15 minutes because each--almost each slide could be a seminar into and of itself but what I wanted to tell you today was sort of a landscape of what is going on within clinical laboratory medicine with respect to the beginning and the use of high throughput next generation sequencing technologies and to kind of paint a landscape, and what are the questions we need to address to accommodate this ongoing development work throughout the United States.

(Slide.)

So the outline of the talk will--I'd like to talk to you a little bit about the progression of what's going on with next generation sequencing, why it's such a technical moving target and will be for some time in the future, and then what we need going forward.

(Slide.)

So essentially the progression that's ongoing is there's ongoing development looking at using this technology for multi-gene panels, whole exome work and whole genome with an accompanying increasing complexity.

(Slide.)

So let's take a moment to look at multi-gene panels. The essence of this is really when you want to examine multiple genes that have a mutational spectrum that lead to a clinical phenotypic overlap. So going in with testing on the patient you're not certain which gene of several could potentially be implicated.

If you look at the kind of areas where this is being developed they include the areas of inherited cardiomyopathies where you'll have anywhere from 10 to 30 different genes, mitochondrial disorders where you want to sequence not only the mitochondrial genome but a whole host of nuclear genes whose protein products interact with the mitochondria and are essential for its function. And, for example, X-linked mental retardation where as many as 95 or more genes on the X chromosome need to be examined and sequenced for a comprehensive diagnostic.

(Slide.)

So if we look at a snapshot of diagnostic development around the country in terms of individuals that I know that are actively working in this area, not only our work at ARUP but a host of other very distinguished universities, laboratories and private concerns whose focus is on diagnostics, and down here the National Center for Genome Research in Santa Fe has been working very diligently on developing a several hundred gene panel to screen for rare autosomal recessive disorders. And there are likely others. This was just sort of a snapshot if you will.

(Slide.)

And so you have scenarios like this work from our laboratory where we're looking in this case at a particular Actin gene involved in hypertrophic cardiomyopathy and looking at a couple of different sequencing technologies, reading out sequence reads and confirming them with Sanger technology. So this type of work is certainly ongoing and is already pressing the envelope of how we're going to do this in the laboratory and perform interpretation.

(Slide.)

So human exome work, which I refer to as

journey to the center of the genome, we're essentially looking at about one percent of the genome that is really coding for protein. So about 20 to 21,000 different genes. And these genes so far to our knowledge harbor the majority of mutations that would constitute Mendelian disorders. And this has been coming out more and more in a variety of journals over the last year, one to two years, using sequencing of the human exome for gene discovery and now moving towards diagnostics in probands and also in kindreds. Our own work in this area is looking at gene discovery in the area of common variable immune deficiency.

(Slide.)

And so an example of data from our laboratory is on the one hand we're looking again at a tropomyosin gene involved in hypertrophic cardiomyopathy as a model looking at a variant identified using a gene panel, targeted gene enrichment approach, or alternatively where you've selected for the gene with a whole exome and essentially also developing confirmatory results with Sanger. So, in essence, you can utilize a gene panel. You could utilize an exome capture technique or alternatively you could use a whole genome

sequencing approach to derive the same information.

(Slide.)

So if we look at some of the groups working with exome moving towards diagnostics, not only our group but a couple of other groups that many of you are probably aware of, and certainly a tremendous amount of work with exome sequencing in the basic science community.

(Slide.)

And so whole genome work that you'll hear more about from Dr. Dimmock following me in terms of applying this for diagnostics in specified medical conditions where other testing has not led you to the diagnostic answer. Prognosis, I think we'll see this used more and more in the area of--prognosis in the area of tumor biology. And I think the area that is most challenging, because our knowledge base is the most limited, is how we will use this type of technology for prediction in terms of otherwise--where we don't have a specific medical symptom and condition that we're addressing.

(Slide.)

So if we look at a snapshot of groups working in the space of genome work--Dr. Dimmock will talk about their work at the Medical College of

Wisconsin and Children's Hospital but a couple of other groups to bring to your attention.

(Slide.)

I think the question for all of us from a laboratory standpoint is we're now sitting at this juncture here at 2010 with about $10,000 in reagents or slightly less to sequence a genome and I think I'm being perhaps a little conservative here by saying that by 2015 we'll certainly be at $5,000 or significantly less than that and we'll see how that sort of unfolds over the next two to three years in terms of the cost. This is primarily reagent costs. It doesn't factor in the considerable amount of cost that's going to be required from the standpoint of processing the data and interpreting the data.

(Slide.)

So will whole genome sequencing supplant gene panels and exomes?

DR. GREEN: Do you want to give an estimate of what you think today a whole exome cost compared to whole genome here?

DR. VOELKERDING: A whole exome cost is probably in the neighborhood of right now about $2,500-3,000 all things wrapped up.

DR. GREEN: For reagent costs?

DR. VOELKERDING: Reagent cost, yes, and that's actually coming down more and more, quite frankly.

(Slide.)

So what we have is a technical moving target. So with gene panels you would take your genomic DNA, enrich for the target genes, prepare your library for sequencing, perform sequencing, bioinformatics and interpretation. Your target genes could be the entire exome. When we move to whole genome sequencing essentially you won't perform that enrichment methodology.

(Slide.)

But here are some of the challenges for laboratories. There are two different major flavors of the gene enrichment methods for either amplification based for gene panels. Array based is what you need to use for capturing the exome. So however you get there you need your enriched genes and then you're going to perform your sequencing. This is actually a lot of technical complexity for laboratories.

(Slide.)

The other technical moving target is the sequencers that are available. The first wave of

sequencers have now been followed by the same groups developing both higher and lower throughput versions of their technology and right now the Illumina technology and the Life Technologies technology are the dominant technologies being used for exome and whole genome sequencing. We have a second wave of technologies that have come on or coming that are available to us now based more on single molecule sequencing. There's a third wave of technologies that's coming along. And also there's a fourth wave of technology that will be based on physical methods of essentially threading DNA through nanopores and that's probably, you know, in the realm of five to eight years out in terms of realistically seeing those technologies coming along commercially, which may ultimately substantially drive down the cost of whole genome sequencing.

(Slide.)

So what we're all transitioning into is a bioinformatic world that's also a technical moving target because there's many different algorithms, alignment methods, assembly methods. There is software now that's available both commercially and academically; a laundry list thereof. The computational power and storage is considerable to

perform these types of analyses. This actually draws a question of how each institution will handle their computational needs and storage. And if we're storing large databases or large datasets offsite from the institution where they are generated there are certainly germane issues related to patient privacy and HIPAA compliance.

Diagnostic databases and interpretation: This is where the lion's share of everything will come forward. The technology will get easier but the interpretation is just escalating in terms of the amount of cognition that's going to be required to analyze this type of laboratory testing. So we have this amazing convergence of chemistry and bioinformatics, and I personally weighted this because this is where we spend increasingly large amounts of our time.

So there's a large cognitive component and so I think this really is a new realm for all of us in laboratory medicine and in medical genetics in terms of the amount of time and effort that will be required to produce meaningful results at the whole genome scale.

(Slide.)

So what do we need going forward? A few

final slides.

(Slide.)

First, though, I'd like to say we need a historical perspective and we need to foster innovation. I think there's a lot of concern about whole genome sequencing. It is both a technology and a medical utility in terms of an opportunity but it is a new technology but so were PCR and so were arrays. So good scientists, bright scientists and physicians and scientists will work through these technologies.

Expand education and training: I know there was a session this morning focused on that. The medical profession is definitely on a learning curve so we're going to need to start at the basic building blocks of medical student education and internship, residency, fellowships to essentially generate a new generation, if you will, educate a new generation of individuals that will be able to address this type of complexity of information.

(Slide.)

We need to develop technical standards and guidelines, and I'd like to put in here also professional guidelines and I think what we need to do is to leverage the existing infrastructure within

professional organizations and there are certainly a lot of grassroots efforts starting to move in this area.

But perhaps one of the most key issues is the interpretive component of this. When we have a list of variants or insertions and deletions what do we do with that information and right now we don't have the type of databases genome-wide that are necessary for interpretation that we ultimately need. There are many individual databases that are gene specific but they only represent a couple hundred and what we need is a database that essentially examines all 20 to 21,000 different genes of our genome. So we'll need to coalesce existing databases, build new databases, and integrate new basic science knowledge into these databases on an ongoing basis.

(Slide.)

And I think we need to promote appropriate medical use. Whole genome sequencing at its core essence is a laboratory test ultimately and, like many laboratory tests, they can be ordered appropriately or not appropriately and, therefore, there's going to be need for oversight in terms of professional oversight of appropriateness of the use

of this laboratory-based test.

And that means we need to understand our limitations in knowledge at any given point in time. And we have to address how this information is going to be used. Who will have access to it? Will patients have access to it? What information will they have access to and the portability therein of that information? So we need to incorporate it into the very active and ongoing evolving electronic health record.

(Slide.)

And with that I'll stop and leave you a quote, one of my favorite quotes, and take questions.

Sorry for the whirlwind but that's the task I was given.

Yes?

DR. GREEN: Actually I think you did a very nice job. I mean you had a lot of ground to cover, I realize, and I thought it was very well summarized.

One question I had is do you think gene panels are going to be relevant very much longer because it would seem to me the cost of doing any sort of a gene panel is going to quickly become

roughly the cost of just doing a whole exome and is there really anything you're learning in the gene panel you're not learning in the whole exome?

DR. VOELKERDING: Yes, I would say that if you look at--because I've been doing a lot of test cost analysis within our own institution so if you look at a gene panel of 30 to 100 genes and you're going to sequence that you're looking at direct costs. If you include laboratory labor you're looking at direct costs in the neighborhood of around $1,500.

DR. GREEN: So that must be by Sanger sequencing then, right?

DR. VOELKERDING: No, this would be based on one of the high throughput sequencing instruments. That's for a single patient sample that's non-barcoded.

DR. GREEN: Isn't it incredibly inefficient to analyze such a small target with any of these next gen platforms for one patient or are you barcoding? I mean you must be doing some trick there.

DR. VOELKERDING: Yes. If you drive--you can drive the cost down by barcoding.

DR. GREEN: Okay.

DR. VOELKERDING: But where you're--where a lot of your upfront cost is in this enrichment technology. You have to enrich your panel of 50 to 100 genes.

DR. GREEN: Right.

DR. VOELKERDING: And all of the current enrichment technologies are quite expensive so although you can leverage barcoding to really drive down your sequencing cost you still have the labor and the cost of doing the enrichment.

DR. GREEN: Which is why I thought it would be far more efficient just to go right to the whole exome figuring that next month there will be more--the gene panel will grow and the month after the gene panel grows. So I'm just surprised people are still investing even their thoughts in gene panels anymore when it would seem to me you would just go right to whole exome at this point.

DR. VOELKERDING: Yes. And it turns out though that to do a whole exome you have to do enrichment. It's just that you're enriching for essentially all the genes so you have a lot of costs built into the enrichment process whether it's a 50 gene panel or whether it's the entire exome.

DR. GREEN: That was my point.

DR. VOELKERDING: Yes.

DR. GREEN: That's why I'm surprised. I was just thinking we must be getting really close so it's not even worth thinking about 50 or 100 genes anymore, just do the whole exome.

DR. VOELKERDING: You know, I think that that's certainly a strategy that we're considering. And then essentially you ask the question, well, I've sequenced the entire exome but all I'm looking at clinically is an individual with an enlarged left ventricle with a family history and I'm trying to look at their cardio--at the genes associated with cardiomyopathy. So what you do is you basically mask the non-relevant genes.

DR. GREEN: But haven't clinical chemists been doing that for years?

DR. VOELKERDING: Yes. So there should be no barrier to masking non-relevant genes if your technology brings you all the genes to the table.

DR. GREEN: Plus I would think that the logic there is that what you are setting yourself up for is a day where you're not going to just be looking at cardiomyopathy, that you'll have the technical capability when there's dozens and hundreds of other conditions that you'll be looking

for at the same time.

DR. VOELKERDING: Yes, I think it begs the question of the box that I showed about prediction.

So you may have a specific medical question that you're seeing your patient for but if the technology has all this other, shall we say, information associated with it that it has brought through the testing modality as we understand that and it makes medical sense to look at those sorts of potential genomic risks that have a significant enough odds ratio to make sense, and an intervention associated with it, then you're absolutely right. It will kind of--I think it will unfold over time in that direction.

DR. WILLIAMS: So a couple of points. One is given your quote I would question whether your musical interlude was actually accidental or not but I'll let that pass but the analogy to the clinical chemist issue raises a couple of questions in terms of exome versus gene panel.

One is there may be an equivalent of a critical value that occurs in exome sequencing and I was trying to think of one but thinking maybe like a Huntington expansion or something like that.

You detect something in your exome

sequencing that is critically important and is perhaps actionable much as if you ran a Chem-20 and they were only interested in electrolytes but you actually had a calcium of 15 you would contact the provider and say, “We have a critical value in a test that you really didn’t order but you need to know about it.” That would be an issue that labs, I would think, are going to have to struggle with.

The second, though, that is not analogous to the Chem panel is the idea that you now have information that if it’s at a high enough reliability it is enduring. You know, your chloride is going to change from day-to-day but your exome presumably isn’t. So if I, as a clinician, wanted to order another genetic test at some point in the future and you’ve already done the whole exome then isn’t it really--wouldn’t it be more efficient for me to say, ‘Hey, I know you did the whole exome and now I want results on these genes,’ and expect that to be done at a fraction of the initial test cost?

DR. VOELKERDING: Absolutely. It really poses the question of reinterpretation of any gene panel, any laboratory test, the exome, the genome, where you revisit it because something else has come forward in the medical record of a patient’s

symptoms.

My hope is that this--this issue of a critical value, you know, my hope would be that the ordering physician and the laboratory would work together to have a really thorough medical history, family history. So that some of these issues might be a priori potentially known so you may have a certain medical condition you're testing for but you want to have a very good thorough family history to help guide, I think.

And, also, I think the question becomes if you see something--if you're masking you're basically not looking for that information from a laboratory standpoint. So I think these have to be understood going in, what's the test, how is it done and whether or not you're masking for certain information.

DR. FERREIRA-GONZALEZ: I think this is a critical issue for the laboratories where you have genetic information that the clinician did not request and you're holding that even though you masked it and you still have it. It is affecting not only that individual but the family of that individual, too.

But the other issue that I think is

important is that as you have this information that is masked maybe to the laboratory, as new information comes about how do we match the masked information that we're not providing because it was not ordered with the new knowledge, whose responsibility is this? And then who holds that information? Is it the laboratory that then--so we need to look at these new paradigms and how we are actually going to practice.

DR. WILLIAMS: Yes, I mean I am thinking--you know, as we were talking I was thinking of a better example. I mean if you had a mutation in a tumor suppressor that was de novo, you know, family history is not going to help you but now you have actionable information. Let's say it was, you know, a mismatch repair gene that you have, you know, a nonsense mutation in MLH-1 that you've detected.

What would be the liability to the laboratory? Because you did the whole exome you know at least in some sense of knowledge that there is--that this is--it's clinically actionable because it would alter surveillance for that individual. You know, we can't rely on family history in a situation like that because even in families with these mutations only about 50 percent of them will

have a family history that would flag as at risk.

This is a real--it's a thorny issue that will require a lot of thought and were this committee to be continuing it would be great grist for discussion.

DR. EVANS: So the other thing I would just bring up is that there is precedent in how to deal with masked information, et cetera. The other thing that there is less precedence for will be in another entire subset of results which would be results you might term sensitive.

In other words, there are things that will come out of a whole exome or whole genome sequence that some people might want to know and some people might very much not want to know.

For example, ApoE status would be one of those things. And we are going to have to grapple in some way with how to deal with that information and how to involve now the patient in a way that patients haven't typically been involved in laboratory tests, and that's going to be very challenging.

DR. FERREIRA-GONZALEZ: But some of the issues are the same as this is going to be a clinical laboratory test. So a clinical laboratory

test will have to follow the same issues that we have, clinical validity, clinical utility and so forth. The magnitude of the question might be bigger but, you know, we already have an infrastructure--

DR. EVANS: Yes.

DR. FERREIRA-GONZALEZ: --we need to continue to leverage and there might be new questions but there are not--

DR. EVANS: Well, I would argue that some of the questions really are qualitatively different. It's one thing to make the very reasonable assumption that most people are going to want to know about whether they have an MSH2 mutation. Okay.

It's another thing to grapple with the issue of who wants to know about ApoE status, their Huntington's status for that matter. I mean--well, 20 percent of people demonstrably who are at risk for Huntington's don't want to know their status.

DR. FERREIRA-GONZALEZ: (Not at microphone.)

DR. EVANS: (Not at microphone.)

DR. WILLIAMS: There is really a more interesting philosophic question here which really

is, is ultimately the economies of scale going to drive the questions so that we're going to have to deal with these? Because it's really changing the paradigm of how we do--because even if--you know, to really break the clinical chemistry metaphor, I mean there we're still only doing 20--a Chem-20 to maybe get four results, and we save a few pennies per test on that. You know, are we going to--are the economies of scale going to drive this to the point that we're going to open up all of these questions that are going to be extraordinarily difficult to grapple with?

DR. DALE: For exome sequencing, has it progressed to the stage where it does not require confirmatory sequencing if it's used as a diagnostic test? Where are the regulations in that regard?

DR. VOELKERDING: So I'm going to give you one person's opinion but this technology at this juncture--all of these high throughput technologies at this juncture for any variant that would be referred to as a pathologic variant of significance in my humble estimation should undergo confirmatory Sanger sequencing and should do so for some foreseeable future until we have a much better understanding of the reproducibility and accuracy of

these technologies; notwithstanding that some of my colleagues in the commercial industries that are bringing this technology forward for us to use.

DR. DALE: Can I ask one other question about the workforce for doing this?

DR. VOELKERDING: Yes.

DR. DALE: You listed a few institutions. Do you envision that this is going to be done in a few centers in the U.S. or the world or that it will be disseminated given the amount of technical expertise to interpret the data?

DR. VOELKERDING: I think it will, you know, be first established. If you look at the groups that have--that are establishing it they are either large reference laboratories or they are university-based laboratories or they are private companies whose forte is sequencing technology. So the question is how disseminated it will become and how widespread.

I think we'll follow--there are two things. The technology can make it--potentially make it more disseminated and I think that will happen but the clinical expertise to interpret the information, to package it and to provide it back to patients in a meaningful way will be a significant

bottleneck. So I think we're only looking at the beginning of this landscape and it will take a number of years, I think, to play out.

DR. MANSFIELD: I was just going to respond to David's question about confirmatory sequencing.

I have been digging into this area of whole genome sequencing and working with the Archon X Prize people for the 100 Genomes Project. And in doing that I have learned that many platforms all have different types of errors and different error rates and that the only way anybody agrees now that you can actually validate something is by Sanger sequencing, which by the way has--

DR. : An error rate.

DR. MANSFIELD: Yes, its own error rates. So I think there is--it's--care should be taken right now as people move into this area. They should also understand that many of these interpretations are based on comparison to the reference sequence which is not the correct sequence. It is a sequence of which there are uncountable variants of pathologic or non-pathologic significance.

DR. ENG: Thank you.

DR. VOELKERDING: So I wanted to again thank the committee. Unfortunately, I'll need to leave fairly shortly to catch a plane out at National airport so thank you again for the invitation to present.

DR. ENG: We're delighted.

(Applause.)

Hopefully, there will be no more burning questions.

We are delighted to have David Dimmock.

He is an assistant professor of pediatrics and genetics at Medical College of Wisconsin and at Children's Hospital. He received his MBBS at St. George's Hospital Medical School, otherwise known formerly as George's in London. He did his pediatric residency in St. Jo's in Phoenix, Arizona, and then moved on to Baylor for his clinical and research fellowship in genetics. He moved to Wisconsin three years ago and is a physician-scientist at the bench and bedside. He studies biochemical and metabolic genetic disorders and whole genome sequencing.

So, David, thank you.

WGS FROM THE CLINIC PERSPECTIVE

DAVID DIMMOCK, M.D., ASSISTANT PROFESSOR,

DEPARTMENT OF PEDIATRICS, MEDICAL COLLEGE OF WISCONSIN

DR. DIMMOCK: So I will talk a little bit about how our use at our institution of whole genome sequencing. But I--it was very hard to do this divorced from the concept of patients in clinical care.

(Slide.)

So I want to start out by one of our--actually our first whole exome case that we did.

(Slide.)

I have no conflicts of interest, financial. But I do have an emotional conflict, which is actually we do care about the kids that we take care of and I hope you guys will see that this is actually really useful in taking care of kids.

(Slide.)

Historically, exome and whole genome sequencing has actually focused on celebrity individuals, individuals where there is a familial disease and collections of individuals with well defined disease. The most notably success recently was Kabuki Syndrome. But I would argue that for true clinical utility the technology must be applicable to a simplex case with an isolated

disease.

(Slide.)

So I want to tell you about a case. This is all with the parent's permission.

This was a male child who presented at 15 months of age with very poor weight gain and a perianal abscess. He had significant progression of his symptoms over a few months with very aggressive refractory inflammatory bowel disease. Pathological studies revealed focal granulation tissue with chronic active granulomatous inflammation consistent with severe Crohn's disease.

(Slide.)

Its clinical course was really very severe. In spite of very aggressive medical and immunomodulatory therapy his disease progressed with mucosal inflammation, strictures, enterocutaneous fistulae and poor cutaneous wound healing, ultimately requiring a total colectomy.

(Slide.)

By his fifth birthday this child had spent the majority of two-and-a-half years actually inpatient in hospital. He had a modestly abnormal immunological workup which showed abnormal anti-neutrophil antibodies with abnormal chemotaxis of

neutrophils, decreased NK cytotoxicity but no evidence of hemophagocytic lymphohistocytosis. He had memory skewing of his D4 cells and an inverted CD4 to CD8 ratio.

(Slide.)

We know that dysfunction have been associated with inflammatory bowel disease. There was a suggestion at least in the literature that in several forms of immune dysfunction the Crohn's-like picture may actually respond to immune reconstitution. This is a very risky procedure and not one that one would enter lightly.

(Slide.)

We felt really at the stage of this child's illness at about four-and-a-half years of age that we really were left with three options. We could continue his current treatment which was leaving him to be hospitalized most of the time. We could blindly attempt significantly risky therapy or we could see if we could obtain information to make a more informed choice. As you guys know because I'm here, we opted for the third choice.

(Slide.)

We used gene capture and this was an

exome-based sequencing on 454 technology. We got just over 16,000 high confidence variants. Because it was exome capture the majority of these were in genes. And over 15,000 of them had--were in protein coding regions. Seven--7,000 of these were non-synonymous changes and using several different bioinformatics pipelines. We were using two models. We had seen that this was a recessive disease and using one model of two hits to a gene we weren't able to find a disease causing mutation. During our analysis a new version of dbSNP came out and we were able to filter down from 878 very interesting variants all the way down to eight. I would point out that we actually analyzed the sequence on over 1,000 of these variants by hand. Of these eight that were novel, four of them altered a highly conserved amino acid. We searched 5,000 referenced genomes and we were left with two changes that were unique in 5,000 referenced genomes. One of these genes about 30 percent of the population carry a known mutation in so we were left with one choice.

(Slide.)

We confirmed it with Sanger sequencing.

(Slide.)

We then actually sent the whole genome

gene out to be independently confirmed because it was clinically available as a single Sanger test. The gene is associated with cancer predisposition. The treatment of which is a bone marrow transplant so we actually performed a bone marrow transplant on this child and have seen a dramatic improvement in the bowel condition. He is about 100 days out from bone marrow transplant now. He's going to be going home probably in the next week or two. His bowel disease has almost entirely resolved and he's now eating normal food, and he's basically a normal five-and-a-half year old.

(Slide.)

More details of this are available and will be published very shortly.

(Slide.)

But I think we have demonstrated in this individual case that genetic sequencing is a useful advance in DNA diagnostic testing and it can inform clinical decision making. And I want to emphasize the "inform" here. It is a lab test.

(Slide.)

Obviously we had one success and then we had a queue of people at our door saying, "My child next, my child next." And we have already had over

120 kids and certainly significant interest at our institution for whole genome sequencing right now.

(Slide.)

But we had very significant ethical concerns and I can't underestimate these. The most obvious one I think to everyone in this room is the fact that you might find things you're not looking for, things that are not pertinent to the question at hand. And we're talking about children here because we're based in Children's Hospital. This is not a new problem to us in genetics. I have seen patients with micro deletions, including RB1 cancer predisposition. This is a common problem but because of the extra information that we get with whole genome sequencing we expect this problem to arise more frequently.

(Slide.)

In addition, resources to analyze data and obtain consent are significantly limited in our institution as I think they are at most.

(Slide.)

The initial genome analysis took us about six months. It takes significantly less time now but we still have limits.

(Slide.)

So we spent a while trying to look at how to choose which cases to go forward and we wanted to be guided by several key principles. One of which was equity of access. The other was because there is a concern about the potential for harm with this approach. We think this should be reserved for individuals in whom the likelihood of success is high and that reasonable clinical testing has been exhausted and that molecular diagnosis has the potential to advance clinical decision making.

(Slide.)

In our institution we have a two step process. The first step is nomination and the second step is a review group.

(Slide.)

During the nomination phase two physicians with expertise in the disease area are required to determine that standard clinical assessments are being utilized, the whole genome sequencing is clinically warranted in the context of the management of the patient and their family, and the patient’s family is at least preliminarily interested in considering whole genome sequencing. They are then referred to genetics to initiate the consent process and then to our review group.

(Slide.)

Our review group is constituted of the hospital's chief medical officer as the chairman, three clinicians with an expertise in the area of interest who are not directly involved in the case, the chair of the hospital ethics committee. Because we have two institutions our medical college ethicist is involved as well. We have always one geneticist, one genetics expert and one genetic counselor.

(Slide.)

Typically in front of the review group the nominating physicians will present the case and the review group will determine what disease information is related to the clinical question. This will allow us to focus on genes of interest. They will ensure that appropriate clinical consent is obtained and ensure appropriate research protocol and consent are in place if information will be used for research as well as clinical care.

(Slide.)

To answer the other question, we require all DNA testing in our laboratories to be confirmed on a second extraction, preferably by a secondary technique. This is true of all DNA testing. When

you send cystic fibrosis testing and even when you send viral DNA testing typically second extractions are tested to confirm. We do not consider whole genome sequencing as a definitive or medically actionable result without secondary confirmation.

(Slide.)

We sought several ethical opinions both from within our institution and outside concerning consent for data return. We had several anxieties going in. One of our families has a very significant family history of breast cancer. One of the questions we had was could we sleep at night if we knew that the child had a breast cancer mutation which would affect perhaps the management of the mom or dad if we didn't tell them? Who should make that decision and who should give the results back?

The final opinion was that the return of all of the information, the genomic information, was morally permissible and such a decision as to what should be returned should remain at the discretion of informed parental choice. The opinion was that the parents were in the best position to decide what information should be returned to them if they were appropriately informed.

(Slide.)

As an institution we decided the parents should be preemptively asked what data they would like returned and this is part of our consent process. This is not a quick process. At our institution it typically takes six to nine hours of face-to-face time to obtain consent with typically additional multiple phone calls, and this is not reimbursed.

(Slide.)

So we use the categorical approach.

(Slide.)

We have taken the opinion that information actionable in childhood must be returned. There is a duty of care to confirm and act on these results, and basically there is no opt out for these results.

However, because we are typically looking for the focus of a single disease we don’t have an obligation to go hunting the genome for everything else. Although we do have the facility to search against, for instance, HGNB database, we don’t feel that there is an obligation on the testing group to actually do that.

(Slide.)

Actionable disease with adult onset can also include mutations in BRCA-1 and 2 and

hypercholesterolemia.

(Slide.)

And non-actionable disease with onset in adulthood examples would include Parkinson’s and Huntington’s.

(Slide.)

As I mentioned for the actionable disease with adult onset, there is an ethical or a moral choice to weigh against the child’s autonomy against the possibility of preventing disease in adulthood. And in genetics we typically review the family of the patient rather than the individual child.

(Slide.)

More controversial is perhaps the question about returning data, for instance, on Parkinson’s and Huntington’s. And the philosophy really behind even considering this--we recognize that this would inhibit or reduce the child’s autonomy going through in the future. But what is currently treatable today will possibly change in the future and many of our parents are at an age where they are considering further children and they may wish to find out this information to make choices of their own about further family planning.

So having whizzed through that, I

anticipate a lot of questions.

DR. ENG: Any questions or comments? I know Steve does.

CHAIRMAN TEUTSCH: Yes. This is fascinating to see how one works through these, hopefully, unusual rare serious disorders. The committee--we also worry and have been thinking a lot about how this relates to common disorders, particularly things in adulthood that are polygenic.

And I wonder if you could--and maybe if it's an unfair question just tell me. Do you all have practical experience with using this in common disorders where one then has to work through many of the complex issues about unrelated findings and other kinds of uses of the data and the implications for clinical care?

DR. DIMMOCK: So I think there are two questions there. Right now for whole genome sequencing we are focusing on rare or ultra rare disorders. So we estimate less than one in 10,000 population prevalence for a disease is the kind of standard for entry requirements because that really makes it more possible to get a result using the filtering techniques we use.

So to answer the question about whether or

not we are using whole genome sequencing for common disorders; no, we are not.

Do I have clinical experience of genetic testing for common disorders? Yes, that's bread and butter for me.

And population based screening? Yes.

Do I think this technology is ready for that today? No.

DR. BILLINGS: I was just curious. In the case that you presented, the first, which I guess is in publication, was there a sibling involved in that case?

DR. DIMMOCK: No.

DR. BILLINGS: And if the parents request prenatal diagnosis in another pregnancy, will you offer it?

DR. DIMMOCK: That is a more difficult question.

Am I confident enough in the diagnosis that I would be prepared to make significant decisions while we did a bone marrow transplant on this kid right in front of us which carries with it a significant risk of death--and that decision was not taken lightly. And we spent a lot of time talking about it. And we actually sent the child

out for a second opinion to another institution with the DNA test results and asked them what they would do blind to what we had already said, and they came to the same conclusion.

Am I confident that this is what is causing this child's disease? Yes. And we didn't have time to go through all the other complementary testing that we did.

We were in the fortunate situation that this gene was known to cause human disease. There was a lab that was offering the testing and so we could send it out as a DNA test and they came to the same conclusion, the testing lab did, that this was a pathogenic mutation.

Prenatal diagnostics comes into a whole moral issue about whether or not one approves of prenatal diagnostics and so I'm going to duck that question.

DR. DALE: I think you've raised some very important and interesting issues, particularly the issue about sharing results with parents or patients and families.

Do you have support from the NIH? Are you not required to follow the rules of the dbGAP that require that data be regarded as research and held

in confidence? Where is that interface now?

Maybe Eric wants to comment about it.

DR. GREEN: These are clinical tests; correct?

DR. DIMMOCK: Correct.

DR. GREEN: So I don't think it applies.

DR. DIMMOCK: This is a diagnostic test.

DR. GREEN: It's diagnostic. It's not research.

DR. DIMMOCK: This is not research.

DR. DALE: So the patient or some foundation has paid for the testing?

DR. DIMMOCK: Correct.

DR. DALE: So the discovery is made which is of a new gene but that's not research?

DR. DIMMOCK: Correct me if I'm wrong, Dr. Green. You can jump in when I get this wrong.

The difference between research and clinical primarily surrounds intent. So the intent in all of the cases that we have done, and some of them will never be published because we don't--the families don't want them published, is to take forwards the clinical decision making in the context of that family. It is not to generate secondary generalizable knowledge. Therefore, it is clinical

care. It is not research.

DR. GREEN: Isn't it also an issue of who is paying for it? I mean these are not being--this is not being funded. The payments for this are not from NIH grants; correct?

DR. DIMMOCK: Correct.

DR. GREEN: Yes. So NIH policy is not going to apply here. It's not NIH money.

DR. MANSFIELD: So I was just curious whether you have tested the parents for one.

And the other question--I'm not sure I understand where you said you asked the parents upfront what information they wanted back. If they had wanted back whether this child carried a BRCA-1 or 2 mutation, even though that wasn't relevant to the clinical issue, would you have given it back?

DR. DIMMOCK: So I think the issue is that the parents testing is a little difficult because of the consent issues we have with the family about discussing in public forum but certainly we have taken care of the family in a clinically appropriate manner.

You did hear me correctly, yes. In the situation where we have done appropriate upfront counseling and the parents have indicated that they

would want to know the information--this family wasn't the breast cancer family. That is a different family I was talking about. But if they were in a situation where they had told us that they wanted to know about a mutation that was relevant for adult onset disease, yes, we would tell them.

And, yes, we are aware of the implications for the child as are the family when we consent them.

But, yes, it is our intention if they request that information, we will return it to them.

But I would also add, as we've already said, we don't consider whole genome sequence data in and of itself to be clinically or medically actionable so we would not consider that data to be confirmed until a separate test had been done to confirm that mutation.

DR. WILLIAMS: So one of the things that was interesting in your criteria was that you had to have a high likelihood of success, which given the fantastically small number of people that this is going to apply to seems almost un-definable, could you articulate a little bit in your mind about what you would think would constitute a high likelihood of success?

What sort of characteristics and how confident are you that you've got the right set of characteristics?

DR. DIMMOCK: This is one of the beauties of having a case selection group that actually talks this stuff over.

I think from the point of view of where the bioinformatics is right now, the rarer the disease the higher the likelihood of success because--and really a recessive disease is easier to find than a dominant disease.

So if we're looking at a disease where we are looking at less than one in 10,000, we can use a filter and say, 'Well, if we don't see this variant in one percent of the population or--' sorry '--if we do see this variant in more than one percent of the local population, it's not relevant to being disease causing. And that's one of the ways we could filter so fast down to where we got with this child. It was by making that assumption that this disease was less than one in 10,000.

As you are probably aware, you know, Wisconsin is not special. There are--well, it is very special but not for these reasons.

(Laughter.)

So really what we're looking for in Wisconsin--we have about 70-75,000 births a year--is a disease that we see less frequently than about 10 times a year in the whole population of Wisconsin.

DR. WILLIAMS: But the assumption still is at some point you have to say this is--we think this is single gene.

DR. DIMMOCK: Yes.

DR. WILLIAMS: And that's the issue that is I find a little bit harder to grasp. What's the high likelihood that you're dealing with a genetic rare disorder as opposed to a rare disorder of things?

I mean one of the strangest presentations that I can recall in my career has been Munchausen by Proxy which aren't going to be detected by this methodology in all likelihood. So how do we--

DR. : (Not at microphone.)

(Laughter.)

DR. WILLIAMS: Only if we test the parents.

So the question is how do you decide that this is likely a single gene caused disorder?

DR. DIMMOCK: I think often there are characteristics of a disease or presentation

individuals within that specialty will recognize as being rare.

Munchausen by Proxy I would agree with you is actually probably about the hardest thing for a lot of the conditions we look at.

This child clearly had severe early onset Crohn's. All of the data pointed in that direction.

All of the other kids that we have done to date have had very clear lab test abnormalities that are well out of the range that we would expect.

Could I guarantee it's genetic rather than environmental? No, but nothing in life is guaranteed and I think it's reasonable to have a hypothesis.

I think even when one considers things like infectious etiologies clearly there are host factors that determine one kid getting hepatic failure with herpes whilst the next kid just kind of has nasal congestion. The same is true of influenza.

So I think even in situations where there's clearly an environmental component, if the presentation is extreme enough then there is probably a rare enough host factor that we can find it.

DR. NUSSBAUM: You have presented an extraordinarily compelling situation with a clinical intervention that made a difference and yet you've given us--you've inferred that there have been others, you know, that make the nomination process. I just wonder if you could share not only the broader experience--and I know you're not going to give examples because you don't have permission but not only at Wisconsin but as you look at other centers like yours that are in pediatric research environments, you know, how many children with extremely rare clinical courses have been looked at through whole exome sequencing?

And have there been 20 percent examples where you could then intervene in unique clinical ways to have an impact or is this so extraordinary a situation?

I wonder if you could share--if you know that or if you--I'm sure--I'm not sure. I suspect you've talked with many of your colleagues about this.

DR. DIMMOCK: There are two cases that I would be willing to talk about. One is this case. There is another case where we were able to make a diagnosis and the diagnosis was of a disorder that

is universally fatal with progressive involvement and the kid was--the discussion was about listing for liver transplant.

DR. NUSSBAUM: So two then. What do you think the denominator is? Is it a few hundred or a few thousand?

DR. DIMMOCK: No, I would say--so we have--most of our other cases we haven't completed yet because the analysis takes time.

DR. NUSSBAUM: But what about other centers? Do you have any knowledge of that?

DR. DIMMOCK: I honestly am aware of one center in Germany that has done one case and they have some preliminary answers that look promising but that has not been finished. I'm actually not aware of anyone else that has done this.

DR. WILLIAMS: I'm sorry. Could I direct a question to Eric if I may?

DR. GREEN: Only if I know the answer.

DR. WILLIAMS: Okay. Is this something that Bill's group is doing in terms of the evaluation of rare genetic disease?

DR. GREEN: Which Bill? Bill Gall?

DR. WILLIAMS: Yes.

DR. GREEN: Doing in terms of what? In

terms of--

DR. WILLIAMS: Are you considering this type of an approach for the evaluation of the rarest of the rare that that group is specifically--

DR. GREEN: A very, very large fraction increasingly of patients being evaluated by the Undiagnosed Diseases Program are--they are all being evaluated to infer whether or not it's likely to be genetic, and many of them are, and in a good subset of those we're doing whole exome sequencing. A couple of them are even doing whole genome sequences, absolutely.

DR. BILLINGS: What's the definition of genetic in that case?

DR. GREEN: Biomedical geneticist sort of, you know, best judgment.

(Simultaneous discussion.)

DR. BILLINGS: If it's a singleton can it be a genetic case?

DR. GREEN: Where they think that genome sequence data might give information but, you know, in those cases everything is a research project so even the definition is.

DR. EVANS: I mean that's a really important issue that we're only going to be able to

answer after we've done a bunch of these, right? I mean we can have some idea.

One of the most useful that we're using is family history. Now the problem with that is that you're oftentimes in dominant diseases, right, and that has its own peculiarities.

Another example would be mitochondrial disorders. There are certain hallmarks that kind of scream mitochondrial disease to us but our ability to diagnose those is very meager and this is the kind of approach that it's only after doing a bunch we'll start to find out what the hurdles are.

DR. BILLINGS: So I just wanted to return--and I might ask Liz to comment on this--to this question of research versus clinical testing. So did you have an IRB involved in this--the management of this individual?

DR. DIMMOCK: Did we have an IRB? We actually have two IRBs because we have two institutions.

DR. BILLINGS: You have multiple IRBs.

DR. DIMMOCK: I actually want to just kind just address the utility question a little bit more. I think really utility is going to depend on the case scenario. When we pick out rare

diseases that we know are genetic we are going to have very good utility. I think the question is when we ratchet down--it's like with RacGH (sic). You know, in the first hundred cases everyone knew they had something and it's true as we use it now with an 18-20 percent clinical hit rate.

DR. BILLINGS: So--

DR. DIMMOCK: Now the question about research versus clinical.

DR. BILLINGS: So I just wanted to clarify.

So a test delivered on a research instrument with--you know, research analyzed but used for a clinical purpose is a research test and not regulated under--I don't get it exactly.

DR. MANSFIELD: No. As somebody pointed out--I can't--maybe it was you but the difference between--well, we actually have three differences. There's research. There's investigational and there's clinical. It's all about intent. It's not what instruments you use or anything like that. It's what you intend to do with that result.

I would classify this possibly investigational in the FDA paradigm but the fact that you use research instruments and so on does not

make it research. The intent was to diagnose the child. The investigational part is you don't know the performance of this instrument and investigating--you don't know the performance of this test in investigating this child. So it's tricky.

DR. BILLINGS: Under current paradigm then what is the regulatory obligation?

DR. FERREIRA-GONZALEZ: It has to be done in a CLIA certified laboratory.

DR. MANSFIELD: Well, certainly it's--

DR. BILLINGS: I think she's saying an IND.

DR. FERREIRA-GONZALEZ: No, no, no, there's a different--

DR. MANSFIELD: Well--

(Simultaneous discussion.)

DR. MANSFIELD: No.

DR. FERREIRA-GONZALEZ: You're making a clinical decision on a result.

DR. MANSFIELD: Because it was confirmed by a medically accepted--which I believe bidirectional sequencing is procedure.

(Simultaneous discussion.)

DR. FERREIRA-GONZALEZ: It still has to

be--

DR. MANSFIELD: Medically accepted doesn't mean approved.

(Laughter.)

DR. FERREIRA-GONZALEZ: But it has to be performed in a CLIA certified laboratory.

DR. MANSFIELD: Right. It has to be in a CLIA lab because you're returning a result on a human. I believe that it--bidirectional sequencing might be on the edge whether that's medically accepted or not.

(Simultaneous discussion.)

DR. MANSFIELD: No, no, no.

DR. FERREIRA-GONZALEZ: A lot of instruments are for research--you know, some of the sequences that we use are not for a clinical purpose and we use them in a clinical environment--

DR. BILLINGS: That's what I'm asking.

DR. FERREIRA-GONZALEZ: Well, the issue is have you validated your assay for the analytical performance and then with the intended use.

DR. BILLINGS: (Not at microphone.)

DR. FERREIRA-GONZALEZ: That's CLIA.

DR. MANSFIELD: So, yes. So for investigational use it's usually analytical

performance and the probable benefit outweighs the probable risk. If there is a medically accepted procedure--and we get to determine what that is, not everybody else--then an IDE is not required.

DR. DALE: I was interested in the decision making process.

You indicated that when you found the mutation then you transplanted.

I was wondering how did you know the mutation you found was the cause of the disease.

DR. DIMMOCK: We didn't have time to go into that. There's a lot more background testing that we did as well in a CLIA lab environment, functional testing.

DR. DALE: So that you identified this as a gene that was associated with a similar disease?

DR. DIMMOCK: So this gene, the XA (ph) gene, is known to cause an immune disease which leads to lymphoproliferative disorder. The decision to transplant was based on the risk of this kid developing a lymphoproliferative disorder. We fully expected that it would provide benefit to the bowel disease as well but the decision was based on the XA gene mutation, which is well established.

DR. KANIS: So going back to the last two

points. In your decision making when you had your three options, in your--if you look back on it without thinking about whole genome sequencing, would you have gone--I mean, I can't see you--you're saying you're failing your current therapy. That would kind of knock that one out.

Don't you think--what would be the likelihood you would have gone to transplant anyhow without any of that whole genome sequencing data and does that then change anybody's opinion as to whether that was research or not?

DR. DIMMOCK: That is a lot of questions. Would have been doing transplant in the face of Crohn's disease being research was the question?

DR. KANIS: No, in this particular case we had this Crohn's-like disease, progressive, early onset, severe, and you sound like you were just antsy to do something.

It sounds like you would--what's the likelihood you would have gone to transplant regardless?

DR. DIMMOCK: So that discussion has been very seriously had and the decision has been made that there wasn't sufficient evidence to risk the transplant but I would argue that actually doing

transplant in this situation is as much as research as doing whole genome sequencing because it has not got a clear indication. It's not FDA approved to treat Crohn's disease.

I mean that--not to sound flippant but I think really when we're in the situation of rare diseases it's very difficult because there is no standard of care. There is no approved route. There is typically no approved treatment.

So do I want us to get more data and go forwards with this so that we can think about it being approved? Yes.

But one of the other questions is--and this is a question that we've talked a lot about and I think the FDA is going to have a huge amount of helpful input into this. We can't on one case get this FDA approved as the test of last resort for a kid with severe Crohn's disease. And one of the problems we have with rare disease testing--and I mean I--once again I don't mean that as a flippant statement. It is defining clinical validity is very difficult when each child that you sequence actually has a different disease and a different endpoint. But really what is--the clinical validity, as I think I've alluded to, is going to depend on the

context. How rare is the disease that you're looking at is going to affect clinical validity and the utility of the test.

So going forward one of the issues that we've really struggled with in the institution is thinking about regulatory approval. To satisfy CLIA's guidelines, even CAP, we can do because we can prove the analytic validity that every time we sequence this specimen we get the same result. We're trying to define some kind of clinical endpoint or even a utility or what even are we actually testing when what we are looking for is going to be different from child-to-child or adult-to-adult. It is very difficult to try and work out how one defines the utility endpoint.

DR. MANSFIELD: I think it's safe to say that in cases of ultra rare diseases that FDA is certainly not interested in intervening to make you require clinical validity before you use it for that. We would probably be more interested in ensuring that the instrumentation was manufactured properly, that the software had been validated, and that you have some idea of how it analytically worked.

DR. EVANS: So I would also say you held

yourselves to a very high standard and, in fact, in some ways a higher standard than what is used clinically now.

In other words, we pursue tests regularly in the clinical arena where the diagnosis is not necessarily actionable, right? We diagnose Huntington's disease. We diagnose all kinds of disorders that, unfortunately, aren't actionable. And that is part of clinical medicine. So I would argue that you actually held yourself to a very high standard to insist upon medical action-ability and those strict criteria.

DR. ENG: And on that happy note our boss says we are well behind and let's move along.

Thank you, David, very much.

DR. DIMMOCK: Can I just say one last thing?

(Applause.)

DR. DIMMOCK: I'm standing here but, you know, we had one person running our instrument. We had 12 programmers, five or six bioinformatics people, and a team of about four clinicians regularly involved, about ten clinicians involved in this patient's care. So this really is a team effort and each rare case is a team effort so anyone

planning on doing this needs a big team.

DR. ENG: Paul will lead the discussion.

DR. BILLINGS: Thank you.

DR. ENG: Good luck.

COMMITTEE DISCUSSION

DR. BILLINGS: Well, obviously we don't have anything else to talk about and we can all go home now.

(Slide.)

So our intention now is to try to define a set of issues that we can include in a letter that will motivate the Secretary to continue to study the affordable genome and its implications.

(Slide.)

So here are the proposed issues that we-- we'll go into these but I'll just review them for you.

Challenges in evaluating the clinical validity and utility of whole genome sequence data and we just had a bit of an interplay about that very issue.

Challenges in communicating whole genome sequence data to patients and patients may include family members of patients in particular.

Coverage and reimbursement paradigm that

does not meet the needs of whole genome sequencing. We discussed this at length at our last meeting.

Timely and appropriate reassessment of whole genome sequence data as research reveals new findings and I think Jim's comment about needing to do a bunch of these to give it meaning is certainly a comment related to that.

And then disparities and barriers to the equitable access to whole genome sequencing technologies; the meaning of affordable.

(Slide.)

So I think the way to do this is probably to go over each one of these topics, talk about the proposed guidance, and then open it up.

Go ahead, Jim.

DR. EVANS: Could I suggest one additional one, which is consent issues. You know, there are many tests which involve consent now in clinical medicine. When we listened to the previous presentation where there were to six to nine hours of consent--

DR. BILLINGS: Right.

DR. EVANS: --that might be an issue--might be a bullet we want to add in such a letter.

DR. BILLINGS: Okay. Maybe that's--maybe

let’s actually--this was our first cut. Maybe there are other key bullets that we want to put on this list before we dive deeper into these bullets. Jim just put up the issue of consent.

Are there others from the committee?

Steve?

CHAIRMAN TEUTSCH: Maybe you have captured this in the first one because the whole issue of not just evaluating the sequence data but conveying that information to clinicians in a form that’s actionable that will lead to appropriate decision making.

DR. BILLINGS: I think that was our intent under that first one but if you feel that there needs to be culled out--

CHAIRMAN TEUTSCH: Well, it can be part of the description that follows if that’s the intent but there is also then the whole issue of we talked about the actionable information that you’d like to act on and then all of the other information and how you manage--how you manage all of that and particularly the potential for false positives or the economics of all the downstream unintended consequences of the testing.

DR. BILLINGS: I think you made that point

quite clearly last--

CHAIRMAN TEUTSCH: But is that embedded in here?

DR. BILLINGS: I took it--

(Simultaneous discussion.)

DR. BILLINGS: I took it actually to be under the first one but maybe it needs to be--

CHAIRMAN TEUTSCH: It is more than a communication issue, right?

DR. BILLINGS: Right.

CHAIRMAN TEUTSCH: It’s the clinical decision making process and how do you--of the whole thing. What are--because it is--the tradeoffs of harms and benefits before you even do the testing, let alone conveying the information once you’ve got it.

DR. BILLINGS: David?

DR. DALE: I will add one to the list and that’s the data sharing aspects. I mean this rare case, the confirm--the confirmation will come when other similar cases are sequenced so that you have some information there. So it’s a challenge in terms of how we as a community behave when discoveries or apparent discoveries are made. It’s a real dilemma. Is this private information?

DR. FERREIRA-GONZALEZ: I think some of the issues also will be on--that might be related to clinical validity or utility but today we don't have a mechanism to share information as we continue to generate more information on the genetic findings versus a phenotypic presentation so there's nowhere to go or anything.

The other issue that might be covered under coverage and reimbursement--there are two issues. One is that the amount of effort that is required to do the interpretation of these data is very different from what we normally do now. So how we go about doing it, one, and then how do we get paid for that secondly.

And another issue or challenge is how you store this information. Informatics technology today are not able to capture that information. I mean today I cannot put a sequence of the Connexin 26 gene on my laboratory information system, let alone the whole genome or even exome. So those are huge challenges that even though we might have the data, you know, we can't put it for everybody to access or even us to access in a very easy way.

DR. BILLINGS: Andrea, can I ask so presumably the ARUP must be developing either a

local solution for putting sequence data, either exome or whole genome sequencing, on their WEMS (ph). Otherwise they couldn't be considering doing this.

DR. FERREIRA-GONZALEZ: No, I don't think they have it in their WEMS. I think they might have it in--there are two issues because you can generate the data and you can archive it so then you have to store it, long-term storage.

DR. BILLINGS: Yes.

DR. FERREIRA-GONZALEZ: They are two different issues.

DR. BILLINGS: I see.

DR. FERREIRA-GONZALEZ: So the archival is when you do the analysis and when you do the long-term storage that's extremely expensive. We were talking about today that it may even be cheaper to rerun the specimen versus storage for long-term.

DR. BILLINGS: Yes.

DR. FERREIRA-GONZALEZ: So those are issues that need to be evolved. So I think they have it taken off line that it can continue to be accessed but it's not part of the electronic medical record or in any system that they can actually easily query with all the clinical information.

DR. MANSFIELD: Paul?

DR. BILLINGS: Sorry, go ahead, Liz.

DR. MANSFIELD: I wanted to add from my experience there are still quite a number of challenges in analytical validation across the genome. As far as I know, nobody is really clear on how to do that in a way that's consistent across the genome. I agree wholeheartedly with the idea of some kind of database or something so we start to connect genotype and phenotype so that this becomes useful for more than just the patient that the discovery was made on.

DR. WILLIAMS: I think related to that is a fundamental decision about, you know, at what level of reliability of sequencing are we at a point where, you know, you can have--this is related to the point that Liz is making. We don't have that--you know, the analytic validity but what's the threshold at which time we would be comfortable, you know, to say how many bases do we miss when we run the genome that we're comfortable that this is going to be clinically acceptable.

DR. BILLINGS: Charmaine?

DR. ROYAL: I think David's talk about sequencing in children raises--David's talk raises

issues about sequencing in children. I thought about a question that someone asked if the parents asked about a late onset disease and incidental findings related to that if you would give it to them, and he said, “Yes.” Normally we don’t test children for those conditions but if you find it as an incidental finding in such a situation then he would give it to them. I think there are issues there that we need to address.

So I think sequencing in children probably raises issues that we haven’t thought about that we probably need to look at.

DR. BILLINGS: Maybe we should just go ahead then and discuss these points, and then we can discuss the new points as well at the end.

Would that be a good way to do it, Cathy?

Okay.

(Slide.)

So here is what we meant by challenges in evaluating the clinical validity and utility of whole genome sequence data. The concern as we thought is limited information about clinical validity and utility for many associations and limited tools and resources for clinicians, including data and analytic tools, as well as just

simple reports. The current regulatory policy is not a good fit for whole genome sequencing technologies.

You can take exception to that, Liz, if you like.

DR. MANSFIELD: I agree with you actually and we're working on it.

DR. BILLINGS: Yes.

DR. MANSFIELD: So a recommendation to the Secretary won't hurt my feelings.

DR. BILLINGS: Good.

(Laughter.)

That's important to me.

So HHS should apply the SACGHS oversight recommendations on clinical validity and utility to whole genome sequence technologies.

Is that--I mean that's a simple recommendation. We've opined on clinical utility and validity before. How do we feel about applying this now to the kind of big world of whole genome sequencing with three million variants per individual?

DR. FERREIRA-GONZALEZ: You mean a lab developed test or whatever you want to call it so it should be under the purview of any of the

regulatories (sic) that we have today. I mean some of the forthcoming for the short-term that we have already identified for other areas of genetic testing will apply for these.

DR. BILLINGS: Let's put--let me put--maybe I'll put it slightly differently. We heard in the morning about the plans for LDTs which are coming under further regulatory oversight. Would a broad application of a new LDT policy significantly impact the translation of this technology into the clinic?

DR. EVANS: You know, I think it would. I think that--and that may be a good thing and maybe a bad thing but I think it would. I guess there's no way to get around the idea that if you're going to use a risk calibrated approach, which certainly makes sense to me, that you basically have to consider whole genome sequencing a high risk level because although there will be heterogeneous results, some of which will have low impact, some of which will have high impact, you probably need to make a judgment based on the riskiest thing you're likely to find, which would be the highest level.

Does that make sense, Liz?

DR. MANSFIELD: That's the way it has

typically worked is that the highest risk element actually establishes the risk but in this case I don't want to go too far into this because I know a lot of people watch this and I don't want to set off a firestorm but we're looking at some different ways of using our regulations in these areas where--and copy number variation is another one--where you can look at a lot more than what is actually meaningful for the diagnosis. And that has its risks and it has its benefits and we're trying to come up with a new way to handle that. I don't know classification-wise if it would be high risk but being that we haven't settled on what we're going to do I don't think this is the first thing we're going to go running out into public saying you've got to come in with a submission.

DR. : A good move.

(Laughter.)

DR. WILLIAMS: So, Paul, I think the other thing related to this is that there's a presumption in the guidance that somehow in our brilliance we have captured everything in the oversight report that's going to be applicable to whole genome sequencing technologies. Having been involved in that and not being particularly brilliant I think

that may be a false assumption.

I guess I would like to see this have an additional step which is the--maybe the applicability of the oversight recommendations be assessed for whole genome sequencing and if gaps are identified to use--you know, to convene experts or whatever to assess what type of additional oversight beyond those recommendations would be applicable.

DR. BILLINGS: That sounds quite reasonable, Marc.

Andrea?

DR. FERREIRA-GONZALEZ: So our next committee will do this?

DR. BILLINGS: No. No, but that could be part of the recommendation for the Secretary.

DR. RANDHAWA: So a couple of issues here. One, it might be useful if you're going to discuss clinical utility to discuss added value or comparative utility or comparative effectiveness so it's not just the validity of the test but in relation to the existing practice.

The second thing that's not quite clear is the regulatory policy is not a good fit. It seems to imply that we are requesting for a regulatory policy for utility which is, hopefully, not the

intent here in terms of the concern but that's how it reads right now.

DR. BILLINGS: I see. Do you have a suggestion on how we might change that?

DR. RANDHAWA: I think it would be useful if we can clarify the concerns as Liz has raised, the analytical validity, the clinical validity and utility, and of course the comparative utility. And then within the extent of applying regulatory policy for other tests to make it applicable for this test also but not to somehow imply that we should add utility in the regulatory policy here.

DR. BILLINGS: But isn't Marc's suggestion the sort of final common pathway, which is to say that the committee has made a statement about oversight of testing, to the extent that we should study how whole genome sequence does or does not fit that model, and then look for gaps and areas where it's not effective and supplement it both on the regulatory side as well as on the definitional side.

DR. RANDHAWA: And that's fine. The oversight is much broader than just the regulatory policy but the way it's identified here it seems to be like that's the solution being proposed.

DR. BILLINGS: Of course.

Jim, did you have something?

DR. EVANS: I was just going to say it seems to me that the operative thing here that makes whole genome sequencing a bit of a poor fit for the regulatory structure that exists is twofold, the magnitude of information return and the extraordinary heterogeneity of that information. Right? Information on everything from your earwax type to whether you're going to die of Huntington's disease. Right?

So it seems to me it's those two things, the sheer magnitude and the heterogeneity.

And that, you know, I think, as has been said, perhaps what needs to be said is something about evaluating whether the existing oversight recommendations are applicable, right, or what ones are.

DR. BILLINGS: Yes.

DR. EVANS: I'm a little uncomfortable just saying, you know, we should apply those recommendations.

DR. BILLINGS: Okay, any other comments about this?

Moving right along.

(Slide.)

So challenges in communicating whole genome sequence data to patients. So the concern is determining if, when and how to communicate incidental findings, variance of unknown significance, off-target results to patients, and assuring a knowledgeable workforce. The guidance that we propose is that HHS should support professional societies in developing appropriate guidelines and implement SACGHS recommendations for genetics education and training. And the professional societies are no big surprise.

DR. McGRATH: Maybe this is the place to put in Charmaine's comment about the parents--the results to parents and guardians. Maybe under the concern because that's the who.

DR. BILLINGS: Sure.

DR. McGRATH: Or we didn't say who, maybe we need to define who.

MS. DARIEN: And--sorry. And of course you know what I'm going to say, which is that the--it's not just professional societies but it's also patient groups that are dealing with it like Genetic Alliance and the National Organization of Rare Disorders. It's really important to have to have the stakeholders in there.

DR. EVANS: And, finally, in the list that is variance of unknown significance, et cetera, I think it might be reasonable here to insert findings of a potentially sensitive nature. The more we learn about behavioral attributes and their correlation with genotype, ApoE, Huntington's, there are a lot of things that are potentially sensitive and perhaps that's where this should go.

CHAIRMAN TEUTSCH: In addition to the specialty societies we of course have the primary care groups that do need to have the clinical decision support systems built to allow them to do that. We should probably say something about clinical decision support systems in here.

DR. WILLIAMS: So this is more about the action-ability. Support is a pretty bushy (sic) word, I guess, to use Steve's language earlier. Are we really talking about, you know, funding a group like say HRSA or AHRQ to develop RFAs for people to compete to develop these guide--I mean what are we really talking about when we say "support" because usually what we're talking about is money.

DR. BILLINGS: So are you really saying about funding--

DR. FERREIRA-GONZALEZ: I think we need to

focus more on trying to figure out what are--how the practice is going to be. When you all have all this information, what you're going to disclose, how do you approach that? I think there has to be a lot of research done in these areas before we--

DR. WILLIAMS: Right. And I think that's what I was trying to get at was that, you know, the HHS and professional societies or the expanded professional societies with support, we're really not defining what the Secretary could reasonably do to move this forward. And I think as Andrea pointed out, a lot of it relates to, you know, convening function to say what are the issues. What data do we have? What data do we need? You know, whether this would be some type of a consensus conference or state-of-the-science or whatever it would end up. You know, I think we need to be a bit more tangible than just to say "support."

DR. BILLINGS: So the Secretary should use her resources to move this agenda along. Is that basically what you're saying?

DR. WILLIAMS: Yes.

MS. WALCOFF: I wouldn't say "resources." I mean, I think "convene" is a good way to say it. I mean just "should convene these groups to develop

something." I think you can use really the FDA model that Liz has been working on with LDTs, which I think has been well received across the board, even among folks who have different opinions on what the end result should be from that guidance. But certainly I think the transparency and openness, and it's really the way that the government at least in the health area has been moving. If you say "use resources" I think people skip to the next bullet.

(Laughter.)

DR. BILLINGS: Other comments on this one?

Okay.

(Slide.)

Coverage and reimbursement paradigm that does not meet the needs of whole genome sequence testing.

Concern: The current paradigm may not be adequate to cover the informatics costs for whole genome sequencing or the cognitive services required of clinicians. That cadre that David just described to us.

Guidance: HHS should assess the remuneration needs of laboratory professionals and clinicians who provide and/or use whole genome sequence tests.

Does that cover--does that grab you?

DR. WILLIAMS: Well, the forum is the one that I'm struggling with a bit and I'm just looking around to see if Jeff is still here.

I'm not certain that the Medical Evidence Development Coverage Advisory Committee is the right forum for that because what we're really talking about here is something that currently is under the purview of the AMA-CPT committee and there is ongoing discussion about issues of interpretive components for--and professional components for molecular laboratory testing that probably will not get to the point of addressing whole genome sequencing but at least conceptually is getting out on the table the issues of the interpretive component, the practice of medicine aspects of this type of testing that's necessary and could provide a foundation for moving into this area.

I think the forum that's proposed here--they are basically looking to say is there evidence to support that CMS should pay for this or not. But even if they said, 'Hey, CMS should pay for this,' there's no mechanism by which CMS could reasonably reimburse because we don't have the procedural codes that they would have to have to be able to actually

do the reimbursement.

I don't know, Andrea, if you can--

DR. FERREIRA-GONZALEZ: You have the right assessment of this coding that we use to provide information to CMS or third party payers to let them know what we have done. Today they are not meeting our needs and right now the AMA is going through the evaluation of different proposals to try to incorporate the interpretation, professional interpretation piece, into some of the coding.

I think it was very clear this morning or this afternoon by Karl Voelkerding.

And from my experience in trying to do interpretation of sequencing of, you know, two or three or four different genes, the amount of cognitive knowledge that you have to put not only to determine the sequence that you're calling--the bases you are calling that are correct but also starting to go into different databases and trying to identify that the changes that you see from whatever reference you use has any clinical significance or is not clinically significant. It is just an incredible amount of professional work that is involved. I would say it is more than the technical aspect.

So this current paradigm that we have doesn't really provide enough remuneration for the professional input compared to the technology input. It needs to be revisited. This is at the level of the AMA but I'm not sure what the Secretary can do at this point.

DR. WILLIAMS: Right. I mean this is really the problem of the $1,000 genome with $100,000 interpretation. I think that we have to understand that in the case that was presented what they were trying to do was to use these interpretive skills to narrow down to a single target. There was no attempt, you know, to really formally assess the whole genome even though they did the whole genome. They were basically, you know, using techniques to try and get down to a target or a reasonable small number of targets that could be done.

So they have no comment, nor did they take a look to say, for example, is there a deleterious BRCA mutation. So there's a presumption that somehow whole genome sequencing is going to get to the point where we are actually going to instantaneously know all this and that's just, you know, not going to be the case. So it really is a much more complex problem and it's not something

that the current laboratory reimbursement is up to.

DR. DALE: I would comment, too, about the cost. Dave didn't say how much that work up cost but I would be sure it would be a lot of money. So you have to think of the relative benefit of doing that. And I think there need to be technical workgroups or something that provides the advice in terms of strategies for who needs it. I mean because many--so many diseases have multiple manifestations but at the ground level the sophistication of the clinician to recognize the clinical features of various genetic variants is missing. So I could envision spending huge amounts of money in the laboratory. It's wasteful if it turns up negative results.

DR. BILLINGS: David, how is that different than let's say a new imaging technique or any other kind of new technology that might be applied to a disease group?

DR. DALE: I can remember our arguments when multiphasic clinical chemistry testing began and being engaged in that debate.

DR. BILLINGS: You just dated yourself, David.

DR. DALE: Of course it has been a while

but we had--

(Laughter.)

--the same argument in the ‘60s about this but this is higher stakes, a lot more money. Or in a--if you say zero sum health care system it has a sucking sound to me. So we don’t want to waste that money. On the other hand we want to apply good technology to diagnose rare problems. So that’s one of our real challenges and I think there is ample room though. For instance, in the mitochondrial diseases somebody said, “Thirty.” It is a round number but most of those diseases have multiple manifestations. If you’re a sophisticated clinician you can make a better guess rather than spending all the money.

CHAIRMAN TEUTSCH: So are you suggesting that we say something about assessing the value of these tests?

DR. DALE: Yes.

CHAIRMAN TEUTSCH: Do you want to be explicit about that?

DR. DALE: Well, I just think that there is going to probably be a hierarchy of development of tests at times or situations where this is useful. I think the case that was presented was

probably a good one where the immune defects and the genetics and the mutations associated with them are pretty well known. So this was a niche for this case to be worked up. I agree with that. But there are other places where it's a totally black box. So I think we'd be remiss if we had primary care physicians sending off whole genome sequencing tests because that's what the parents wanted.

DR. WILLIAMS: And in some sense the coverage and reimbursement presumes that we understand that there's value. I mean the first decision as a medical director, you know, that you're going to make is, you know, is this test medically necessary? What are we going to learn? Is this an experimental investigation? We use those terms in a very different way than FDA or NIH or the Office of Human Subjects Research. You know, irrespective of whether or not those people consider what was done experimental investigation, there's not a health plan in the world that wouldn't have said this is experimental investigational and it's not something that we're going to reimburse you for, which is of course why they have established funding that's independent of third party payers to be able to move this forward.

So I guess maybe in some sense this may be premature to put forward in an actionable recommendation to the Secretary today since the validity and utility questions are much, much more important to try and get a handle on at present.

DR. BILLINGS: Go ahead, Sam.

DR. NUSSBAUM: I'm trying to think through a pragmatic set of ideas here.

We know that the cost curve of whole genome sequencing is coming down and will certainly intersect soon--we've seen this in previous meetings--with the cost curve of BRCA testing and testing for other composite DNA.

So the question is then for CMS and others and other payers, including us, is at what point do you then just cover whole genome sequencing?

So you basically cover and get lots more information than you ever envisioned. So women with a family history of breast cancer and meeting certain criteria would get whole genome sequencing rather than BRCA testing or if someone has breast cancer and you're looking at whether to use chemotherapy or other interventions.

So it strikes me that over time this is going to become a reality that we're going to have

this information and whether you mask it or not it's going to be ultimately known. So in a practical way it strikes me that while we always want to be forward looking and make recommendations well in advance, this may be one where the science just isn't ready for prime--I mean isn't ready for prime time because maybe we would conclude that certain things like storing cord blood should be a universal health care need. And having your genome sequenced a universal health care need at birth and then that just can be--this information can then be used as science evolves.

But it strikes me we're in a sort of very, very--sort of an area where there is just so little clarity that I don't know what we could say and I just envision that if you had payers, unique situations of very critically ill kids, that there could be--if those things get worked out, you know, independent of what's research investigational when you're trying to figure out the model of best and appropriate care.

DR. WILLIAMS: Yes, I mean the point that you also bring up that I think is really important is we've already--if you look at gene panels, we've already gotten to the point where there is a test on

the market that is being marketed solely for the fact to say we cannot only do these two recommended panels, CF and Jewish Disease, but you'll get 100 more diseases and at a lower cost. That's being heavily marketed to practitioners.

If we only focus on the cost of the test itself we are going to be misled because the big cost, and this is relevant to the imaging, too, is the downstream costs of, you know, what is--what do we do with what we've found that we weren't looking for in the first pace. You know, the Isaac Kahone incidentalome (sic) issue, which was focused more on whole body imaging but I mean in this case we're even beyond that.

There is definitely--people are going to want to follow up on things that are found in these tests that we're--that are probably not going to ultimately be of relevance but will consume resources and will not necessarily be attributed to the cost of the tests as we define them.

DR. FERREIRA-GONZALEZ: I think we can draw from some of the array CGH studies being used for inherited disorders in pediatric patients because it's a different level on the investigation of the whole genome but we're starting to get

information in areas that you don't know. So we already have testing that is becoming some of the practice that then gives you more information and being submitted for reimbursement and being reimbursed so maybe that could be an area that we can start looking at some of the issues since it is already being used.

DR. WILLIAMS: Yes. I mean I'm not sure it's exactly translatable in the sense that we're looking at pretty gross rearrangements even at high density array as opposed to single, you know, deleterious mutations. So while there may be some things that can be learned from that, I'm not--I wouldn't be so sanguine as to assume that that is going to be a fully powerful model going forward.

DR. EVANS: David?

DR. BILLINGS: Did you want to go first, Liz?

DR. MANSFIELD: Well, I just--

DR. EVANS: I'm sorry.

DR. MANSFIELD: During this conversation it occurred to me that while we were looking at direct-to-consumer testing from the regulatory point of view, we heard quite a number of voices stating that it was--it's my right to know my genome, to

know my sequence, which fundamentally I don't disagree with. But to know your genome because you're entertained by it and may seek medical care is very different than to know your genome for a defined medical purpose.

I wonder if there isn't something in that that we need to address here.

I haven't heard anybody say it's my right to know my copy number variation but--

DR. EVANS: But we will hear people say I want to know my whole genome. You can kind of--I mean, I guess I feel like we've gotten very far afield from what this particular slide is supposed to cover and I don't think it is controversial to say that the current model may not be adequate to cover both the informatics cost and the cognitive services.

I think that as long as we perhaps put in something about if whole genome sequencing becomes perceived as a useful clinical test or is demanded as a test, we are going to need new models for reimbursement.

DR. BILLINGS: Perfect.

DR, EVANS: Right.

DR. BILLINGS: I mean that's exactly--

DR. EVANS: Yes, and we can debate all day about exactly who has to do that and how it should be done.

DR. BILLINGS: Okay.

DR. EVANS: The Secretary needs to hear that.

DR. BILLINGS: Okay.

DR. EVANS: Okay. Good.

DR. BILLINGS: So I'm going to move this along a little bit.

(Slide.)

Timely and appropriate reassessment of whole genome sequence data as research reveals new findings. The concern is that whole genome sequence data will need ongoing reinterpretation and re-annotation. It's unclear who will be responsible for not only doing this updating and obviously maintaining the databases that would be required for doing this updating and delivering that data, and its significance to the end user.

HHS should support the development of tools and--again I guess--support--there's that word "support" again. We might want to change that. Should support the development of tools and resources that help assure the interpretation of

patient data is current.

DR. WILLIAMS: There have been tangible suggestions in a couple of different times during this about the actual creation and in this discussion and the previous discussions about creating, you know, something that would be--you know, go beyond the current dbGAP to really collect and refine these genotypes and phenotypes in some sort of a systematic way to try and facilitate learning.

And it seems to me that we're getting the suggestion from a number of different subjects that we're discussing. So if we could somehow put this into the recommendation that we need some sort of a systematic way to collect and analyze this information, and that that is reasonably assumable under the Department of Health and Human Services, that that would be something to--

DR. BILLINGS: Well, do we--it seems to me that we don't know how to do this in our health care system very well. I mean we can say some things. We need an IT system. But we actually--for whole genome sequence data we just don't know how to do it yet. We don't know what tools are necessary exactly and we don't know how to integrate those tools into

a delivery system.

So this one cries out for study it seems to me, along with further recommendations.

Gwen?

MS. DARIEN: So the other side of this which we talk about a lot in cancer meetings, the cancer community, is how and when you deliver new information to patients and what is the consent process there, which I think is something that's left out of this.

DR. BILLINGS: Okay.

Yes, Jim?

DR. EVANS: Finally, the only other thing I'd mention is it's--I think the hardest part is not going to be necessarily updating. One could imagine sweeping--you know, informatically being able to sweep through a gnome to pick things up. It's going to be deciding what the findings are. Right? And that's--so I think the concern should include--

DR. BILLINGS: What qualifies as a finding?

DR. EVANS: Yes. It's unclear who will be responsible for updating, the meaning and significance of the data, and how significance will be determined. Right? And that I envision needs to

ultimately be similar to the way the newborn screening community has grappled with the issue of what diseases, you know, should be screened for. It has to be a centralized transparent process using defined criteria to determine what the variants are that need to be swept, you know, and looked for in the genome.

DR. FERREIRA-GONZALEZ: But we cannot hold the information today. There is no way. There are no tools to put the genome information there. So you--

DR. EVANS: Say that again.

DR. FERREIRA-GONZALEZ: There is no way to deposit that information in the electronic medical record today. So you cannot query anything--

DR. EVANS: Right.

DR. FERREIRA-GONZALEZ: --because you cannot put it so we have to put that tool first.

DR. EVANS: We have to have that tool but it has to be in the service ultimately of clinically significant issues.

DR. FERREIRA-GONZALEZ: Yes, I understand but we also have to be able to put it and we don’t have that. So today maybe that’s a recommendation

to develop the tool to deposit that information.

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: Paul, I'm going to have to--because I know we're running out of time and we could talk a lot about these.

Why don't you run through the last one and then let's figure out how we're going to somehow package this in a succinct fashion that the Secretary can actually get her arms around?

So, Paul, why don't you go ahead?

(Simultaneous discussion.)

(Slide.)

DR. BILLINGS: Aside from the newly added issues to the list, the last issue in our list was is the affordable genome really affordable and accessible to all.

The guidance would be to assure equitable access to whole genome technologies. The HHS should assess the feasibility of using whole genomes as part of a public health mandate, such as newborn screening, and what would be required to the extent that newborn screening represents affordable widely available testing.

DR. MANSFIELD: I think this is great.

CHAIRMAN TEUTSCH: So, Paul, can I--

DR. MANSFIELD: Health care accessible to all.

DR. : Yes, we're all in favor.

DR. MANSFIELD: Do you want to get your whole genome screened if you can't do anything about it?

CHAIRMAN TEUTSCH: So, Paul--

DR. : I think it's a real issue.

CHAIRMAN TEUTSCH: --and Charis, I guess here's a question for you and for the committee. We've been through each of these and we've got lots of good things. We've heard a lot of discussion. My guess is--that's why we were planning on doing this for the next year.

DR. : How about two years?

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: And I've heard a lot of things. Sam is right. You know, we're sort of in the middle of a very gray area and it will be a while until it sorts itself through.

So I guess the question I've got in terms of what we're going to do for this report, one is we can take the outline that you've provided and use that with some tweaks that we've heard today. Another suggestion would be that we simply indicate

this is really an important area and then we can highlight not only the issues that you've bullet pointed but a few of these here that we've had--that have been raised but which we are totally unable to get to resolution about in anything like real time to get things done by tomorrow.

So I'd like to hear at least a little discussion about what it's going to look like that we tell the Secretary so that we can work from this and modify that or whether you like the summary idea that I had or whether you think there's another solution here or whether we should--

DR. EVANS: I like the summary idea. I think that the overarching message should be that whole genome sequencing is being pursued. It will likely in some manifestation become part of medical care and that it raises huge problems, and many of them. And then we should just bullet some of those without even attempting to offer solutions. Because like you said, that's what we were going to do over the next two years.

CHAIRMAN TEUTSCH: Or being complete.

DR. EVANS: Or being complete.

(Simultaneous discussion.)

DR. BILLINGS: So, Steve, we heard when

Francis was on the phone last week that one suggestion which was that some of us might fall under the granting purview of the NHGRI.

Eric, do you think that that's--you know, (1) is that a reasonable way to handle these issues; and (2) is that going to get us to the kinds of answers that we need now? I mean it's not really research we're talking here.

DR. GREEN: I actually think the research might inform a lot of this. I mean--

(Simultaneous discussion.)

DR. GREEN: Early next year we will publish a new strategic plan for the field of genomics. The institute will publish. I mean we touch on lots of these issues. We don't own all these issues and many of these issues are bigger than us but we're driving a lot of this, especially in the technology arena. And we raise a lot of these issues.

And I will certainly tell you that some of what NHGRI will be funding in the next five to ten years for research will help inform this. I wouldn't make it synonymous. I mean I would say that's one part of a larger picture that needs to be painted.

DR. ENG: Why don't we do the paragraph as suggested by Steve? The way he said it was very broad. Here are the concerns. And then at the recommendations would be, among other things, research or convening panels of stakeholders to examine this issue and encompass it in some of the verbiage that's used in the education--

DR. GREEN: I'm not even sure we should have recommendations.

DR. ENG: Well, that is--

DR. GREEN: Well, that's the recommendation.

CHAIRMAN TEUTSCH: Sheila, how does--

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: --the Secretary accept such a document?

MS. WALCOFF: Well, I can tell you that senior staff to the Secretary would say that, you know, I think identifying something as an important issue and one that has--not just problems because I can't totally agree with Jim on everything in every meeting. We have come close this meeting.

(Simultaneous discussion.)

MS. WALCOFF: I'm only going to take issue with one word and that is just "identifying

problems" because I think there are opportunities and/or challenges.

I will say at the risk of even saying these two words together but even when the issue related to gene patenting was first brought to me by, you know, near and dear to our hearts, Greg Downing, you know, it was something that we didn't know a lot about, that I didn't know a lot about, the Secretary certainly didn't know a lot about. But it sort of, you know, raises it as part of your overall--as Eric said, you know, your strategic plan and what you're trying to look at as this moves forward. There is going to be more and more discussion as the cost of this goes down and certainly Dr. Collins has been talking about that for some time.

But I think it just needs to be on the radar, you know, and I think that's important because there are a lot of big things going on right now but we need to keep these types of issues on the radar of the Secretary and the senior staff to the Secretary so that action can be taken.

CHAIRMAN TEUTSCH: Gwen?

MS. DARIEN: I was just going to underscore how much I agree with you and Jim about

putting something in as a summary because I, for one, would feel uncomfortable turning in something as recommendations that weren't thoughtful because I think the quality of this committee's work has been phenomenal. So to kind of rush in with something that's not fully thought through I think is--I think would not represent us well. I think it wouldn't set up a thoughtful discussion for the future which is what we want to do.

CHAIRMAN TEUTSCH: So what I'm hearing is the recommendation is actually--we need to keep paying attention to this issue and there needs to be attention--and then we can begin to list a set of what the considerations are which are from the research end all the way over to the clinical decision support, reimbursement, all those kinds of things that we can begin highlight in a paragraph without sort of saying what the answer is.

MS. WALCOFF: And I think one last thing to add to that is to sort of maintain the communication among the different agencies that this group has been able to offer in bringing folks together because I know a lot of the work that we did was really just figuring out that so many of the

different HHS agencies were working on a particular issue related to genetics and genomics and either were somewhat aware or not at all aware or very aware but working in their own sort of fashion on the exact same thing. I think having some cross department coordination is positive with all these issues.

CHAIRMAN TEUTSCH: Are you all right with that?

DR. : Yes.

CHAIRMAN TEUTSCH: I know you guys--

DR. ENG: You--

(Simultaneous discussion.)

DR. ENG: --our discussion.

CHAIRMAN TEUTSCH: Well, I appreciate that and you've laid out a lot. In fact, I think the sessions that you guys have chaired have been really helpful in bringing many of us up to speed. I speak for myself who was way below speed.

Do you all--can you craft sort of what that might look like tonight so we can actually look at it? I don't think we're looking for something long but a fairly simple statement and then a set of considerations, issues, things that we think they need to pay attention to without being judgmental

about them. Something honest.

(Laughter.)

CHAIRMAN TEUTSCH: This will break the budget of the health care system.

(Laughter.)

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: All right. Let me just get a sense. Are most people comfortable with that?

DR. : Yes.

CHAIRMAN TEUTSCH: Okay. Great.

Thank you for helping us through that process.

I know this is a very short circuit on a very complex topic.

So with that we go into a break. I should tell you Sheila--is it mother or mother-in-law?

MS. WALCOFF: I have to make one plug for my mother Ruth Ann Darryberry (ph), who as many of you all know, and were very gracious in offering your support to me, she was very seriously injured in a car accident in February and has come such a long way. She’s famous for these things that she has been making since I was in kindergarten, butter pound cakes, and she is now able to stand and move with a cane and make her cakes again.

I have brought some cake to share with everyone for our last meeting kind of in honor of my mom.

CHAIRMAN TEUTSCH: Thanks, Sheila.

MS. WALCOFF: So enjoy.

(Laughter and applause.)

CHAIRMAN TEUTSCH: All right. With that we'll reconvene at quarter of.

(Whereupon, at 3:32 p.m., a break was taken.)

GENETIC INFORMATION NONDISCRIMINATION ACT

UPDATE ON THE IMPLEMENTATION OF THE GENETIC INFORMATION NONDISCRIMINATION ACT (GINA) AND PUBLIC AWARENESS OF GINA

CHAIRMAN TEUTSCH: All right. So we have two more topics for the afternoon.

So first before we hear our afternoon speaker I want to provide an update on the implementation of GINA.

I think you know that a draft final regulation implementing Title 2 of GINA, the provisions that prohibit employment discrimination on the basis of genetic information, was cleared by the Office of Management and Budget in April. That regulation is currently under review by the EEOC.

We had hoped to have them here today but obviously that process isn't complete. We haven't talked about that today but that process isn't complete.

So once the commission votes to approve the rule it will be sent for a final review by OMB, after which it will be published in the *Federal Register* and we'll see the final reg.

Although that final rule hasn't been issued the statute did become effective on November 21st of last year and the EEOC, therefore, began enforcing the protections against use, acquisition and disclosure of genetic information in the employment setting as of that date.

So that's where we are with that but obviously that's not the only thing that has been going on with GINA.

So to that effect I'd now like to introduce the next speaker, Juli Murphy-Bollinger, who is a project manager at the Genetics and Public Policy Center at Johns Hopkins University. As you know, we've turned to them before for information on what's happening in the policy in the real world arena.

She is going to report on findings from the center's studies on public awareness of GINA and

the public's attitude towards genetic privacy.

We'll have a few minutes for discussion and questions for her, and then we can have a brief discussion about whether there is anything regarding the presentation that we want to convey to the Secretary.

Juli, welcome.

MS. MURPHY-BOLLINGER: Thank you.

CHAIRMAN TEUTSCH: And we look forward to what you have to say.

PUBLIC AWARENESS OF GINA

JULI MURPHY-BOLLINGER, M.S.

PROJECT MANAGER, GENETICS AND PUBLIC POLICY CENTER

JOHNS HOPKINS UNIVERSITY

MS. MURPHY-BOLLINGER: Great. Thank you.

(Slide.)

Thank you very much for inviting me to come speak today.

I'm going to talk a little bit about some of the research findings that we have obtained in our work--

CHAIRMAN TEUTSCH: Could I ask you to speak up? You are not alone because I've had a hard time understanding the other speakers as well. Anything you can do to speak more loudly into those

will help us to pay attention.

MS. MURPHY-BOLLINGER: All right. Is this better?

CHAIRMAN TEUTSCH: Yes, thank you.

(Simultaneous discussion.)

MS. MURPHY-BOLLINGER: Okay. So I'm just going to share with you some of our findings of our research that we've done talking with the public surrounding a proposed biobank study, and we'll get to some issues of what we've heard in the field about people's awareness of genomes but I thought I'd do a quick back up of what we're studying and in what context so that we can see the background here.

(Slide.)

So we have been in the field talking to the American public regarding a proposed biobank that is under consideration at the NIH in which they would like to enroll a representative sample of 500,000 Americans, collect medical, lifestyle, environmental exposures, lifestyle histories, and follow these individuals for a period of a decade or more. So we were asked to go and solicit public opinion.

(Slide.)

We've done this as two projects.

One which has completed and that started off, as you can see, in 2006 and went through 2008. And in this project we surveyed the landscape of people's opinion about the proposed study to inform the design and implementation. We did it through a whole different variety of mechanisms.

And what you can see here is that the project ended in 2008 right at the time when GINA was signed into law. So this data was collected pre-GINA being funded into law.

We further have recently received funding to talk with the public more and to dig deeper into three issues that came out of our findings from the first study and those focus on returning research results, concerns about privacy and consent. We are halfway through that project right now. We have completed our focus group data which I'll share some of that with you today about privacy and GINA.

And we're about to go into the field with another large population survey of 3,000.

So I'm going to share with you some data that came out of our first public consultation grant used to inform the second. They are all relative to public attitudes about privacy, concerns about privacy and data sharing.

(Slide.)

So from our initial consultation data, this is all the quantitative data coming out of our survey which was fed by our earlier work on focus groups and interviews. I think it's just important for everyone to know that there was a lot of wide support for the proposed study just as a background of where these opinions are being held.

(Slide.)

So people thought that the proposed study was a very good idea. A majority of them thought it was a good idea and most are willing to participate as well.

(Slide.)

However, when we talked about privacy it was a very widespread concern for all people who are considering participating in the privacy.

(Slide.)

Over 90 percent of individuals identified privacy as a concern.

(Slide.)

When we talked about what were they concerned about in terms of what parts of information they considered privacy and concerning was financial information and medical information.

And like we've seen in other surveys we've done, financial information was more concerning and protecting that than their medical but both were still very large concerns for people considering this project.

(Slide.)

We also asked what type of information or is there any type of information in a medical record that would need additional privacy protections. And only a fraction of additional types of information need additional privacy projects. Most thought it should all be protected equally.

(Slide.)

And when we asked them what types of information they thought, of the people who thought there should be additional protections, these are what they identified. Again social security, number, things that are related to financial are ranked very high, other types of histories were still identified as concerning but, as you can see, genetics is somewhere in the mix a little bit lower than we had anticipated where it would show up.

(Slide.)

When thinking about participating, aside from privacy being a large concern, having

researchers having access to their sample was concerning and having the information in the study used against them was identified as concerning. So people widely identified privacy as a concern. But in terms of harm from the information or being used against them, concerns like discrimination or other harms. That was ranked lower. So we were very interested in what was going on when people said what were their concerns about privacy.

(Slide.)

And just as a quick aside of some data about access I was asked to address the issue of access. What we have heard in the first go round is in terms of who would they feel comfortable sharing, U.S. academic researchers ranked the highest and then with lesser thrill government funded researchers, pharmaceutical companies were down there, and surprisingly international academic researchers ranked lower than pharmaceuticals. So there was a very strong patriotic effect here.

(Slide.)

So here we are currently through our-- halfway through our consultation data and this was the consultation. We were digging more deeply into privacy concerns. So I'm going to share with you

some of our focus group data which is qualitative which we have not yet tested in a quantitative format but we can give you some themes of what we're hearing.

One is that privacy is dead. It does not exist anymore. We heard this widespread in all the groups that we have spoken to. We did ten focus groups representative of the country. And people think that there isn't any privacy anymore, particularly now that the internet age is here and everything is out there on the web.

For some actually the fact that there was no privacy in the world anymore made them more-- actually more comfortable. They thought everyone already knows everything about me so what's there that I am going to provide to you that they don't already know so I don't worry about it.

(Slide.)

We asked them some questions of what exactly are you concerned about when you say you're concerned about privacy. And what we heard overwhelmingly was discrimination for sure. The majority that we heard was insurance discrimination and some cases of employment discrimination. And a very big one was identity, identity theft, identity

and fraud.

So what we heard was very interesting that people thought having this information collected into these scientific databases, that this information being out on the web and the interconnectivity that the information that will be collected will somehow be able to have people's financial information vulnerable. So they thought of this big sort of database connectivity making it more vulnerable financially, which sort of speaks to some of the concerns we saw in the earlier data.

"So I worry about people stealing my identity." We heard a lot of that in these groups.

(Slide.)

Also concerns about being stigmatized, being labeled, and even though we always take cloning off the table when we have these discussions, people still fear being cloned participating in this type of research.

(Slide.)

Another point that we have heard--and we heard this in several focus groups--is again speaking to this idea that information being collected in a database could contain information that would be of interest to other outside entities.

More than one person had mentioned being spammed by drug companies. So that people would be able to get a hold of their information that was collected as a part of this study and put into a database and have it used to market and solicit other marketing materials to them.

So a perfect example of this is people finding out--are you tired of your blue eyes and being spammed by another company that's going to sell different color contact lenses.

So why I put this in was it speaks to the point that they really feel there is this connection of information out there that would make them vulnerable, particularly financially.

(Slide.)

Many people thought privacy breaches were inevitable and that they were not overly concerned. They felt that the information being coded would help them and that the data that would be out there would not be--would only appeal to a very small segment of the population so that their medical information wouldn't be as concerning to people.

(Slide.)

So then we asked them--you know, we heard a lot about insurance discrimination and some

employment discrimination. We asked individuals in these focus groups whether or not they had heard of the Genetic Information Nondiscrimination Act, and most participants hadn't heard of it at all. It was absolutely dead silence and this was predominant in all the focus groups that we did.

When we went on to describe GINA and what protections that GINA offered, most were not reassured by our description of what GINA was going to do for them. So I've pulled a few quotes just to give you a theme of what we were hearing.

"So does the fact that GINA is in effect give you any reassurance?" "No, not really."

(Slide.)

They felt that there were ways around GINA. And I pulled some of these quotes to show you what we're hearing.

"Because it's just a law and ten years down the road some cowboy gets elected and he changes the law. So the fact that the law is there--laws can be changed." So there wasn't reassurance there.

"Would GINA help your concern about insurance companies having access?" "No, because insurance companies are large organizations that

have ways of getting information whatever law comes out."

So there is a very strong theme that insurance companies have large tentacles that can creep their way in to getting a hold of this information on them regardless of whether there is this law there to protect them.

"Again there's always red tape and there's always a way to get around GINA."

So there wasn't a lot of confidence that GINA could provide the protections that it has been designed to do.

(Slide.)

Also this speaks to my last slide about the access to the databank that individuals want to hear and this also speaks to the theme of insurance being able to get around GINA.

"Despite NIH's best intentions it would be difficult to control access to this dataset. An insurance company could be attached to another research firm and then that way they can obtain access to the database and NIH wouldn't even know that they were coming on into it."

So what we're hearing is that individuals are not hearing about GINA in terms of just

awareness. And when we describe it they are not very much reassured by it, and they feel that there are many ways around it particularly due to savvy and crafty insurance companies.

So that is just a brief synopsis.

(Slide.)

Oh, and just because I was asked to speak a little bit more on access, besides the usual players of insurance companies and employers not getting access to the data, scientists performing cloning were not popular, and individuals seeking transplant donor matches. These are different types of people that were identified as not wanting to have access to this type of data.

(Slide.)

So I just wanted to thank those who are involved and I'll take any questions you have.

So the summary is most people haven't heard about GINA.

(Laughter.)

COMMITTEE DISCUSSION

CHAIRMAN TEUTSCH: And those who have don't seem to think it does much.

Do we have any--a couple of questions for Juli?

Yes, Barbara?

DR. McGRATH: That was really interesting. Thanks.

You probably said it at the beginning but you were speaking so quickly. The age of the sample--because especially the privacy issues I am picking up are big generational differences in how people think of confidentiality and privacy. What was the age of the sample in this study?

MS. MURPHY-BOLLINGER: IT was a wide range of ages. We did--you had to be over 18. So in terms of the survey data people were 18 or older. We tried to get a representative survey of the U.S. population so that we had an age spread.

In the focus groups we tried to do in the first round of consultations variation by age and in terms of just getting different groups by age and race and other factors we thought might influence their opinions about participating in research. People who have done research before and things like that. So we did have some young--we had a wide range of ages from 18 all the way up to in the 60's and 70's.

We did in this round do focus groups with individuals who are social networkers, self-

identified social networks, wondering if they might have different thoughts just on privacy in general. And so we solicited people using Craig's List advertising, whether they had Facebook accounts, whether they posted to Facebook, and our announcement to date has shown that we haven't seen much difference. We thought they might be more open to be sharing online information.

And they actually were just as concerned and actually were quite astute about how they protect their information when they participate online.

CHAIRMAN TEUTSCH: Sam?

DR. NUSSBAUM: Did you have a chance to ask--I don't know if it's a question of whether anyone actually experienced discrimination, whether they personally or knew of someone who experienced this?

MS. MURPHY-BOLLINGER: We didn't--

DR. NUSSBAUM: Because it would seem to me that would be a nice balance to be sort of a perception that--in ways of insurance companies and even government--

MS. MURPHY-BOLLINGER: Right.

DR. NUSSBAUM: --and everyone getting

around the issues.

MS. MURPHY-BOLLINGER: Right. We didn't actually specifically ask the question of have you been discriminated against but we were asking what concerns they had about privacy and people did tell anecdotal stories of why they were concerned about privacy. But it was more just general concern about privacy. What exactly are you concerned about, whether it was based on a real experience or not. So, no, we didn't ask that. We just asked what their concerns about privacy was and then went on to say there is this law that has just recently been put into effect that is designed to do this. How did this change, if at all, your feelings? And it did not erasure. So--but, no, we did not.

CHAIRMAN TEUTSCH: Any other questions?

Great. Well, thank you for that.

(Applause.)

I guess it's not entirely surprising people don't know the details of our laws.

But a question for us now based on the kind of preliminary information that Juli presented, is there anything that we--that you all feel we need to include in the letter we send to the Secretary on this issue. Obviously GINA has been a major topic.

We really don't--we are not armed with all the information we want.

Dr. Billings?

DR. BILLINGS: Yes, that would be me.

I'm curious how many topics are we going to discuss in this letter to the Secretary because , for instance, GINA is past law and, yes, I understand that we need to study it more and more and how it's being applied and whether people really know what discrimination is or not. But is it going to--you know, is it--does it deserve more than we've already published on this issue?

CHAIRMAN TEUTSCH: Well, I will repeat Sheila's admonition to us earlier in my channeling of Reed. KISS, keep it simple. And--

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: That was me, the stupid.

(Laughter.)

CHAIRMAN TEUTSCH: We probably do want to deep it to two or three of the high levels issues. I merely--and I'm not suggesting that we actually want to weigh in on GINA. We have in the past. I just wanted to make sure that folks had an opportunity to make--to say something. We have a

number of things on the record already. I think it just dilutes our message.

I see a lot of head nods.

DR. WILLIAMS: Yes, I would agree. I think there would be--I mean for groups like the public education wing of NHGRI and that--I mean I think this is really important information in terms of what could be brought forward. So I would think there are actionable things here that at the committee level that wouldn't necessarily need to go to the Secretary.

And we've identified others in previous meetings, other issues, which hopefully will still rise to the surface and be addressed.

So assuming that we're good with what we've already said, I see Dr. Williams running on because--

(Laughter.)

--or shushing down a hill.

So the last topic for today is on clinical utility and comparative effectiveness research on genetic tests. As you know, Mark has been leading the task force in this arena and is going to provide an update, and lead a discussion on what the committee would like to convey to the secretary on

this topic.

Marc, I assume I do not need to ask you to speak up; is that correct?

CLINICAL UTILITY AND COMPARATIVE EFFECTIVENESS

UPDATE ON THE CLINCIAL UTILITY AND COMPARATIVE EFFECTIVENESS RESEARCH OF GENETIC TESTS

DR. WILLIAMS: Yes, that was the first observation that no one is going to have any problems hearing me since I'm old enough to have had to project into auditoriums without any sort of amplification devices.

The second observation is I'm glad I'm not working in the insurance industry any more based on that last.

(Slide.)

So I wanted to just bring you up-to-date in terms of where we are. In June we spent some time talking about the third pot of recovery act money has not been publically disbursed, which was the Secretary's discretionary monies. And we spent--unfortunately, spent some time crafting a missive to the Secretary that turned out to be not necessary given that the monies, in fact, had been spoken for but had not been publicly announced.

The final words were announced as of

September 30th and it's a bit embarrassing to stand up here and say that I'm speaking on behalf of the task force when in reality I'm really speaking on behalf of me because there was just really no way to convene the taskforce to try and do the last review in the short amount of time between the announcement and the meeting.

So what you're going to see is a review that I did of the inventory of the funded projects which supplements the previous inventory that you've seen presented in the previous meetings.

(Slide.)

The first approach I did was to do a title search using search terms "genetic, genomic, genome, GWAS and personal" against all of the titles from this last bunch of projects. There were seven NIH funded projects that were identified. Four of which were in oncology. There were no projects--at least the titles of which indicated that they had anything to do in the Secretary's discretionary funds or in the alphabet soup of other Secretary responsible agencies.

(Slide.)

The four studies I think are worth spending just a bit of time on because it represents

a total investment of nearly $16 million.

Programs in clinical effectiveness of cancer pharmacogenomics, comparative effectiveness in genomic and personalized medicine for colon cancer, Center for Comparative Effectiveness Research in Cancer Genomics, and clinical validity and utility of genomic targeted chemoprevention of prostate cancer.

So I think these are projects that really have the opportunity to do some groundbreaking work in determining clinical utility and comparative effectiveness in the realm of oncology.

(Slide.)

The other studies were $4 million for comparative effectiveness in genomic medicine. In some sense when you think of the task of this group when you consider that $4 million was given to the comparative effectiveness of cancer pharmacogenomics and another $4 million for the comparison of cancer genomics, they really have their work cut out since they've got to do all the rest apparently.

There is about $1.5 million that is allocated for the use of genome-wide association study data for enhanced Mendelian randomization studies.

And then of particular interest to me is $3.5 million to build a genome enabled electronic medical record which I think is really very important to highlight given that we've been on record as a committee on several occasions to say that this is really a critically important infrastructure need if we're really going to be able to do anything going forward. So it was very gratifying to see the funding to this project.

(Slide.)

Now, I then did a manual search on all of the titles of all of these projects just to see if there was anything else that could conceivably fit under the rubric of genetics, genomics, personalized medicine, family history, and identified 23 NIH funded studies of possible relevance to genomics. And in some cases these were diseases that were under study where I recognized that there was a significant genetic or genomic component and hoped that that was going to be accounted for.

Another five of these were in oncology. Six were in rheumatology and autoimmune disease. There were five projects specifically devoted to polycystic kidney disease, the autosomal dominant form which is a single gene Mendelian disorder. One

study in autism. There was an interesting warfarin dosing study in the pediatric population which I thought was intriguing and then there four general infrastructure grants that could potentially have some relevance.

(Slide.)

In the other HHS agency monies, this would include AHRQ, HRSA, CDC, FDA, CMS, and I think spell check changed--I'm not sure what HIS is now.

DR. : (Not at microphone.)

DR. WILLIAMS: Indian Health Service. That's right. So that's it. You type "HIS" and it changes it to "HIS." So that's what it was.

(Simultaneous discussion.)

DR. WILLIAMS: So I was desperately going for all the different combinations of those three letters to say, okay, which one is it? So thank you for that.

These were three projects that I identified. One is enhancing cancer registry data for comparative effectiveness. That's a CDC funded grant. There is the registry of registries, which is an AHRQ funded program. And then there's a Maternal and Child Health Pediatric Research Network program which is a HRSA funded project.

(Slide.)

There are also some other monies that have been devoted to some broader issues relating to comparative effectiveness and I wanted to highlight a couple of these because they are relevant to proposed recommendations to the Secretary.

(Slide.)

AHRQ was charged to establish an entity for identification of new and emerging issues for comparative effectiveness research and I think it's fairly safe to say that there would be general agreement around the table that genetics, genomics, personalized medicine and that is certainly one of--has the potential to be one of these emerging issues.

There is a group that was formulated to look at evidence gap identification. This consisted of eight task orders and these were all--the competition was among existing United States evidence-based practice centers. None of these task orders specifically reflect genetics or genomics. There are monies that have been designated for dissemination and translation of findings from comparative effectiveness research.

One is to develop a comprehensive

informatics framework for CER dissemination and then there's an innovative adaptation of dissemination of CER products that specifically relates to autism.

(Slide.)

AHRQ was also charged to disburse ten grants of up to $10 million each related to evidence generation in the clinical and health outcomes initiative in comparative effectiveness. None of these ten grants address genetics or genomics.

Enhancing clinical effectiveness research with natural language processing of electronic medical record--we all know that in EMR there is lots of free text that we really can't do much with. Natural language processing has a way to extract information from free text and create coded information that's computable.

Two grants were--I'm sorry. A grant was awarded that was specifically asked to focus on issues related to asthma and to smoking cessation. There was no specific information about whether family history information would be one of the things that would be looked for with family history but that would be a specific interest for asthma.

There was a request for creation of additional registries and then there is a group

called “unfunded meritorious applications.” So these are applications that have gone in and were deemed meritorious but did not meet the threshold for funding. There is the potential that if other monies are available or if certain projects--if money is not renewed that they can be funded. These are multiple grants with duration of two to three years and funding amounts would be roughly a million dollars each.

(Slide.)

And then finally the Secretary’s office created or I should say issued a contract to develop an inventory of comparative effectiveness research and a second group to research the evaluation and impact the assessment of the research portfolio. In other words, did we get what we think we spent back out of the research?

And there may be others that are related in some way, shape or form to our topic but given the short time for review and the inability to actually look through the abstracts they would have gone unnoticed.

(Slide.)

And I also wanted to bring one other thing to the attention of the group and that is something

that has been referenced previously today which is the Patient-Centered Outcomes Research Institute or PCORI, which was established by the GAO. The Board of Governors has been announced. Apart from the NIH Director--and we understand--at least there are rumors to the effect that the NIH Director actually knows something about genetics and genomics. I'm not sure but I think that may be the case.

There is no member that has had a dedicated career specifically in genetics, genomics or personalized medicine but the chair of the Board of Governors is an obstetrician/gynecologist who has had a research interest in prenatal genetic testing. And one governor is a board member of the NCI Board of Science Advisors, American Association of Cancer Research Foundation, Duke University Cancer Center.

So while there is no one that is a geneticist per se, there are probably at least two board members who are familiar with a significant amount of the science and the ex officio NIH representative obviously is.

There's a methodology committee that is also going to be constituted. The members are currently being solicited with nominations due on October 29th.

(Slide.)

So, overall assessment at least from my perspective is that there has been additional funding given for topics of interest to SACGHS with probably an emphasis on oncology and rheumatology. However, I think it's also fair to say that a number of the 14 priority diseases that are affected by family history, genetics and genomic information, have projects that do not reflect the importance of this.

And there are also some general projects that involve genomics and informatics, which as I mentioned before has been a priority SACGHS issue. So there is a potential I think to enhance genetics and genomics in several of the projects that have evolved infrastructure, registries, dissemination, translation, and evaluation.

(Slide.)

Which brings me to the next or, in this case, the last step from the perspective of the committee and relates to the letter that we intend to send to the Secretary, and in conversations with Steve and with staff I was asked to propose potential recommendations in this area that could be forwarded to the Secretary.

So again I want to represent this fairly as being my work, which I hope reflects the general principles that the taskforce would have applied. I will also mention that from this morning I've actually modified it based on one of the task force member's comments earlier about dissemination and translation. So I've actually modified the recommendations to reflect David Dale's comments earlier. So I guess it wasn't completely out of mind.

I have tried to make these recommendations extremely specific, which I think you'll see, and we will have some time to discuss whether or not these are appropriate.

(Slide.)

I wanted to just give you a brief sense of the background that would be contained in the letter. The workgroup activity recognized the following needs: We have a need for evidence-based recommendations and guidelines. We need definition of thresholds of evidence that reflect context of specific tests and interventions such as rarity of the disorder, clinical situation, the economic impact, the population likely to be affected, and the type of test. All of these are themes that

we've heard this morning and this afternoon as we have discussed the issues that we have been talking about.

We need to determine the value of any given test or intervention which is not only the impact on patient outcomes but also the economic impact on the health system.

We need to understand the ability of our current infrastructure, particularly our information systems and electronic health records, to support implementation and the ability to actually capture post-market data.

Aspects of translation are--there may aspects of translational science that are unique to genomics and personalized medicine, and we need to understand those as well.

(Slide.)

And so here are the recommendations and I'm just going to read through those. The power point that was handed out contains them. And then we can decide how to go forward.

1: Support adoption of recommendations from the American Health Information Community's Personalized Medicine Work Group, as well as the incorporation of knowledge from the ARRA funded

study building a genome-enabled electronic medical record by the Office of the National Coordinator of Health Information Technology or ONCHIT. So again this I think simply reinforces the message that we've sent a number of different times saying that we really need to have the ability to capture this information in a useful way in electronic health records if we hope to do any of this.

2: Encourage incorporation of family history, genetic and genomic information into comparative effectiveness research studies for all 14 priority health conditions as appropriate. So, as I mentioned earlier, in the background we're doing a good job in oncology. We're seeing some progress in rheumatologic disease but for many of the other priority health conditions such as cardiovascular disease we know that there is information that's important but it's really not being reflected in the studies that have been funded to this point.

3: Provide ongoing funding to support and expand development of systemic--I'm sorry, systematic evidence-based recommendations by Department of Health and Human Services funded centers. And in the text--the background text this

is specifically referring to existing groups such EGAPP, GAPPNET, the work that AHRQ has been doing with its evidence-based practice centers in the area of genetics and genomics, and we need continued investment to develop evidence. And while that's-- resources are not going to be solely the purview of DHHS, clearly there has to be a role there. And I suppose 1 could also include CMS and specifically the MEDCAC related to that.

4: Increasing visibility of family history, genetics and genomics for ongoing inventory and evaluation of comparative effectiveness research studies. And here I basically specifically articulated some of the studies that we have just reviewed.

A: Direct the entity charged with identification of new and emerging issues for CER to include family history, genetic and genomic issues for consideration.

B: Designate at least one of the eight centers charged with identification of evidence gaps to focus on issues relating to CER/CU family history, genetics and genomics and health care.

C: Direct the entity charged with

developing an inventory of CER to explicitly collect and report information related to the use of family history, genetics and genomics in all inventory projects.

D: Direct the entity charged with the evaluation and impact assessment of ARRA CER to specifically account for the contribution of inclusion or exclusion of family history, genetics, and genomics information for these projects.

E: Direct the entity charged with developing the comprehensive informatics framework for CER dissemination to ensure that this framework supports information related to the use of family history, genetics and genomics. So this is one that I added this morning so that we can bring the translation piece forward more visibly.

5: If funds are available in the AHRQ unfunded meritorious applications program direct that some of these funds be prioritized to address the gaps in number 3 above. And I added the sub-bullet this morning “encourage some of this funding to be directed to projects that study the translation of personalized medicine into clinical practice.”

6: As openings become available on the

governing board of the Patient-Centered Outcomes Research Institute encourage the GAO to solicit a member with specific expertise in genomics and personalized medicine, and assure appointment of individuals with expertise in evidence-based genomics to the methodology committee.

So I'll turn it over to the chair for how to proceed.

CHAIRMAN TEUTSCH: So this is open for discussion.

I think Marc provided a level of specificity to things we have already discussed. We should talk about whether these are the right things we want to say.

Clearly they are different in specificity to some of the other things that we discussed earlier. So it would probably be just as well to walk through these recommendations first and then see which way we want to go to make sure they are the right ones and what's the level of depth we want to go into for each.

DR. WILLIAMS: Okay. So we'll start with number one.

MS. FOMOUS: (Not at microphone.)

DR. WILLIAMS: I was making sure. I was

looking around to see if there is puzzled body language. I'm not detecting any at least at a level that I'm able to detect it.

So maybe, Steve, it would be appropriate just to do a straw poll to see if this seems appropriate.

CHAIRMAN TEUTSCH: Right. You may want to remind people AHIC (ph) was the organization that was the--it was public-private, right?

DR. WILLIAMS: Well, actually the AHIC was an advisory committee to the Secretary of DHHS and there were ten workgroups associated with the American Health Information Community to address specific aspects of electronic health records and develop standards and recommendations.

The Personalized Healthcare Workgroup of the AHIC made recommendations relating to family history, newborn screening, genetic and genomics to the Secretary. There was to be a follow-up group that would have been a public-private partnership but that has really not emerged.

CHAIRMAN TEUTSCH: It has not materialized, right?

DR. WILLIAMS: Correct. So we did reference this in the meaningful use letter that we

sent several months ago as part of the public comment to say that we think that it was important to take the recommendations from the Personalized Medicine Workgroup forward.

CHAIRMAN TEUTSCH: So that's what those are.

Andrea?

DR. FERREIRA-GONZALEZ: A question. The RC2 grant building a genome-enabled electronic medical record, has it finished?

DR. WILLIAMS: That is funded.

DR. : It just started.

DR. WILLIAMS: And so the recommendation here would be to make sure that the Secretary or a representative would say, "You in the Office of the National Coordinator of Health IT need to be aware of the results of the study and incorporate that into your ongoing work to develop a medical record for use in this country."

CHAIRMAN TEUTSCH: Yes, Barbara?

DR. McGRATH: I think that's a little odd because you don't--we don't even know if that study is going to have recommendations. It may--various things happen with studies. They could have different outputs. So it seems funny to ask them to

adopt recommendations that haven't been made yet.

DR. WILLIAMS: Well, we are not saying "adopt." Well, perhaps the incorporation of knowledge is what I--you know--because there will be knowledge that will be generated by the study presumably. And what I didn't want to have happen was that the study gets done over here and it never gets to the people over here that are actually making the decisions about that.

So I tried to make it in a way that was not too directed but to say we need to make sure that there's communication of this.

DR. McGRATH: So maybe if it just said "and incorporate the knowledge."

DR. WILLIAMS: Yes, Sam?

DR. NUSSBAUM: Just to second what Barbara said. There may be many other studies that are going to address issues that relate to genome-enabled medical records so just the idea of incorporate new information that has been funded by ARRA and other sources because maybe PCORI will fund new initiatives, too.

I think it's a bit proscriptive.

DR. WILLIAMS: Too detailed.

DR. NUSSBAUM: Detailed and proscriptive

when it doesn't need to be. Now whether AHIC--the AHIC workgroup--I'm surprised that that work didn't have a--I know AHIC sort of folded very--went away very quickly, right?

DR. : Yes.

DR. WILLIAMS: Well, the AHIC sun-setted at the end of the last administration.

DR. NUSSBAUM: Right. But I'm saying they didn't pass on the results of all of their deliberations and recommendations necessarily.

(Simultaneous discussion.)

DR. WILLIAMS: We surely attempted to.

CHAIRMAN TEUTSCH: I think they were all made available but I don't think--you're right. They did not seem to have a life after that.

DR. WILLIAMS: Correct.

CHAIRMAN TEUTSCH: I think what Marc is saying is that there was some thoughtful work done that now needs to be incorporated.

What I hear you and Barbara saying, Sam, is that we probably want to just say that that--as work goes forward in the area of developing the electronic health record as it relates to genomics that we need to be cognizant of those recommendations.

DR. NUSSBAUM: Yes. Let me--perhaps let me share where I think this should go. The Secretary is going to be busy for weeks reading all of our recommendations. This might be one where with a lot of specificity we might be better off actually crafting a thoughtful statement that says that here in a time of comparative effectiveness research and all of this ongoing study that we encourage or we support--and then sort of capture these same themes. But you know it just feels recommendation after recommendation that--

DR. WILLIAMS: Yes.

DR. NUSSBAUM: --hitting hard with stuff that not us but others have done two years ago with a study that's not funded with PCORI that actually--I'm not sure who it reports into. It was determined by GAO. Does it report to the Secretary? PCORI? It's in the Affordable Care Act but--

CHAIRMAN TEUTSCH: Well, it's public-private partnership.

DR. NUSSBAUM: Right. But who is making nominations to PCORI should there be openings? Is it the Secretary? I'm not even sure it's her jurisdiction. That's the point. I think that a lot of these issues--they're all meaningful. They're

all good but maybe they can be shaped in a way that is--that it captures that. I just don't--

DR. WILLIAMS: Well, let me pull back to one because we'll get to PCORI. One of the things--all of the studies that I referenced here were ones that were funded out of the Secretary's discretionary funds. Now some of those discretionary funds were seeded to other--to NIH and to other organizations to do that but these are all ones that--these are all monies that were discretionary to the Secretary and so that's why I thought it might be appropriate to highlight issues of which discretionary funding was used to reflect back to say here is how you could actually apply this in the general scheme of things.

Now it may well be that, you know, we have--we have previously communicated and maybe we don't need to communicate again about the AHIC recommendations. I think we do personally because we're still not seeing a lot of movement there. But because funding was specifically designated with the idea of creating the genome-enabled electronic health record it just seemed a shame not to say, 'Hey, you know what? You're doing this, don't waste the opportunity.'

But you're quite correct there are other studies that may also--

DR. NUSSBAUM: I guess--let me try this one more time. I guess I'm just--when all of this funding took place under ARRA, the $1.1 billion, it seems to me a little bit presumptuous of us to believe that people wouldn't use the output of that research to actually make a difference in how information is gathered and how care is given. That's the whole point of comparative effectiveness research.

So for us to sort of say, you know, in a sort of dogmatic way use the information to drive better outcomes I think is valuable but it's premature. Of course one would hope that all the work that gets funded, whether it be in cardiovascular disease, gets used. I just don't know why without any output yet we should be, you know, pretty demanding about it. That's all.

CHAIRMAN TEUTSCH: Go ahead, Sheila.

MS. WALCOFF: I thought you were about to say something.

CHAIRMAN TEUTSCH: I was but I'm glad to hear you.

(Simultaneous discussion.)

MS. WALCOFF: I think--I want to try to say it a little bit differently because as I look at this in terms of how to get the attention of the Secretary or folks working on comparative effectiveness now, and I think there are a lot of very excellent points made all the way throughout but the first thing that really comes to my mind is there's obviously a well known and substantial focus on implementing health reform right now. And I think that's very pervasive throughout the department, throughout the government and certainly throughout the White House.

If it's possible to try to capture the good points that are made through here in a way that says kind of with the banner as you work to implement health reform related to comparative effectiveness research specifically related to the establishment and commencement of activities under PCORI, here are the three things that we think that you need to keep in mind or, you know, as you process that. As you develop this in an organization that's quite unknown to everybody because it is so brand new--what are they going to do--as you walk through all of those other issues keep these three top key points right at the

forefront of the development of that kind of comparative effectiveness research as something that's sort of pervasive throughout.

I think that is something that is maybe a little bit more concise and probably a little more general than this but also something that I think would get some attention just because it ties into exactly what they are focused on and looking at right now.

CHAIRMAN TEUTSCH: So--

MS. WALCOFF: I didn't help that much.

CHAIRMAN TEUTSCH: No, it helped. I'm just trying to think what the three main points would be.

DR. NUSSBAUM: In my thinking that helps--

MS. WALCOFF: If I turn my mike right off after this.

DR. NUSSBAUM: Sheila, in my thinking that helps beautifully because that's what I think we want to do is bring attention to the field, the space, the work that's being done but again it's--I think everything is perfect up there. It's just a little bit, I think, too premature, too prescriptive, too unknown. And I'm not even sure--if we're not even sure of the reporting structure,

how these seats are going to be fill, to write to the Secretary with specific information may be--may show our lack of understanding rather than our deep understanding.

CHAIRMAN TEUTSCH: So I'm hearing a couple of things at least in this discussion. One is we still have the pervasive issues that we need to have electronic health record systems being built that allow for the incorporation of genomics in a systematic way. That's sort of what this one--this first one is about, right?

DR. WILLIAMS: Mm-hum.

CHAIRMAN TEUTSCH: The second I've heard is that in comparative effectiveness research where it's appropriate that there should be--we should encourage the genetics component to be included as part of those studies. Isn't that the second one that you've raised? I'm not sure what the third one is other than that PCORI itself, you know, will need to address the issue of genomics and will need the requisite expertise as part of its methodology committee.

MS. WALCOFF: I think that's a very important as they try to decide who is going to be on the committee.

DR. NUSSBAUM: I think the answer there is to emphasize--and, Marc, you've done this--is that there has been an underrepresentation. That's your point, an underrepresentation on the Board of Governors. We don't know what's going to be on the methodology committee. So to emphasize the vital importance of this information both for effectiveness research, outcomes research. So I think that's the frame of doing it and encouraging that there be consideration of even greater expertise as other subgroups are developed. That's a positive response.

CHAIRMAN TEUTSCH: David?

DR. DALE: I was just going to comment. I think you've got it right, Steve. The inclusion in the record and then the comparative effectiveness of genetic testing or genetics and genomics because there is an important role compared to other traditional ways of making diagnosis. It's a big unknown and it's part of the central issue in terms of paying for genetic testing is how valuable is it.

So we need to encourage that and I think from Marc said, and he's my only reference, not enough has gone into that area. So that's where--we appreciate what's happening but we would encourage

more and then a strategy to make that information available and interpretable by clinicians.

CHAIRMAN TEUTSCH: Gurvaneet?

DR. RANDHAWA: If I can add some context here. There are at least two grants that I'm aware of within our PROSPECT program which is one of the RFAs that I wrote for building a new clinical electronic infrastructure for prospective outcomes. And two of those grants have genomics and biomarkers as part of that.

The challenge is not just having an EMR that can contain family history or genetic test results in an easily identifiable field but also how do you extract information from different EMRs using different methods. And so it's not just only building an EMR but building the methodology to do comparative effectiveness research.

And one of them that you might want to think about is we also have a new cooperative agreement with Academy Health on electronic data methods forum, which is doing exactly what David said, which is using methods or advancing the field of methods in using electronic information for new comparative effectiveness research. Its specifics are still to be defined. The fields of action are

still to be defined so that might be a place where we can focus our energies also.

CHAIRMAN TEUTSCH: So I've heard two things regarding the electronic health record. One is to make it so it's capable of doing research and the other I thought you were also saying was so that it facilitates the translation into practice.

DR. DALE: An example of that is if you test one member of a family where all the members appear to have the same disease, how do you incorporate the genetic testing of one individual into the diagnostic strategy for another because it's a common thing particularly in autosomal dominant disorders.

CHAIRMAN TEUTSCH: So if we go in this direction, in sort of a more summative two or three high level kinds of thoughts--Marc has a lot of detail in here--its detail that my guess is--those who are listening to this conversation--have not really been reviewed within HHS. Maybe I'm wrong. We could capture it in other ways besides a letter.

In an appendix as an example of at least some of the preliminary analytics that have been done on this. So we don't--I only worry that we don't lose some of the work that you've done.

DR. WILLIAMS: And if I can just interject.

I mean looking specifically at four I think there is--we have an opportunity here in the sense that these are grants that have just been announced and it's not clear--and I was talking with Gurvaneet earlier--it's not clear from the summary paragraph that the investigator provides what it is they are actually intending to do.

So in some sense I think four represents an opportunity to provide direction to the project officers of these grants to say you need to make sure that these include this information or you need to assess whether this is something that's going to be critically important.

I mean so in some ways I'm pushing back a bit because I think we have the opportunity to actually change the playing field for some of this that's going to be critically important to answer some of the bigger questions that have been identified moving forward.

CHAIRMAN TEUTSCH: Charmaine?

DR. ROYAL: I was wondering whether we should nominate someone for the methodology committee. Is that something that would be

appropriate for us to do as they're soliciting nominations or is it not?

Sheila, what do you think?

MS. WALCOFF: As far as I know. I actually don't know in detail how the--I think they are supposed to take nominations from any group. I don't think there are particular limits. I think we certainly could.

CHAIRMAN TEUTSCH: With *Federal Register* announcement for--

DR. WILLIAMS: Yes.

CHAIRMAN TEUTSCH: --solicitation.

MS. WALCOFF: So I think that that is something that we could put in there.

I also--just to follow up on this point on point four. Just in terms of being specific on grants that were just announced maybe what we really should be saying is direct the project officers on these grants to do X, Y and Z because that actually is something that you can undertake to do that doesn't involve getting appropriations or making major policy changes.

It's actually a legitimate step that is very focused. It's not kind of the three key points but it's here with respect to these recently

announced grants here is some action you can take in the meantime while you're working on figuring out what PCORI is, what led to it, what the methodology of it is going to look like and what methods they might actually put into place.

CHAIRMAN TEUTSCH: So one could either--if we have a general statement about the importance of incorporating genomics into comparative effectiveness research agenda we could either in the text or as part of that say "and as a first step in that process one could look at the projects that have already been funded and to the extent possible incorporate them in there," and then provide this list as an appendix.

You'd like it in there whole. You are--

DR. WILLIAMS: Well, I'm just--

(Simultaneous discussion.)

DR. WILLIAMS: --listening to what everybody has always said about the reports about where people actually read and the appendix never comes up.

(Laughter.)

CHAIRMAN TEUTSCH: Although the project officer might look at them.

MS. WALCOFF: That's what I mean by

saying, you know, really putting it up at the top. Because when you start with increasing visibility of--you know, and sort of--it starts to sound very general and you have the very specific points below.

I think my point on that would say direct the project officers to X, Y and Z.

DR. WILLIAMS: Yes.

MS. WALCOFF: So that's so they can actually undertake to do something that's starting at the right time and ongoing but it fits under I think the more general importance of incorporating this in.

CHAIRMAN TEUTSCH: Preferences, folks, which way you want to handle that?

I mean one is you'll end up with a fairly long list in this recommendation, which is okay too, and a level of specificity.

DR. WILLIAMS: It's a long list but it's--as Sheila points out, it's easily actionable by the Secretary's staff in the sense to say, "Okay, we've even referenced what the projects are. The project officer--this is--we think this is a good idea."

MS. WALCOFF: I think the rest of this should be shorter. So if we can try to fit it--as you said, when you go to the appendix, I think if

we're going to have a lot of additional details it's not going--everything is going to get lost. But if we are able to say these issues are important throughout development and execution of comparative effectiveness research. And as a first step the project officers for recently announced grants should do X, Y and Z, and here are these six things that--here are some examples.

CHAIRMAN TEUTSCH: So if you back one slide to two. That's the general statement it seems about incorporating them.

DR. WILLIAMS: Yes.

CHAIRMAN TEUTSCH: And then what we've got for four is a level of specificity.

DR. WILLIAMS: Yes.

CHAIRMAN TEUTSCH: If I hear--if I understand what you've done, Marc, is a level of specificity and you can sort of say if we--leave 2 as the main point and then sort of have that bullet as a first step.

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: That would at least simplify things a little bit.

CHAIRMAN TEUTSCH: If we look at--let's look at three for a second, whether we want to ask

for funding. It probably needs to be a little bit more specific about how--what we want--I mean the expansion of systematic evidence-based recommendations is fairly broad. Is there something we want to say specifically about that?

DR. DALE: I think that--I would suggest making 3-4. And there's another word that you might think about. It's the word "visibility." We may be concerned about visibility but I'm not sure that's what we want.

DR. DARIEN: Aren't you talking more about integration?

DR. DALE: I think so, yes. Something--

DR. WILLIAMS: Integrating genomics and family history into the systematic evidence-based recommendation process. Right? Isn't that what we want to say?

DR. DALE: Yes.

MS. DARIEN: Yes, that's what I would say.

MS. WALCOFF: (Not at microphone).

DR. WILLIAMS: Now, just to be clear--and I didn't articulate it here. It's in the proposed text of the letter. What we were talking--what I was thinking about at least here were the specific genomic evidence centers that currently exist, EGAPP

(ph), GAPPNET, the AHRQ projects that are specifically around genetics and genomics. In other words, we're already funding some of that, you know, systematic evidence review and we know that we need more evidence. So it's not so much the visibility of that evidence but it's really actually increasing the throughput of evidence evaluation around existing tests.

DR. DALE: Marc, if I understand it, though, I think that 4 as you have it numbered there is the bird in the hand.

DR. WILLIAMS: Well, 3 is a bird in the hand, too.

DR. DALE: I think 3 is the bird in the bush in the sense that it's a gimmee (ph). You want more money for this but 3 is 4. What you have listed is concrete.

DR. WILLIAMS: Three is very concrete in the sense that at least in my--in the text in the letter which you haven't seen it articulates the current evidence work that's being done in genomics, EGAPP (ph), GAPPNET, AHRQ, et cetera.

But I look at 3 as being very tangible as well as 4. These are things that--you know, because one of the issues quite honestly that's coming up

with GAPPNET is the sustainability discussion about how to--you know, CDC has basically said we can't fund sustainability out of our funds.

So if that's the case then are we going to continue to limp along as a volunteer organization. That's going to impair our ability to actually generate more evidence.

So even though the statement 3 here doesn't reflect tangible entities, and maybe it should, the reality is that my intent in putting that there was to fund tangible entities that currently exist and are currently working.

MS. WALCOFF: I think the ESGs (ph) that are currently existing and currently working, in particular AHRQ and the work that they've been doing for such a long time in comparative effectiveness research, you know, one of my concerns is that we get lost because we have sort of a new thing, a new entity in PCORI and everybody is talking about it.

I'm wondering if there's a way to say that though that doesn't start with "funding" because I think that--I think that the work that they are doing has been funded and is being funded. Of course, everyone wants more funds but what I really want to do is make sure that people recognize that

work and incorporate it because PCORI can't do everything. They are not going to be the one stop shop. I mean it's already integrated throughout in particular with AHRQ.

So I think I'm--I feel like what you're trying to say, Marc, is we don't want to lose that. We want that to continue to be ongoing just because there's a new organization that's working at this and doing it in a more public fashion perhaps, and we don't want to lose the work that's being done there and it should continue.

DR. WILLIAMS: So I just want to make sure we're not confounding two things because, you know, PCORI is sort of six but there's work that's already going on that's specific to genetics and genomics in terms of doing the evidence-based reviews. So I'm not sure I understand how those two recommendations are--

CHAIRMAN TEUTSCH: Let me see if I can help, David.

I hear two different things. One is the comparative effectiveness research agenda.

DR. WILLIAMS: Yes.

CHAIRMAN TEUTSCH: Which we are supporting, and that is where a lot of those ARRA

funds went. Right?

The other then is developing evidence-based recommendations, which has been done by EGAPP and others, a little bit by--some by AHRQ. So we have the recommendations. So those are two things that we want to--I think want to get across, right?

Then we have the institutional issues which are more confusing because we have all of--a variety of federal agencies plus this new entity, PCORI, which have somewhat overlapping and yet to be teased our issues. I would suggest that at least on that score that we not get into that because that's not particularly a genomic issue other than we think that PCORI needs to be strong. The research agenda needs to be developed with appropriate genomic information and we need to have evidence-based recommendations.

I wonder if we can sort of keep--sort of separate those out in a way so we can keep them fairly neat and not confound the research and the evidence with the institution.

DR. WILLIAMS: Right. Yes, I mean, I think that that's good because as I think about the charge to the workgroup it was comparative effectiveness and it was clinical utility. So 3,

the EGAPP, the GAPNETT, and that is really more, I think, the recommendations relating to utility at least as I think about that.

And then the--as Steve had previously proposed combining 2 and then adding the more specific recommendations under 4 as more related to the comparative effectiveness research agenda and how that needs to reflect family history, genetics and genomics.

When then leaves, as you say, the other issues, PCORI and the other agencies, and we still have the informatics and infrastructure pieces that are sitting out there.

CHAIRMAN TEUTSCH: So talk to us a little about 5 or what on this one is number 5.

DR. WILLIAMS: So this is again--it's very specific and again this could be--this could be condensed if we want to include it at all. It could be condensed into the whole section on comparative effectiveness research because these are monies that are designated to AHRQ to fund CER meritorious applications that are not currently funded but where there's a presumption that either because there will be non-renewals or withdrawals or additional funds AHRQ has been charged to fund additional proposals

and projects.

So this would be an opportunity to in some ways to prioritize some of these 14 priority diseases to incorporate the genetics, genomics and family history.

Or are these monies already spoken for, Guvraneet?

DR. RANDHAWA: No, these are--it's just a reflection of the grants that we didn't have enough funds to support but they are meritorious. So they could come in for another round of funding. We have our baseline funding for supporting research and that it's on a rolling basis where the applicants can apply, revise and resubmit their applications.

DR. WILLIAMS: Okay. So maybe the other question as to whether or not this should even remain is would AHRQ be amenable to direction to say that in terms of the prioritization of funding for these grants that are in the queue that consideration of incorporation of family history, genetics and genomics could be used as one way to prioritize which would receive funding through this program.

DR. RANDHAWA: I cannot speak to that.

DR. WILLIAMS: You may not be able to

answer that question in a public venue.

(Laughter.)

CHAIRMAN TEUTSCH: Let me see if I can try this because again this is--that gets into a very high level of specificity on some specific proposals.

I think what we want to say is that we believe it's important to do research on the translation of appropriate genomic--use of genomic testing and family history into clinical practice. We can make that statement. In which case I think if you like--if you buy that I think we have five things we want to say.

Steve, let me try these on you.

So we're talking about this in the context of health reform. There are five things. One is we need to have the electronic health record developed in such a way that it incorporates genetic information for use in practice and facilitates research. That's one.

The second is that it be incorporated into the comparative effectiveness research agenda, and you can then have a sub-piece with all your specifics.

The third is the capability, expand the

capability to make evidence-based recommendations for clinical practice.

The fourth is to conduct research for translating effective technologies into clinical use, which is what I think 5 is.

And then the last one would be to assure that PCORI has the expertise it needs to take advantage and to understand the use of genomic information as part of the comparative effectiveness agenda that is--patient-centered outcomes research that it is going to have in its purview. That's sort of a simplified version of what you have here, I think. I don't know.

Just running a trial balloon up, folks.

MS. WALCOFF: I think the simplified version is good. I think it's hard because it's late in the day and we can't really see it but I think if you get those down--is this something we're going to discuss to try to clarify and get the fine details down?

CHAIRMAN TEUTSCH: Because we're going to assign Marc the task of clarifying all of that tonight.

DR. WILLIAMS: Marc may not accept the task.

MS. WALCOFF: Somebody has been typing furiously, though, haven't they?

CHAIRMAN TEUTSCH: I hope so. I hope we have some good notes.

The question is really what we want the thing to look like. I have tried to sort of distil it down into the longer term recommendations as opposed--and getting away from the very focused piece. I guess that's the question for all of you.

If you look at number 5 it's very focused on a specific set of things and the question is do we like that or do you want a more generic statement about the importance of the translational research?

DR. WILLIAMS: Well, obviously I prefer a little bit more focus because of the opportunities that current exist from funding but that's just me.

CHAIRMAN TEUTSCH: Well, that's what we need--that's what I would love to get the sense of this group about is--I mean it has the advantage of being more directly actionable, right, here and now, a little less forward looking but that's what we want to hear. There are tradeoffs depending on how we do it.

Or you can make the general statement and then put it under here as an example. We can sort

of have our cake and eat it, too, I suppose. But we don't want to make these overly complicated.

DR. DALE: Well, I'll take the initiative and make a general comment. I think that despite our senescence or termination--

DR. WILLIAMS: You didn't say dementia. I was appreciative of that.

(Laughter.)

DR. DALE: --that this field needs a demonstration of its value and utility, and that's near term most likely to come by what Marc suggested in terms of practical application of funded areas. So I would make a pitch for doing that.

The longer term issues will then fail on their own if, in fact, some utility is shown by evidence-based review and comparative effectiveness analysis of genetic testing but we need some evidence.

CHAIRMAN TEUTSCH: Gwen?

MS. DARIEN: So I think Sheila's recommendation was a really good hybrid of this because I think that it gave a context within which we were making these recommendations which demonstrated an awareness of what was going on outside of this room, which I think is really

important, but it allowed for the specificity in that one particular example. So I actually--I think that is a really--I think that was--that's a really good approach because I also think as soon as you start getting more you get lost in the specifics and you forget the high level point that you're making.

CHAIRMAN TEUTSCH: So help me with number 5. What will that look like under that scenario?

DR. WILLIAMS: Well, if I understood what Sheila was saying, and actually I did have some sense of affinity for that as well, I could see this being added to that sort of laundry list that you would compress this into a sub-bullet in terms of direct the project officer for the unfunded meritorious applications program to do this.

In that way you would--all of the specifics then would be captured under one recommendation as opposed to elevating any of the specific things to an overarching priority.

I think where we got distracted was the--we then got confused around the EGAPP, GAPPNET, PCORI and other alphabet stuff. So--but I think the overall organization that Sheila had proposed was--I thought it was pretty reasonable.

CHAIRMAN TEUTSCH: So tell me what the

overarching one is going to say?

DR. WILLIAMS: I am going to turn back to Sheila because I'm not sure I can capture it.

MS. WALCOFF: I was trying to capture that in number 2.

DR. WILLIAMS: Yes, but if it's--

MS. WALCOFF: Although we can't say 14 priority health issues because I feel like then you're wondering where does that reference back to.

DR. WILLIAMS: Well, the 14--

MS. WALCOFF: Or maybe it's related to the--

DR. WILLIAMS: That's all part--that was all embedded in the ARRA funded CER projects that they are specifically focused on these 14 priority conditions, which is--so I pulled that directly from the enabling.

MS. WALCOFF: I think actually maybe just end it after encourage incorporation of family health, genetic and genomic information into CER studies. Is that kind of the biggest overarching--

CHAIRMAN TEUTSCH: Yes, I would think--I would had one word. The CER and translational studies because this last one is about the translational work rather than the evidentiary work,

right?

DR. WILLIAMS: Right. Okay.

CHAIRMAN TEUTSCH: So that--

DR. WILLIAMS: Okay. And I'm assuming either Sarah or Kathy are capturing this.

MS. WALCOFF: Maybe you could even be more--instead of encourage, you could just say incorporate.

CHAIRMAN TEUTSCH: Right, right.

DR. WILLIAMS: Okay. So incorporate family history, genetic and genomic information into CER and translational studies.

CHAIRMAN TEUTSCH: Right. And then we'll have that set of--

DR. WILLIAMS: Period.

CHAIRMAN TEUTSCH: --you know, as a first step.

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: We'll have that laundry list from--

DR. WILLIAMS: As a first step direct the project officers to blah, blah, blah. Okay.

CHAIRMAN TEUTSCH: So that simplifies.

DR. WILLIAMS: So that takes care of 2, 4 and 5.

CHAIRMAN TEUTSCH: Right. That's good.

And what do we want to say about 6?

Do we want to be specific about these particular boards or do we want to be more generic?

DR. WILLIAMS: Well, you know, I had the same--somebody raised this issue and I wasn't clear on this as to what role the Secretary actually has in the constitution of these committees given that GAO is actually doing the population. So that wasn't clear to me either. If the Secretary really doesn't have anything to say about this then it's not appropriate to make a recommendation to her.

CHAIRMAN TEUTSCH: She certainly has people on this governing board.

DR. WILLIAMS: Well, the methodologies committee also will have a representative from NIH and from AHRQ.

CHAIRMAN TEUTSCH: Gurvaneet, who does PCORI report to?

Do you know?

MS. WALCOFF: I can't remember right off.

I ought to know because I read an article about this but I don't remember right offhand who they report to but I would say that in terms of getting attention because this is sort of happening

right now I was thinking of it more as a banner framework. But I didn't want to do that in a way that diminished the work that was already ongoing by the other parts of our alphabet soup that we have been working so closely with for all these years that are doing important work.

So I guess my point was really not to worry about so specifically whether--this is against what I typically say. But, you know, sort of what her role is in directing it--but the fact that it's ongoing ought to get the attention overall and has got the attention overall of HHS certainly and others that work with HHS very closely on the implementation of health reform. And just sort of by acknowledging that and then move into incorporate into our actual specific recommendation and then to even our more specific steps that staff could actually take right away, and then check in the box to say we did this, we actually did push it forward.

DR. WILLIAMS: So, as written, do you think 6 is actionable or not?

CHAIRMAN TEUTSCH: She can certainly encourage.

DR. WILLIAMS: Yes. I'm not sure she's going to assure.

MS. WALCOFF: I think that really what you need to say is that this expertise is necessary.

CHAIRMAN TEUTSCH: Right.

DR. WILLIAMS: Okay.

CHAIRMAN TEUTSCH: I would think she has a role in ensuring the availability of the necessary expertise in genomics and family history--

MS. WALCOFF: Of course you could argue that is being accomplished by the agency representatives that are participating.

CHAIRMAN TEUTSCH: And who she nominates.

MS. WALCOFF: Right.

CHAIRMAN TEUTSCH: The governing board, at least as I thought, didn't tend to have a lot of subjects. It wasn't designed for subject matter--

(Simultaneous discussion.)

CHAIRMAN TEUTSCH: I think it's the methodologies group that actually needs the expertise and then the people who actually select the specific studies, which is more of an internal mechanism rather than a governing mechanism.

Do you agree?

MS. WALCOFF: Also, too, how it's communicated out because one of the charges is to communicate it rather rapidly publicly. So I guess

the short answer to that is to narrow this down to a more--in a way a broader statement that this expertise is essential to PCORI in particular and perhaps the methodologies group.

DR. WILLIAMS: So perhaps something that says the SACGHS thinks that expertise in evidence-based genomics is essential to the PCORI methodology committee and urges the Secretary to assure or encourage that this expertise is represented on this committee.

CHAIRMAN TEUTSCH: Ensure the methodology committee has expertise in evidence-based genomics.

DR. WILLIAMS: I mean the verb to some degree is a little bit difficult because if the Secretary doesn’t have direct control over who is going to be on the methodology--

MS. WALCOFF: You could say “should identify specific expertise as an essential component or the expertise necessary to form the methodology committee or to be broader and say PCORI but specifically the methodology committee.

DR. DALE: But to solicit the expertise, not necessarily to be politicking for a member.

CHAIRMAN TEUTSCH: Right.

DR. DALE: That has a negative

connotation.

MS. WALCOFF: Well, whatever her role will be with respect to selecting agency personnel or simply, you know, responding to an inquiry of another senior official who might have the direct responsibility of doing this. For example, they do talk. You know, the department heads and so we could recommend that she identify this as an important specific expertise that needs to be there. It's proactive but it doesn't sort of limit her.

DR. WILLIAMS: So we need to work on the verb.

MS. WALCOFF: She may not be able to assure.

DR. WILLIAMS: Work to assure or whatever.

MS. WALCOFF: But she could certainly raise it and identify it and speak to it.

CHAIRMAN TEUTSCH: Do you have enough direction and can you help us craft something for review tomorrow?

DR. WILLIAMS: Well, before we--I mean in some ways I would almost ask if Sheila could help on 6 because I--

CHAIRMAN TEUTSCH: Can you help with 6, which is now 4?

MS. WALCOFF: My bullet will be a bullet.

(Simultaneous discussion.)

MS. WALCOFF: You can number it however you like.

DR. WILLIAMS: Yes. I think that would be helpful because I'm not exactly sure how to phrase that.

CHAIRMAN TEUTSCH: If you could work on the first three.

DR. WILLIAMS: Well, okay. So 1 is basically going to sort of stay--it's going to change in the sense that we're going to make this an overarching issue with perhaps a couple of sub-bullets. It specifically says "The AHIC recommendations of this and other research related to incorporation." Is that--

CHAIRMAN TEUTSCH: If you want a sub-bullet that's fine. I would keep it simple. The EHR has the capabilities for clinical genomics.

DR. WILLIAMS: Okay.

CHAIRMAN TEUTSCH: And if you want to--if you feel like you want to be specific I'd only caution that since AHIC is no more--

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: --and was done by a

prior administration--

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: --it may be just as well to be--

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: --you can refer to it in the next as having--as being a good resource for this purpose. That's probably what I would do.

DR. WILLIAMS: Okay.

CHAIRMAN TEUTSCH: And then the second one is the research agenda, right?

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: Comparative effectiveness and translational research with that list.

DR. WILLIAMS: Yes.

CHAIRMAN TEUTSCH: As a sub-bullet. And the third is about the evidence-based recommendation generation.

DR. WILLIAMS: Right.

CHAIRMAN TEUTSCH: And the fourth one is the one Sheila will be working on about the PCORI capabilities.

DR. WILLIAMS: Okay. So just to go back to the third one which is--so do you think I should

include specific examples in this or is 3 as currently written adequate?

DR. : (Not at microphone.)

DR. WILLIAMS: It's not related to 2. It's not a sub-bullet of 4. It's separate.

CHAIRMAN TEUTSCH: Do we want to have funding in here or do we just want to talk about the capability of--of expanding the capability to do this?

DR. WILLIAMS: Yes. Okay.

CHAIRMAN TEUTSCH: And I think what I would probably do is the same thing we just talked about. Rather than prejudging what that's going to be, EGAPP, GAPPNET or whatever, or NIH, whoever is going to--or AHRQ, whoever is going to assume all this, you can put that in the text. We can just make sure that we have it captured there that these are the entities that are moving that forward. I think you do mention it in the text, right?

DR. WILLIAMS: That's my recollection.

CHAIRMAN TEUTSCH: I'm trying to remember.

DR. WILLIAMS: But I'm a bit kerfuffled at this point.

CLOSING REMARKS

CHAIRMAN TEUTSCH: So if we're good here--

Sarah, you have a draft letter that you've already begun to craft; correct?

And who has seen that letter?

Nobody.

One at 11:00 o'clock last night.

Do you plan to make that draft available to everybody in the morning? Is that where you are?

And what we'll have then to insert into that are what Charis is doing with Paul in terms of whole genome sequencing work.

We will have some of Marc's language, I think, because you incorporated the text already of Marc's in there.

MS. CARR: Yes.

CHAIRMAN TEUTSCH: But modify the recommendations along the line of what we just discussed. Correct?

MS. CARR: Right.

CHAIRMAN TEUTSCH: And then we will have from Charmaine tomorrow some of the last piece--the main piece, I think, on the data sharing.

MS. CARR: Data sharing.

CHAIRMAN TEUTSCH: The good news, Charmaine, is you have the benefit of all of our angst today so that might help with figuring out how

we want to do this since you won't have the benefit of a night to redraft unless there's something you want to get feedback on at this point but it's probably a little hard to do. We'll deal with it tomorrow.

The last thing, of course, is Barbara and folks will be working on--hopefully it's the final version of the recommendations for the education and training work as we have re-discussed them.

So we have a lot to do tomorrow, folks.

Yes, Marc?

DR. WILLIAMS: I would like to add one more thing which is the suggestion that Charmaine made, which I think is a good one, which is to consider whether we as the SACGHS wish to put forward a nomination for the PCORI methodology committee. I think that's something that we could potentially act on as well if there was a name that came up that we thought would be worthwhile.

CHAIRMAN TEUTSCH: I would suggest if we want to do that we just nominate that person. That doesn't need to go in the letter, right?

DR. WILLIAMS: No, I know. No, this is separate from the letter.

CHAIRMAN TEUTSCH: So do we--let's open

the floor. Do we want to do that?

Could we do that?

Would we know who to pick?

DR. : (Not at microphone.0

CHAIRMAN TEUTSCH: What's that?

DR. MANSFIELD: I think we should nominate Marc Williams.

CHAIRMAN TEUTSCH: There you go.

DR. : I second that.

CHAIRMAN TEUTSCH: There you go.

DR. WILLIAMS: I am not a methodologist.

CHAIRMAN TEUTSCH: I'm not sure the methodologies committee is going to be made up of all methodologists either. That remains to be seen.

Well, let's do this in two steps.

How many people think we should make a nomination? And we have not generally done that I don't think.

(Show of hands.)

But I see one, two.

How many people think we shouldn't be doing this?

How many abstain?

(Show of hands.)

(Laughter.)

I'm concerned about all those abstentions.

MS. WALCOFF: I was just thinking--I'm struggling because I'm not sure--I don't think there's a down side to it. I just--I know that there is a lot of--you know, there's more supporting than just putting a name forth to accomplish that.

CHAIRMAN TEUTSCH: Could I suggest this because, I mean, I think Marc is a great candidate--and, Marc, I assume--you have the prerogative of putting your name forward. You have also the prerogative of having anybody in here put your name forward, which can be done. But we not do it as an institutional nomination.

DR. EVANS: (Not at microphone.)

CHAIRMAN TEUTSCH: Former chair?

(Laughter and simultaneous discussion.)

CHAIRMAN TEUTSCH: I can see we have gotten to that point in the meeting.

So let's--if I were to put your name forward, Marc, which I'd be happy to do, it would be as a private citizen and not as the chair of this committee.

MS. WALCOFF: Is that--I'm actually wondering can we do that under lobbying rules.

CHAIRMAN TEUTSCH: What?

MS. WALCOFF: Nominate somebody.

CHAIRMAN TEUTSCH: Well, we can do that as individuals.

MS. WALCOFF: No, no, no. That I know we can but I meant as a committee.

CHAIRMAN TEUTSCH: I don't know.

MS. WALCOFF: But I guess that's off the table.

CHAIRMAN TEUTSCH: Sarah, as our keeper of parliamentary truth, are we allowed to do that? Are we allowed to nominate somebody?

Well, we only make advice the Secretary and this nomination--it was strange. If I remember, seeing the *Federal Register*, it didn't go to GAO but it went to some other non-HHS part of the government; right? Where did it go?

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: Yes, it was something odd like that. It was odd that it didn't go to GAO, too, and I don't remember why.

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: Comptroller General. There you go--all right.

With everyone's permission--I got the sense we're not doing it as a committee. We can do

this independently. And obviously there are other groups out there who can and should be submitting nominations and reinforcing nominations of, you know, some of the individuals whose names are being put forth by others.

Okay. So I think--Sarah discreetly moved far away from me today. She is usually here holding my hand.

So are there other things we need to do before we adjourn for the day, Sarah?

MS. CARR: No.

CHAIRMAN TEUTSCH: No. All right. So it sounds to me like we've got a fair bit of work to do tonight.

And logistics--we get the shuttle where we got it before; is that right, Allison?

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: We presumably catch the shuttle where we did before?

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: Okay. And presumably it is out there, right?

DR. : (Not at microphone.)

CHAIRMAN TEUTSCH: Yes, it's not very early. And then we've got--then at 6:30 for those

who are going to dinner.

And then we start tomorrow morning at 8:30 so that means we’re meeting--for those who are coming back--at 7:30 to catch the shuttle tomorrow morning.

Thanks, everyone, for a huge amount of work.

(Whereupon, at 5:15 p.m., the proceedings were adjourned.