SECRETARY'S ADVISORY COMMITTEE
ON GENETICS, HEALTH AND SOCIETY

Twenty-First Meeting

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I N D E X

Updates from Federal Agencies

P R O C E E D I N G S

OPENING REMARKS

CHAIRMAN TEUTSCH: Well, good morning, everyone, and welcome. It's good to see everybody here. Hopefully, we'll have a productive meeting and I hope everyone had safe travels. I know there's some anxiety about travel tomorrow and we'll talk about that a little bit later as we see what we can do about the schedule but thanks to everyone who is here and—

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

We want to welcome everyone in attendance. We certainly are delighted to have members of the public, as well as viewers on the webcast. We appreciate everyone's interest in our work.

We have scheduled public comments for later this morning and again tomorrow that we'll look forward to hearing from members of the public at that time.

We have a lot of things to cover this morning and I wanted to give you all an update on

activities and sort of the plans for the meeting as a whole.

We'll begin today with some preliminary planning for a June session on the implications of the affordable whole-genome sequencing, followed by an update on activities of the Clinical Utility and Comparative Effectiveness Task Force.

The rest of the morning will be devoted to the review and discussion of the committee's draft report on Genetics, Education and Training, and its draft recommendations, which we hope to have ready for release for public comment.

After lunch we will be exploring objectives, mechanisms, and policies for genomic data sharing and review five genomic data sharing models and consider future directions, and health information technology.

Tomorrow we will discuss the SACGHS Gene Patent and Licensing Report and conclude our meeting with updates from our federal agencies.

So, a lot has happened since our last meeting. In September we transmitted a letter to Secretary Sebelius that outlined four critical priorities in the area of genetics that will support effective healthcare reform. And in November we

received a response from her in which she thanked the committee for its vision on priority areas and for providing comments to the Office of the National Coordinator for Health Information Technology on the importance of using electronic health records for the integration of genetics and genomics into healthcare. Both letters are in Tab 9 of your briefing book and they are also available on the SACGHS website.

Last month we received a letter from Myriad Genetics Laboratories in response to comments we received at our last meeting by Face Our Risk of Cancer Empowered or FORCE. As you'll recall, FORCE had indicated some potential problems and we had advised them to provide specific information to FDA, and they've notified their membership about how to do that. The response we got from Myriad to our letter is in your Table folders along with comments from CMS, FDA, and FTC on Myriad's characterization of their regulatory activities.

On Friday, Alberto Gutierrez will be talking to us about new mechanisms that the FDA has developed on reporting mechanisms for laboratory developed tests.

On January 13th, CMS, the Centers for

Medicare and Medicaid Services, and the Office of National Coordinator for Health Information Technology published regulations that help implement the Electronic Health Record Incentive Program enacted under the American Recovery and Reinvestment Act of 2009. The proposed rule by CMS outlines provisions governed by the EHR Incentive Program, including defining the central concept of meaningful use of EHR technology. The interim final rule issued by the Office of the National Coordinator sets initial standards, implementation specifications and certification criteria for EHR technology. Both these regs are open to public comment and we will discuss later in the meeting whether SACGHS should provide additional comments. Excerpts from the regs are found in Tab 8 of your briefing book and tomorrow we'll hear a presentation by David Hunt from ONC.

The paper on Direct to Consumer Genetic Testing, which the committee approved in October, was revised based on edits that staff received from you after the last meeting. The executive summary of the paper is in your Table folder so you can review the revisions to the action steps. We'll be moving forward with the final steps to transmit that

to the Secretary. If you have any additional edits or comments regarding those action steps, please give them to Cathy Fomous by the end of the day.

And, again, thanks to Sylvia for getting that work on getting that paper completed.

In response to a suggestion by Dr. Francis Collins, at our last meeting we formed a small group to draft a journal commentary that highlights the committee's prior work on emerging issues in genomic medicine. The draft commentary is in Tab 9 of your briefing book. I hope you have had a chance to read it.

I would like to thank David Dale, Gwen Darien, Jim Evans, Andrea Ferreira-Gonzalez and Julio Licinio for their work in developing the draft. It was an amazingly efficient process and with great staff work from Cathy Fomous, I think it’s in good shape. We appreciate your reading the document tonight and letting Cathy or me know if you have any questions or comments before we submit it, and the target is to submit to *JAMA* for publication as a commentary.

I would also like to call to your attention the materials in Tab 8 of the briefing book regarding the Healthy People 2020 objectives.

The goal of Healthy People 2020 is to promote health and prevent disease and to guide individuals towards making informed health decisions. Setting Healthy People objectives is a process conducted by the Department of Health and Human Services and the Office of Disease Prevention and Health Promotion that leverages scientific insights and lessons learned from the past decade to set and monitor national health objectives for the next decade.

For the first time the process includes a new set of objectives in the topic area of genomics. Public input and stakeholder dialogue is important to insure that Healthy People 2020 is relevant to diverse public health needs and, because of its relevance to our work, staff developed comments based on our previous recommendations, and these were forwarded to the HP2020 Advisory Committee and the Office of Disease Prevention and Health Promotion, along with an overarching recommendation to include genetics and genomics as a necessary component. The comments we sent are included in Tab 8, along with a list of objective areas for Healthy People 2020. Muin Khoury will be providing more detailed information tomorrow on the genomics objectives so we’re making progress.

Finally, at our last meeting we received updates from the Departments of Labor, CMS and Treasury, IRS, DHHS, Office of Civil Rights and Equal Employment Opportunity Commission, EEOC, on the various regulatory developments that were underway to implement GINA, the Genetics Information Nondiscrimination Act. As we know, GINA prohibits an individual's genetic information from being used on a discriminatory basis by health insurance companies and employers and we were pleased to learn of the progress that these agencies are making in implementing the regs which are designed to help insurers and employers comply with the law.

The interim final regulations implementing Title 1 of the law, the insurance provisions, took effect December 7, 2009. Three departments, Labor, HHS and IRS that jointly issued the regs will review the public comments received on the interim final rule before setting the production schedule for a final rule.

The Office of Civil Rights received about 25 public comments on the proposed regulation issued also on October 7, 2009, to implement the privacy provisions of GINA. Most commenters responded positively to the proposed changes to the HIPAA

privacy rule and OCR is currently considering the public comment received to determine what changes may be needed to the final rule. They expect to publish a final rule later this year after coordinating any changes with the other agencies.

The final regulation implementing Title 2 of GINA, the provisions prohibiting employment discrimination on the basis of genetic information are awaiting clearance at OMB, the Office of Management and Budget, and will be issued at the end of the clearance process.

Although the final rule has not yet been issued, the statute actually became effective 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 on that date.

Now, I would like to let all of you know that we now have two new members of the committee. They have been nominated. One is Charis Eng and the other is Janice Bach.

We are delighted to have you. Welcome to our group.

Charis is the chair and founding director of the Genomic Medicine Institute at the Cleveland

Clinic and founding director and attending clinical cancer geneticist at the Institute's Center for Personalized Genetic Healthcare. In addition, she's a professor and vice chairman of the Department of Genetics at Case Western Reserve University, School of Medicine, and professor of molecular medicine at the Cleveland Clinic Lerner College of Medicine, and a fuller description of her bio is in your folders.

Janice is the state genetics coordinator and manager of the genomics and genetics disorders section in the Michigan Department of Community Health. She has worked for more than 15 years as a genetic counselor in pediatric settings and has led the development of Michigan State Genetics Plan and has served as the project director for federal grants and cooperative agreements relating to birth defects, newborn screening and genetic service delivery.

There's still a bit of paperwork left to finish before both of them can become voting members of the committee and we expect that it will be completed by our next meeting.

On behalf of the committee, I'd like to welcome both of you to SACGHS. As you'll hear, we put people to a lot of work and so we look forward

to engaging you fully, and we look forward to all the contributions you can make.

Whenever we welcome new members, it also means that we lose members and we are going to be saying good-bye to two of them after this meeting. And, because it's really hard to let them go, we are not even going to say good-bye to them until tomorrow but, tomorrow, Sylvia Au and Julio Licinio will be having their last meeting as formal members of the committee but, as they know, they never truly leave.

I'm pleased to let all of you know that Eric Green, who is the newly appointed director of NHGRI, is going to be joining us as NIH's *ex officio* member. He's a geneticist and bench scientist, and is going to be a great addition to our group as well.

Finally, I want to introduce a new member of the SACGHS staff. She's over there probably changing the airline reservations. Allison Lea. Allison has a B.S. degree in psychology from George Mason University and an M.A. in professional writing from Chatham University. She joined the staff in December and was put immediately to work, and was instrumental in helping getting all of us here and

getting this meeting organized.

Before we go any further—

SARAH CARR: (Not at microphone.)

CHAIRMAN TEUTSCH: What's that?

SARAH CARR: (Not at microphone.)

CHAIRMAN TEUTSCH: Oh, okay. I didn't realize that. Sheila, are you on by phone?

Sheila will be joining us so I'm sure that we'll hear the beep shortly.

And now we come to the highlights of the morning session, the briefing on our ethics from Sarah.

MS. CARR: Thank you, Steve.

Good morning, everybody.

As you know, and I know you look forward to this little lecture of mine, you have all been appointed as special government employees, or will be soon, and that's how you serve on this committee and, because of that, there are special rules that employees have to follow and I just want to review a couple of them.

First, about conflicts of interest. Before every meeting you provide us information about your personal, professional and financial interests, information that we use to determine

whether you have any real, potential or apparent conflicts of interest that could compromise your ability to be objective in giving advice during committee meetings. While we waive conflicts of interest for general matters because we believe your ability to be objective will not be affected by 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 deliberations and we ask you to recluse yourself and leave the room if those discussions happen.

I also want to remind you since we are not too far from the Capitol that government employees are prohibited from lobbying and thus we cannot lobby, not as individuals or as a committee. If you lobby in your professional capacity or as a private citizen it's important that you keep that activity separate from activities associated with this committee, and always keep in mind that our role is advisory to the Secretary of Health and Human

Services, not the Congress. As always, I thank you for being so attentive to these rules. We appreciate your conscientiousness very much.

CHAIRMAN TEUTSCH: Great. Well, enough from me. Now we need to hear from all of you.

(Telephone disturbance.)

DISCUSSION OF JUNE 2010 SACGHS SESSION ON THE IMPLICATIONS OF AFFORDABLE WHOLE-GENOME SEQUENCING

CHAIRMAN TEUTSCH: Is that Sheila?

No.

Anyway, our first topic is to talk about our plans for addressing the issues surrounding the affordable genome. This is a topic that has come up repeatedly over the last few years and, as we near the time when the affordable genome is likely to be a reality, we thought it would be important to actually take it up as a topic in its own right.

The next generation sequencing methods are bringing the clinical use of whole genome sequencing data closer to reality. We know there are a variety of technological issues but they seem to be being surmounted but there are a lot of downstream consequences to the affordable genome as well and how that information can be and should be incorporated into clinical care.

In Tab 3 of your binders is not only some articles which hopefully you have had a chance peruse but also a set of questions. What I would like to do is spend a few minutes this morning having a discussion about what all of you see as the issues that the committee should be taking up so that we can begin to formulate our plans for the future.

So I will open the floor to thoughts about how we might--what are the kinds of issues we should be taking up.

(Pause.)

Good, Mara, thank you.

MS. MARA ASPINALL: Well, first I'm going to ask a question.

Have we received any specific guidance or questions from the Secretary or from the Secretary's office of high-priority issues, whether short-term or long-term, that the Secretary would like us to consider?

CHAIRMAN TEUTSCH: To my knowledge we have not received any such things but when I met with Dr. Collins-- Back when? In September? --this was clearly one of the items that was high on his priority list and thought was a way to bring

together many of the things that we have been dealing with in terms of DTC and oversight of genetic testing and clinical utility assessment, all of those sorts of things.

MS. ASPINALL: "This" meaning the implications of the affordable genome?

CHAIRMAN TEUTSCH: Yes.

I think what we are looking for here is your sense of what our priorities are. What are the issues that you see if we're going to take up the topic of affordable genome and—

MS. ASPINALL: Oh.

CHAIRMAN TEUTSCH: I'm sorry if I miss—

MS. APSINALL: No--

CHAIRMAN TEUTSCH: --so there are technological issues that we want to talk about. We may want to talk about issues surrounding how it gets incorporated into DTC or where it fits in with clinical testing, where it fits in with newborn screening, where it fits in with--what are the downstream consequences because—okay--we have a $1,000 genome. There are enormous human consequences. There are clinical downstream testing, all kinds of things that would need to be done. So we have a broad range of topics we could

be taking on. My guess is we will end up forming a task force to help us with all of that and have some informational sessions but we would like to get your thoughts about where we might focus our energies.

Gwen?

Gwen and then Mara.

MS. GWEN DARIEN: I was just—one of the things that occurred to me is that this ties into the whole—some of the work that we did on the DTC task force, especially as it relates to the clinical utility of an affordable genome if people are doing it outside of a provider context.

CHAIRMAN TEUTSCH: Mara?

MS. ASPINALL: Jim was first.

CHAIRMAN TEUTSCH: Oh.

DR. JIM EVANS: Yes, I was going to echo what Gwen was saying. I don't think--in reading the materials beforehand, I don’t think that we should focus on the proximal issues that is what are the challenges in closing the gap between the $10,000 and the $1,000 genome. That’s happening and I think that’s going to happen with or without us much more rapidly than we can mobilize. I think that we should focus on downstream issues and keeping in mind the kinds of things we’ve always emphasized, I

think clinical utility is a big one. And I think the other Gwen also alluded to. I suspect much, if not most, of this type of sequencing will be done outside of the clinical arena and will only filter in to the clinical filter in roundabout ways because people bring their genomes to providers, et cetera. So I think we should focus on interpretation and trying to bear it out clinically.

CHAIRMAN TEUTSCH: Okay, Mara, and then Muin.

MS. ASPINALL: So I would agree as well that we should assume that there is an affordable genome and define affordable at the beginning of the report because some would say an affordable genome at $1,000 isn't truly affordable but that we get to that piece. I would probably be less inclined to focus on the clinical utility issues but rather take an assumption that if there are tests within there that have important clinical utility and say, if indeed, that is the case, similar to what we did in the early years with genetic testing, here is talk about, in my mind, three areas.

First being the health IT piece, which clearly how is--what are the implications in terms of data that comes out of this, both from a

magnitude of data and the issue around privacy of data and how that data, especially if it's done outside of the traditional system, is shared or not shared.

Secondly, I think the issue of the payers and starting with the public payers is an issue. So if, indeed, someone who is on a public payer system has information, how is that integrated or not into their care, what are the implications for reimbursement for the testing or the implications related to that.

And, lastly, with maybe Education Task Force, what this means for physician education in the broader perspective as to if, indeed, this is available and everyone is bringing it to--lots of people are bringing it to their physicians, what kind of information does the physician need to be equipped with in order to best integrate or choose not to integrate that information.

So to me those are the three core areas.

CHAIRMAN TEUTSCH: Let me push you on one thing. You said you would not focus on clinical utility. Given that there’s obviously a huge amount of information, some of which is actionable, presumably related to health benefits, but also a

huge amount of information we don't know what to do with or would lead to additional testing that may be good or ill that you don't think that's an issue that we should be taking up in this context? Not necessarily gene by gene but as an overall how to think about the problem.

MS. ASPINALL: I would very much agree with your conclusions, lots of actionable items now, lots that isn’t and that may flip-flop and change over time as we learn more. My concern is the amount of time and effort it takes to put together an assessment of the clinical Utility may be beyond what we can do in this committee in a reasonable amount of time. So it’s not to say that it's not important to be looked at. I see that less as our core competencies to do in the period of time that I think this is relevant. So I think it's—as I’ve said, there have been a couple of areas before more important to have a core of opinion on some of the issues than a lot of opinion on something else if it takes another year to get there. So my issue is that clinical utility is a bigger nut than we can crack short-term.

CHAIRMAN TEUTSCH: Okay.

Muin?

DR. MUIN KHOURY: Okay. Well, I think this dialogue between you and Mara sort of jogs my memory here that probably clinical utility is the most important thing that this committee could focus on and the fact that it will take some real-time effort and studies and money to establish the clinical utility of the personal genome should not discourage us from doing it. After all, we spent billions of dollars to get to where we are now and, I think, it's very important to evaluate from a societal perspective the balance of benefit and harm.

I agree with you, Mara, but there are actionable things in the genome but many more non-actionable things but people will take action on the basis of these. They might even remove their prostate or, you know, other more drastic surgeries as a result of knowledge of the genome.

So I think in addition to all what you said, I think the importance of the balance of benefits and harms has to be explored from a societal perspective.

I just wanted to refresh the committee's memory here. Last year CDC and NIH held a workshop on personal genomics, the results of which are

published in Jim Evan's *Genetics in Medicine* illustrious journal here, for which many people, including Francis Collins—I think, Steve you were on that committee—made some recommendations for actions. So I think it's important to put that in the context of what we are trying to do here.

If you think that we are struggling with what to do with one million data points, we ain't seen nothing yet. I mean there will be three to six billion data points and how we deal with that from an IT perspective, from the act of consumer education, or whatever, I mean it touches on all the areas that this committee has been exploring over the last few years, including clinical utility.

CHAIRMAN TEUTSCH: Sylvia, Marc and Mike.

DR. SYLVIA AU: I think it's really important that I urge the committee to keep the report as practical as possible because with the whole genome sequencing there's so much public health issues.

And if we were doing this in newborn screening, the whole shift in paradigm in how medicine is going to be given to families because if you have your whole genome from the time you are a newborn, you know, what does that mean because we

usually don’t test minors. There are a lot of legal issues. There are patent issues. I just want to make--there's education issues. We don't have the workforce. We don’t have an educated public.

So the practical issues, I think, are what need to be highlighted to the Secretary that these bring all those genetic discrimination concerns that we have, all those reimbursement issues that we had concerns on, the education or patents. So this really—again, like direct to consumer--brings back some of the prior reports the Committee has done and really to show that this is going to make all of that explode even faster.

DR. MARC WILLIAMS: So I would make two points, probably both of them relatively less practical but I think philosophically very important. One is that the issue of whole genome sequencing is really not going to be--we can't look at it from a paradigm of what we have traditionally been doing relating to testing. This is really going to be a huge problem of knowledge management. It’s not going to be an issue of understanding all of the different data points. It's really—we’re going to have phenomenal amounts of knowledge and we’re going to have to manage it in a different way

if we're really going to understand how to do it. So I would—for the session I think that we would be well-served to hear from someone who has a content expertise around knowledge management.

And then I think the second area that is important to consider as we're--I am kind of just—just it slipped away here for a second so hang on. Let me just get it back. Oh! I think that having some of the people--the person that comes to mind specifically is Zach Kohane—who has written on the incidentalome. The idea that, you know, we have faced some of the problems that Muin and Mara have mentioned before, which is we are going to find some things that we know what to do with but we're going to find a lot of things that we don't know what to do with and they do have implications. And certainly at least when that was looked at from the perspective of say whole body scanning there were some very interesting concepts that from looking at that process that I think could potentially be relevant here as well. So I think someone that has done some thinking about what do we do with incidental findings, what's the response that people have to information that they don't know for sure what to do with, those are conceptual things that I

think are going to be necessary to frame this.

CHAIRMAN TEUTSCH: Mike, and then Jim, and then Charis.

DR. MICHAEL AMOS: Jim, did you want to say something relevant to follow on to—

DR. EVANS: No, you go ahead.

DR. AMOS: All right. I just want to bring to mind some of the practical issues that probably the Committee might want to consider, things like data quality. It's not—data—you know, base colony is not perfect yet and so the issue of that. Integration of, you know, the whole genome with electronic health record because it's going to have to be--you don't want to have these things separate because both are going to be important; interoperability of the systems that are used to store the data and to manipulate the data. If all sorts of different companies make these systems independently then they will never be able to talk to each other and they won't be able to be useful.

Data security is absolutely critical and data transmission. The issue of just moving large amounts of genomic data from one place to another with perfect integrity is not simple, not trivial.

And then I think probably the most

important thing is developing the systems to connect the genome to the—the genotype to the phenotype because genotypic information in and of itself is only as important as it relates to the patient. And there are some really, you know, practical issues of how to do that. We've actually been talking to the National Library of Medicine on how to integrate the systems to standardize the way that genotype is annotated and integrate that with electronic health records. So it’s not only beneficial to the current clinical situation but also downstream for any type of large scale clinical studies.

CHAIRMAN TEUTSCH: Great. Jim?

DR. EVANS: Yes. I just wanted to try to focus for a second on what our main role and our capabilities are as a committee. I think, like Mara points out, this is going to be an absolutely huge issue, right. There are going to be gigantic issues having to do with utility, with privacy, with the medical record. And, therefore, since it is such a big task, I think probably the best thing we can do is help the Secretary prioritize what the most important aspects are.

And, you know, I would again come back to the point that even though—well, like Marc says--

this is a qualitative game changer with all of this information but, having said that, the rules haven't changed about the application of this kind of information to clinical medicine. We have to, I think, continually enforce to the Secretary that all of this wondrous information and all of these great ideas still need to prove out as actually useful to patients. And I think that that--we need to focus on perhaps a role of prioritizing and triaging for the Secretary because we sure aren't going to be able to solve these problems ourselves.

CHAIRMAN TEUTSCH: I understand Sheila has joined us.

Welcome, Sheila.

Charmaine?

DR. CHARMAINE ROYAL: So Mike already—

CHAIRMAN TEUTSCH: Turn on your mike.

DR. ROYAL: Mike already made one of the main points that I wanted to make in terms of integration of the information with other information about the patient or about the person who is tested, and then to piggyback on Sylvia's point about public education, I think that how people use the information, what happens when children get tested, how they handle that. So I

think the public education piece of it is major.

CHAIRMAN TEUTSCH: Andrea, and then Eric?

DR. ANDREA FERREIRA-GONZALEZ: I agree with every comment that has been made but I want to point out two different issues.

CHAIRMAN TEUTSCH: Could you talk into the mike?

DR. FERREIRA-GONZALEZ: I think we have two different—or more than two different issues but I want to point out issues that need to be brought out to our attention.

One of the things is that the $1,000 or affordable genomes happen—it's going to happen. It's just—there's a race to continuously decrease the cost that it's going to happen. Issues about data management are also being dealt with expeditiously but they still will need some help.

But I think from our Committee point of view we can look at some of these more--issues that are practical to what we are going to foresee they are going to be needed to bring these type of testing or type of information into a clinical electronic medical record.

We know there are informatics needs for standardization of vocabulary. Today even for other

genomic information we don't have a genetic standardized vocabulary. So these are crucial issues that are important.

The issues around analytics, around quality control, mentioned by Mara, it's crucial how we are going to call these issues but also how we are going to do proficiency testing for these. So these are things that we can start prioritizing or identifying for the Secretary maybe somebody else can work but we can do these.

There are interface issues between connecting devices, not only connecting devices but interoperability into the different systems. So these are practical issues that need to be solved or we can bring to attention.

The other component to this is how we are going to practice having the whole genome sequence there. Who manages the information? How are we going to coordinate information, do education and so forth? So maybe we can start looking at these issues from the practical point of view that will affect how we practice and then also I think the clinical utility is a huge issue that we need to deal with, so just looking at different aspects, not just the clinical utility.

CHAIRMAN TEUTSCH: Eric, and then Paul.

DR. ERIC GREEN: The only point I was going to make, and I've heard several speakers allude to it, I think Jim Evans said it directly and I just want to emphasize it, is I would hope the discussion doesn't try to focus on subtleties related to whether it's a $10,000 genome or a $5,000 or a $1,000. What I can tell you just in two months of being NHGRI Director but prior to that for the previous 12 years being the head of a production DNA sequencing facility and so having some expertise in this area that the pace at which these technologies are advancing is truly breathtaking. I know it sounds very—you know, just like there's a wow but truly—I mean, I have been involved in production of genomics for almost 20 years and what I see happening now in sequence technologies, even in the past 12 months, is truly spectacular.

So no matter what you think you are planning, what issues you are dealing with, trying to get to it is almost impossible. It's happening faster than a committee like this can even operate. So I would really think very ambitiously as to the amount of data that is potentially going to be generated. And all the discussion about bottlenecks

of information handling, connecting it to phenotypes, to patients, to medical types, all of that is real and then probably multiply it times five.

And what I--there's no sign that the pace at which these technology advances--there's no sign it's slowing down. What I've probably learned in the last six weeks, announcement after announcement after announcement, phone call after phone call I've gotten from some of these—both the vendors but also scientists who are working on this, it is absolutely here and it's going to--the pace of acceleration is going to continue.

CHAIRMAN TEUTSCH: Paul, and then Mara.

DR. PAUL BILLINGS: So I think following on that, just on that last comment, which was I think a breathtaking review of the technology at some level, I would return to the first comment, which is affordability. You know, that said in the context of thousands of our fellow citizens not being able—you know, going to free clinics because they can't get any kind of healthcare and can't afford any of it.

So I think we do have to deal with the notion in a critical sense of what affordability of

this information is and do we actually envision that all members of our society are going to present to whatever healthcare they are getting or not getting with their genome sequence in hand because I am not so sure that the pace of the technology and the pace of our being able to provide that are equal.

So then the other aspects that I would like to sort of re-echo are the medical and non-medical implications of broad based full genomic knowledge. Are there significant non-medical implications of this? I don't know if there are or not. Certainly maybe to genealogy and a few other things but I don't know. I think that needs to be certainly considered.

I really do agree with the knowledge management and the whole comments about the incidentalome. And I would ask Jim and others, there's also a patent issue in here and—

(Laughter.)

DR. BILLINGS: And so there's another life for Jim. We'd like you to stay on for a few more years to deal with that if you don't mind.

So the question is do we deal—you know, how do we get--how do we deal or do we deal with the patent issue there?

CHAIRMAN TEUTSCH: Mara?

MS. ASPINALL: Well, that's just too easy to tee up but I am not even taking on the patent issue and maybe just a broad comment and a recommendation to the committee is Wayne Gretzky had a great quote, the hockey player, which is when somebody asked how he scores all those goals and he said, "Skate to where the puck will be; not to where the puck is."

And that to me has to be the overriding principle with the comments both about the technology and the movement going forward. We need to skate to where the puck is going to be and that alone will give the Secretary insight that given the thoughtfulness of this Committee I think we can do in a very unique way.

CHAIRMAN TEUTSCH: Jim, and then why don't we figure out what our next steps are.

DR. EVANS: So in a spirit of camaraderie, I am not going to—with Mara, I'm not going to talk about the patent issue either.

(Laughter.)

I did want to just bring up one kind of interesting thing. When you think about the whole issue of privacy, I think it behooves us to think

about what drives that. And, to me, what drives that, the reason that people accord their DNA and their genetic information some increased level of protection or privilege is that it can tell us something about the behavioral aspects of a person, something about our proclivities towards certain behaviors, et cetera, and that kind of gets to what Paul was talking about, the non-medical issues. And I think that's germane to a consideration by this group because it brings up the issue of whether parts of the genome should be treated in the medical record, for example, in the same way that, for example, psychiatric information is accorded special status in the genome.

So I think we--it might be worthwhile, it might be productive to not think about human genomic information as a monolithic entity but to think about the qualitative differences in the information that will arise and whether those should be accorded different treatments.

CHAIRMAN TEUTSCH: Muin?

DR. KHOURY: I like the Gretzky's "where the puck is" analogy and just following the puck, at least the way I follow it is it's not about technology, it's about health. And I think that's--

to the extent this information, like any other biomarker information, can improve health and can be affordable and can be used by all segments of the population, I think, we will have a winner. Otherwise we will have a mess on our hands. So I am hoping SACGHS will tackle all of these things.

CHAIRMAN TEUTSCH: David, and then—

DR. DAVID DALE: An interesting discussion. I am glad we have taken this up. And I agree with Eric that the price tag shouldn't be the focus. It looks like we have established the price.

The key thing in my mind, I think, that goes along with some of Jim's comments, is somehow to be in the position of helping to integrate the scientific development of technological development with the physician's office based problem of what do you need to know and what do you need to do. We need to help as much as we can with thinking about that process as given that the genome is going to be sequenced for somebody somewhere, somebody is going to need to know then what do I do with the information. And I think that's not a very orderly process at all right now. And if we can define these steps or help to define those steps, we will really do a service to our colleagues in the

country.

CHAIRMAN TEUTSCH: So I am hearing a lot of enthusiasm for lots of different issues.

I just want to say one thing, before we bring some of this together, on the affordability issue. In fact, my guess is whatever the price of this is going to be, that's the smallest part of the cost of the test.

What's going to happen is other consequences of it and it’s going to be cost-inducing and presumably benefit inducing. We need to understand what all of that is going to be about.

But hearing sort of the array of the issues that are out here, this isn't about whether this technology is going to come; it's really about how do we bring it to reality in a way that enhances the health of the population.

My suggestion, and I think having heard from others prior to the meeting, is that we use some of our time at the next meeting, which I believe is in June, to have an informational session so we can all get up to speed on various aspects of this and then probably form a group to help us create a charge.

Does that seem like a reasonable plan?

So we will need folks to help us pull that together, at least for June.

And presumably on—I know, Paul, you expressed interest in that.

And Charis is raising her hand.

Could I ask—Paul, this is perfect. As someone who has been around the block here with this, you can help.

And, Charis, you'll help because I'm afraid we're not going to get this done so fast so that will be great.

And then I think if you need more, you can draw on others but my guess is following June we will probably expand the group to figure out how we will go from that information session on to a working group.

Great! Well, thank you. That should be an exciting process and an important one.

So having seen the baton apparently passed to Marc, we will turn to the Task Force on Clinical Utility and Comparative Effectiveness Research, which we discussed last in June of 2009, and we established a task force that Marc chairs to help create a charge to identify the issues that we should explore.

So, Marc has been working diligently on that and will give us information about what he proposes we do that will be constructive in this actually pretty new and changing area, and one that is particularly challenging, I think, right now because we don't actually know what's happening with all of the funding for comparative effectiveness in the health reform bill but take it away, Marc.

UPDATE ON THE CLINICAL UTILITY AND COMPARATIVE EFFECTIVENESS TASK FORCE

DR. MARC WILLIAMS: Thank you and thanks for the opportunity to present today.

(Slide.)

I also want to thank the task force members who are listed here for all their contributions.

(Slide.)

Our charge was to determine which issues, if any, SACGHS should explore in the areas of clinical utility and comparative effectiveness research. And so our immediate focus was to try and access where things were at in terms of federal funding in CER that concerns genetics and genomics, and that’s what I’m going to be talking about today.

(Slide.)

So in the American Recovery and Reinvestment Act of 2009 there was a billion dollars—I'm sorry, $1.2 billion—I have to do my math. $1.1 billion that was appropriated for comparative effectiveness research divvied up $400 million to the NIH, $300 million to AHRQ and $400 million to the Office of the Secretary of the Department of Health and Human Services that were to be targeted for comparative effectiveness research.

The $400 million for the Secretary must be used to "conduct support or synthesize" comparative effectiveness research or to "encourage the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data."

The act also required the Secretary to task the Institute of Medicine with a report recommending national priorities for CER funds appropriated to the Secretary and required the Secretary not only to consider the IOM recommendations but also recommendations from the Federal Coordinating Council for Comparative Effectiveness Research, which I will refer to

subsequently as FCCCER for obvious reasons, and spending $400 million appropriated to the Office of the Secretary.

(Slide.)

So our strategy was to review the recommendations that emerged from IOM and FCCCER and identify those relating to genetics and genomics, to assess the degree to which these projects—the projects that were funded by NIH and AHRQ with their CER funds--satisfied recommendations and identify recommended studies or projects that are not yet funded inasmuch as we could.

And then it led to the opportunity then that we could potentially recommend to the Office of the Secretary directions for the funding that could support projects that were recommended either by IOM or FCCCER but were not funded, at least currently, through NIH and AHRQ.

The FCCCER is composed of senior federal officials, most of whom are physicians with responsibilities for health related programs. They issued a report on June 30, 2009, that recognized FCCCER can promote personalized medicine by examining the effectiveness of interventions by patient subgroup. And what I'm going to be talking

about here is really a synopsis that we did of the report that focused on genetics, genomics and personalized medicine, or the purview of that. And the written synopsis of this report and others is behind Tab 4.

Now, I also included a report by the Lewin Group that was produced for the Personalized Medicine Coalition that had assessed—they had provided input both to IOM and to FCCCER about how monies could be used for comparative effectiveness research. And the Lewin report, I think, does a very nice job of crystallizing how comparative effectiveness research and personalized medicine can complement one another.

(Slide.)

Now, the FCCCER recommended that the primary investment of the Secretary's funds be in creating data infrastructure for CER. So one example of that would be patient registries and, secondarily, recommended significant investments for dissemination and translation of CER, particularly those CER studies on priority populations, and priority types of interventions. And they defined priority populations as racial and ethnic minorities, persons with disabilities, multiple

chronic conditions, elderly and children. And priority types of interventions could involve comparing different medical home models or comparing surgery versus medical management, et cetera.

(Slide.)

The report notes “As the Secretary develops HHS’s full portfolio of ARRA investments, it will be critical to consider both CER and health IT holistically.” As such, our committee may want to continue to encourage health IT policy that supports collection of genetic information useful for CER and barriers to genomic data sharing are also barriers to comparative effectiveness research, and we’re going to spend the afternoon obviously talking about some of these issues so I won’t go into any more detail.

(Slide.)

The IOM report was also issue on June 30, 2009, and they generated 100 prioritized research topics and 10 recommendations. Of the 100 research topics, there were two that explicitly mentioned genetics or genomics. One of them was a first quartile priority looking at effectiveness of genetic and biomarker testing with usual care in preventing and treating breast, colorectal,

prostate, lung and ovarian cancer, and then the third quartile priority was to compare the effectiveness of biomarker information, including genetic information with standard care in motivating behavior change and improving clinical outcomes. There were eight other prioritized research topics that could conceivably include genetics and genomics within scope but were not explicitly mentioned.

(Slide.)

The NIH reviewed all of the 100 recommended study topics and concluded that most of the 100 IOM study topics are already being studied through ongoing NIH research projects.

The review by our task force did identify numerous funded projects in the genetics and personalized medicine space. So I think that there is good progress relating to this, particularly in that first quartile priority of cancer.

Of the 10 recommendations there were two that we thought were of particular relevance to the committee.

Number 7: HHS should devote sufficient resources to research innovation in the methods of CER and so we would posit that beyond CER we also need innovation around how we look at clinical

utility, as we already heard in the discussion about affordable genome.

And Number 8: HHS should help develop large scale clinical and administrative data networks for use in CER. Now, this goal obviously raises privacy and informed consent issues, and that will likely overlap with issues that are raised by genomic data sharing and it does reflect ongoing efforts to create such data networks. The recommendation also implies that we need to collect clinical level data.

So, in some ways, what we're going to be discussing around meaningful use will also relate to this issue because if we are not representing some of this in meaningful use we are not going to be able to collect it.

(Slide.)

Now, I did get a chance to play around--and thank you to Mike Lauer for helping me with searches on this--to look at the NIH ARRA funded CER grants, and there were several funded projects that are going to directly relate to genetics issues that the IOM recommended. Twenty-four of these were specifically funded under the comparative effectiveness research monies, and I have detailed

those under Tab 4. There are many others and I did not—I was exhausted but I didn't do an exhaustive search, so if you want to parse it, but there's probably at least 50 to possibly hundreds that address genomic and personalized medicine issues that are not directly related to the IOM top 100 and there seems to be very good coverage across a broad range of conditions, and some of these funded studies are using the methods of comparative effectiveness research even though they are not specifically funded by the CER-designated funds.

I think that many of these funded projects will also serve as investments in data infrastructure and in dissemination and translation of CER findings which would be consistent with the FCCCER's recommendations.

(Slide.)

Now, we don't have much information yet on the AHRQ CER-funded grants. Gerberding (sic) did provide me some information that two of the announcements, the CHOICE and iADAPT are closed, and the rough estimate of applicants is about 118 and 91, respectively. The titles indicate that a small proportion will have a focus on genomics but detailed reading of the applications may reveal

others.

The PROSPECT and the EDM announcements are still open. And Gerberding was estimating that perhaps 10 percent of the these may have something to do with genomics, which would be a substantial number. All of these grants will be reviewed, funding decisions and awards will be done before close of the fiscal year 2010; that is September.

(Slide.)

So if we are to look at gaps in terms of what actually is happening, I think that there were three that could reasonably be characterized as such. The first is definition of adequate evidentiary standards for different applications; the second is this third quartile IOM priority healthcare delivery systems; and the third the coordination of efforts, And I'm going to briefly talk about each of these.

(Slide.)

I thank Steve for allowing me to borrow his slides. Some of you have seen these in another context but this slide overlays Muin's T-1 to T-4 translational efforts against when do evidence-based guidelines actually come out. This sort of represents what might be considered sort of an ideal

model with everything in balance where our evidence-based guidelines are occurring before we go into health practice.

The problem, of course, is we really don't know where that evidence bar should be and if we lower the threshold for translation into practice then we may have things moving into practice that have little evidence on clinical validity, utility that may impact their coverage. There's a potential for increased harms and also the potential for increased benefits for moving things out that actually work. Usually we're relying on expert opinion at this level but this type of evidence bar would stimulate innovation.

(Slide.)

In contrast, if we move the evidence bar way to the other side, we are likely to have very good and useful tests that emerge with good prospects for reimbursement but there's lower incentives for innovation because of the cost of developing the evidence. We do reduce the likelihood of harms but by the same token we may diminish the benefits because we're having some treatments that never make it into the clinical arena that are beneficial where we just can't

generate sufficient evidence.

(Slide.)

Now I am not going to go through this decision factor matrix but this is something that has been discussed at least superficially at the eGAP working group about the different ways that we can think about where we would need best evidence.

(Slide.)

And you could imagine, you know, saying in each of these bars, you know, what evidence do we have around efficacy for regulation, we've got to get good evidence there, we've got reasonable evidence and feasibility, we've got no evidence on cost or these type of things. You can fill that out and use that in some type of decision-making process.

(Slide.)

So, I think this is an area where we have heard about this before at this Committee. We have definitely heard about it even this morning about where does that evidence bar have to be, and we think that this is something where the Committee could potentially play a role in helping to determine this.

I would also mention, though not in Tab 4

but in another part of the packet, there's a comment of the CMS MEDCAC that was recently surveyed on what type of evidence do you really need to make a coverage decision, and there are some interesting findings from that that I think support the same issue. You know, we are really struggling to say what is the evidence bar that we really need?

(Slide.)

The second gap is this third quartile priority, which is to compare the effective of biomarker information, including genetic information in standard care, in motivating behavior change and improving clinical outcomes. There are very few of the funded projects that I reviewed that specifically address these critical issues. There may be more of these that emerge in the AHRQ projects. But this would be something where I think it would be a fair point of discussion for our committee as to whether this should be point of emphasis for the Secretary. I think particularly related to the issue of behavioral changes, both for providers and for patients.

(Slide.)

And then the third thing is coordination. There are all of these different projects. They are

all collecting information and they're creating a lot of registries but are we really using standardized data representation and storage? Is this going to impair our ability to share findings across projects? So could we learn something about the genomics in one condition associated with risks for another condition that's associated with risk for another condition and we could combine that information?

I used psoriasis and coronary artery disease just because this is something that came up in our own institution where I was contacted by a psoriasis researcher that said, you know, "I'm looking for a larger control group for psoriasis. Do you have genotyped individuals?" I said, "Well, we've got a big pool of them in our cardiovascular research group but they're consented to only be used for cardiovascular disease research." He says, "Well, did you know that psoriasis is a huge independent risk predictor of risk for coronary artery?"

Well, I didn't know that and it turns out none of our cardiologists knew that. Now they are very excited about working together. So I think that this is something where there could be a lot of

opportunity for synergy if there were some type of coordination overlay and so that was something that we were thinking about as a possible role for the Secretary.

(Slide.)

At present, the Secretary's funding decisions are unknown. The Secretary was required to send operating plans to Congress in July and November of 2009 concerning funding decisions but that report is not as yet publicly available.

(Slide.)

I almost took this slide out because I was depressed. There was a bill that was introduced into the senate I believe, that--an independent bill indicating that studies should take into account molecular and genetic subtypes. So that basically codified this type of work.

That bill was folded into the overall healthcare reform bill and was, in fact, represented in both the house and senate versions that were passed but, as we all know, the status of that right now is unclear. So whether this particular bill will be extracted from healthcare reform and brought up independently or not, I just wanted you to know that there are some things at the legislative level

that may also impact what it is we are going to do.

(Slide.)

So here are some potential next steps for the task force. One is to try and get a handle on these evidentiary standards for the use of genomic tests, outlines for considering adjusting an evidentiary bar. So, for example, if we have something like a Warfarin pharmacogenomics where we're potentially going to be applying this to hundreds of thousands of individuals a year, we probably need pretty strong evidence this is going to work. On the other hand, if we have a situation where we have two treatments that are in therapeutic equipoise, and it's a coin flip in terms of whether you do A or B, then perhaps we don't need as much evidence to say, well, we think that there's some genomic information that would distinguish between going with therapy A or B, it may be reasonable in that type of situation to move forward with a lower degree of evidence since right now we are essentially equal.

(Slide.)

There are other entities that have begun to address this issue. This was one of the major areas of focus at the initial gap meeting that took

place last fall. It may be that the Secretary could charge this entity with taking ownership of this particular issue but it's one that we thought was quite important.

We could create an inventory or clearing house of genomic CER projects with identification of prioritization of gaps in the CER agenda which could inform how money should be distributed, again potentially with this special attention to the healthcare delivery system point.

We also thought about the possibility of having an informational workshop on this issue for the June meeting. We need to continue to monitor the health IT issues that continually arise and, in particular, reviewing the meaningful use rules, which we will be doing.

By the same token, I think we could say that our work here is done, that there’s really enough happening, and maybe there isn't a role for the task force to move forward. So that would be a potential next step.

And some of you may come up with brilliant ideas that I haven't thought of, in which case we could consider other options.

(Slide.)

So, with that, I will end and we can have discussion.

CHAIRMAN TEUTSCH: Muin?

DR. KHOURY: Thank you, Marc.

I would not suggest to dissolve the task force. I think we are just beginning to do the work.

I think CER, when it's all said and done, is sort of a good sort of medium by which this committee and other groups can tackle the so-called issues of clinical utility. I mean, it's just a way to address the clinical utility in the real world. Whether CER will live or die in congressional language, I think the issues that it has raised are real and they are already on the table.

Just by the way of clarification and just additional information, I was looking at the 24 projects you identified from the NIH list. Many of them have nothing to do with genetics or CER but they were coded as such. I'm wondering if you have issues on that but let me just finish my thoughts.

As part of my other hat, I have two jobs, one of them is an NIH job and I spend so much time at the NCI, we actually from the NCI perspective funded seven out of these 24. They are part of a

network of CER and genomic and personalized medicine. We had our first meeting with the grantees in January and we have connected those groups with both GAPNET and eGAP. And they are going to—and I'm hoping we can find across all of NIH other worthy projects that can actually join that network from a non-cancer perspective because I think cancer is sort of the dominant field in CER right now and the IOM, I guess, priorities reflected that breast cancer, ovarian cancer, et cetera, but I think there are other worthy areas other than cancer. So I think if this committee actually keeps shining a light on CER from what its true meaning is, for clinical utility in the real world, have a discussion and inventory, and then work with the other groups and develop some kind of report to the Secretary with specific encouragement or recommendations, I think it's a good way of spending the time because it's a window, it's an opportunity to shine the light on so-called clinical utility issues.

Thank you.

CHAIRMAN TEUTSCH: Let me just expand on the on the issue of what are talking about on clinical utility, and sometimes that's a fairly

defined thing that we know about in harms and benefits in health terms. But the decision factor matrix that you put up, Marc, talks about how different people make different decisions and context is very important. And FDA has a specific set of regulatory requirements of how it makes decisions, safety and efficacy; payers have other criteria; patients have a different set of criteria.

So you can think about all of these things not just as sort of clinical utility but I think we can add real value perhaps saying how do we help get the information necessary for decision-making, which the clinical is one, and I would suggest that patients and clinicians think about these things rather differently than a regulatory agency or even a payer but different people need different information, and help people understand that and the information that's needed and where they get it so that they can be making better decisions is one of the pieces that I think should come out of the slide you showed.

Jim?

DR. EVANS: I just wanted to put a plug in for--you highlight something in your synopsis early on that I think we should make a conscious effort to

address and counter, and that is the kind of bizarre accusations that you hear a lot that somehow comparative effectiveness research is antithetical to personalized medicine and I think that Muin and Steve's commentary beautifully articulates why that's not the case. But I think because you hear that a lot that should be high on our radar screen to counter because it's just simply not antithetical.

CHAIRMAN TEUTSCH: This group is rarely at a loss for words.

Mara?

MS. ASPINALL: Just for fun I will say I very much agree with Jim. I think that you continue to hear that about comparative effectiveness and I think the issue around comparative effectiveness looking more broadly than just against the standard of care today is the key change to that perspective because there was misinformation, I think, at the beginning that it was only looking at the current standard. And that brought about some of the concerns that personalized medicine was not always in comparison to the current standard and, therefore, by changing, it would not be appropriately viewed.

But in both the report and other work, the broader definition of comparative effectiveness has done that but I do think that misinformation and perception is very much still out there.

CHAIRMAN TEUTSCH: Gwen?

MS. DARIEN: I think it plays into a lot of emotional fears. It's the same thing as a lot of the genetic discrimination fears and the fear is that it is going to lead to health rationing. So I think than Jim and Mara are really correct it has to be very, very clearly articulated and taken out of an emotional context.

DR. WILLIAMS: You know, it's interesting that you mentioned the R word since the funding, the ARRA funding, specifically articulated that you couldn't include that in the research, which, you know, for most of us sort of said, "That's really tying our hands to some degree."

So there are a lot of issues and, of course, the other issue that we really haven't talked about that isn't specific to genetics and genomics is the whole idea of how we do the research is still up in the air as well. The FCCCER report spent a lot of time talking about alternative methodologies, you know, methods that not

traditionally assessed or scored well in NIH funded opportunities, perhaps a little bit less so in AHRQ, but the idea of, you know, adaptive trials and things that are really new types, new ways of doing research, doing research off of the clinical data that we are beginning to accumulate is going to be a critical piece of this. That emphasizes the need to be able to capture the data that is really critically important and some of that data is going to be genetic and genomic, which means we have to have the capability within our clinical information systems to pull that information out.

CHAIRMAN TEUTSCH: Andrea?

DR. FERREIRA-GONZALEZ: To add more to what Marc is saying, there’s something that I find missing in the use of genomic and genetic information because these tests may be being performed maybe in research laboratories and we have to be very concerned about the quality of the test that is being performed. There are clear regulations that establish that even for research purposes that information transmitted for decision making should be done in a CLIA certified laboratory and throughout here I didn't see anything about that.

The other issue is not only that the quality of the testing, it is how the results will be transmitted to healthcare providers or researchers. Being a practitioner, I know the challenges to really convey specific information, what you can test, what are the limitations of the test is and what you cannot do.

Also something that missing here that is very important is comparative methodology research. Her2neu, for example, and I can give you an example, you can have different technology to use to do the detection and make changes or decisions on your treatment. So that research is--I didn't see anything of that but I think it's critical that you add that part of the information.

To talk to Mike Amos' reference materials, normal way to do proficiency tests and also no part of anything that I have seen, I would like to maybe recommend the Secretary to create a clearinghouse for information similar to the clinicaltrial.gov website where this information is already put for clinical trials. So there's already a model there that we can use or recommend the Secretary to use to put some of the comparative effectiveness research in publication.

And lastly is biobanking. I mean as we continue to work through all the issues we talked in the previous session, and the current session, and session that is going to follow, the user and storage of specimens is well-annotated under quality control is critical not only for continued research, but then we can go back and do other testing with new methodology.

So these are issues that need also to be part of our discussions.

CHAIRMAN TEUTSCH: Marc, this is what you had put up first for us to think about but something tells me you are not totally agnostic about which of these we should be pursuing and when. Do you want to lay out what you think a reasonable agenda would be?

DR. WILLIAMS: I am not sure I can define a reasonable agenda.

CHAIRMAN TEUTSCH: An unreasonable agenda?

DR. WILLIAMS: I am much better at that. I think that from a practical perspective, the--you know, some guidance on evidentiary standards is going to be critically important. Whether this is something that really could reasonably be expected to be completed by a task force of this committee or

whether this is really something where we need to get an idea of who actually is in the game relating to this and say, okay, here are the people taking ownership of this, and this is something we need to support and hear back on, I just really don't know on that. Again, I think it would be beyond the scope of the task force to be able to create an inventory or a series of inventories but I think it's a critically important thing to do. So one thing the task force might reasonably do is to say we need a clearing house of information and we need it on these different issues and we would recommend that be created within some entity. Again that was something discussed at the initial GAPNET meeting. One thing GAPNET could do to provide value would be to have a clearing house of projects so that people know what actually is going on in the space.

In terms of the informational workshop, we already know we’re going to be having a workshop on affordable genome so it may not be reasonable in the June meeting to have another informational workshop or it may be that people think we have heard enough from prior presentations that we don't really need to go there again. Certainly that would be something the task force could very reasonably take

ownership of in terms of pulling that together.

That doesn't really answer your question all that well, I don't think, but that's—

CHAIRMAN TEUTSCH: Well, the good news is that Muin is raising his hand and since he's mixed up in almost all aspects of this, he can tell us what's going on with some of these other—with GAPNET, EGAP and assorted other nets.

DR. KHOURY: Okay. So, yeah, there's just an alphabet soup out there but here's what's going on, and I suggest that this committee can actually weigh in towards the end of the year, maybe after June. The reason why I say that is for a couple reasons. One, the projects that are actually being funded now, in the 24 plus or minus 10, I think, are doing the work, plus getting together and trying to develop that number one, and the roadmap type issues, and they are going to have maybe joint meetings with an IOM roundtable on genomic translation that's chaired by Wylie Burke and also the IOM forum on the cancer forum. So that discussion is already occurring in the background.

Of course, GAPNET will try to have the clearing house of projects and maybe even knowledge base on the genomic applications. ARC is doing all

kinds of things this year and Gurvaneet can tell you more about that. So I think waiting a little bit until the end of the calendar year and then having just another session to figure out really what's going on could inform this committee as to what the next steps should be, just waiting and seeing what the other groups are doing. So there is really no need to rush immediately because the work is being done, and maybe if we put the place holder maybe at the June or the October meeting for a quick update on the various efforts by NIH, CDC, Gurvaneet, AHRQ and the IOM roundtable could actually give us more information to play with because this is rapidly moving target this year.

CHAIRMAN TEUTSCH: Muin, do you see any gaps at the moment which others are not addressing or do you think we should just wait and see—

DR. KHOURY: I think there are gaps in all of these things obviously. Whether or not these other groups are going to address them fully is not clear. I would suggest that we work with them somewhat since many of us are involved in these things and wait to see towards the latter part of the year what kind of recommendations this committee wants to make to the Secretary. Now remember all of

these other entities are doing it from various vantage points. I mean AHRQ is doing their thing, NIH is doing their thing but this is the committee that provides advice to the Secretary. So I think there is always a role for this group to weigh in and we shouldn't wait too long. I'm not suggesting to push it another year or two but maybe towards the October meeting we will be in better shape information-wise.

CHAIRMAN TEUTSCH: Andrea, and then Marc?

DR. FERREIRA-GONZALEZ: I agree with Muin that these issues may have to wait until the fall, but I'm wondering if we can do something in the meantime. The issue of the CER where testing is being done, not only for genomics and genetics in research laboratories, and the information is being used to trigger patients, that needs to be done in a CLIA certified laboratory under rigorous quality control, if we need to bring that to the attention of Secretary or somebody in those areas.

CHAIRMAN TEUTSCH: Andrea, I am just wondering if that falls under this general rubric of clinical utility, and we've had the oversight report. We're clearly dealing with the genomic data sharing and the kinds of issues that we heard

earlier.

DR. FERREIRA-GONZALEZ: But these grants are already being granted. They are granting the money and testing is being done so do we need to bring these issues up?

DR. WILLIAMS: Yes, I guess I would share the issue about whether that's something that this task force would be primarily tasked with because, as I hear about this it, really seems much more related to the work we have done in oversight and that I am not saying that we shouldn't and we probably as a committee should respond but I am not exactly sure of the best way to do it so I would defer to Steve on that.

I would certainly not disagree with what Muin has said. I think that there is some wisdom in that. I think there are two things that we can probably do as a task force even if we were relatively inactive. One would be to continue to monitor the Secretary's report so when that actually emerges into the light of day we can review that and see what are priorities that the Secretary has identified will be. The second thing would be is when we do actually have the information on AHRQ funded projects, take a look at those from the

perspective of how is genetics, genomics and personalized medicine represented in those, and that would give us a better idea of the overall scope of what's going on.

CHAIRMAN TEUTSCH: Let’s take two more quick comments from David and Mara, and then we’ll try and wrap this up.

DR. DALE: I was going to comment that I think probably the space for us to be in is in the second two words in our name, health and society. That is, the patient's question often is does this information matter to me? Or the parent's question is my child healthy? The piece we need, which really doesn't fit with the acute stimulus money, but is the long-term, that is information sets that provide the clinical information to link to genetic analysis. And so we need to encourage the government and other sources to invest in--people say registries, but patient databases that allow for drawing good conclusions. Those are long-term investments. But I think of the huge value of the Framingham project in terms of what we have done with that because we made a long-term investment and looking for ways structurally to fund those kinds of projects, I think is very important.

CHAIRMAN TEUTSCH: Mara?

MS. ASPINALL: Well, maybe it's a good summary following up on Andrea's question. Are there some time-sensitive issues that need to be addressed in the short term? I understand Muin's comment about from October on there are other issues but, in the light of this set of grants now, are there comments, are there summaries on what's been put together to date that need to be—to be useful and actionable need to get to people before the October timeframe so that to me is the key time-sensitive question because, as I understand the health questions, but I also focus on the relevance of this committee and want to ensure we are doing something that people need the information.

CHAIRMAN TEUTSCH: Well, I'm hearing that we should be monitoring those and looking at them—

MS. ASPINALL: I guess I'm—

CHAIRMAN TEUTSCH: --but what I'm also hearing is that we probably should defer until October to get a real presentation of what's going on with these other entities and then we can make a decision about what's going forward but we can do some--ask staff to monitor these and maybe provide us some information for June.

MS. ASPINALL: Well, and are there any implications for which there are action items that can be impacted by the Secretary's office for which our view of it, even if it's an initial look at the data, is relevant.

CHAIRMAN TEUTSCH: So maybe I could ask, Andrea and Mara, since you seem to have a good notion of this, and I don't, maybe you could coordinate a little bit with staff about what could be done in the interim and then we'll look to the fall to get an update on the other activities and decide where we can add some value.

DR. WILLIAMS: So if I understand this, the issue is, as I see it, that you're putting forward is in these funded research projects currently that are doing genomic testing there are concerns that you have about how the testing is being done and whether the results of that are going to actually represent the quality that needs to be-- that we would need to have to actually draw conclusions.

DR. FERREIRA-GONZALEZ: Well, there is already a federal regulation that covers those types of testing. If you are going to make a clinical decision on how to treat a particular patient, even

for research, it should be done in CLIA certified laboratory. So bringing to light to the agencies that there are these issues they need to be very mindful of.

DR. WILLIAMS: So is this really something that--since right now the primary funding is through NIH, I mean is this something that would need to go—this concern would go—rather than going to the Secretary would go more directly to NIH?

DR. FERRIERA-GONZALEZ: Whoever is funding this research.

MS. ASPINALL: My issue was just slightly different. It was really a question. Are there any decisions that are being made, less on the previously-granted grants, which Andrea has mentioned, but more on those coming up for which the analysis that we have done and that you, Marc, have done in conjunction with others and taking other pieces, is useful to get in front of the Secretary or others. So basically is the work that’s been done so far useful to anyone in the granting of additional work between now and the end of the fiscal year?

DR. WILLIAMS: I think I can answer that question, which is right now everything--I don't

think that there would be any way to insert anything into AHRQ process would be my guess. And my understanding is that the Secretary's report is actually also done. It's just under consideration. So I don't think for either of those two things, which are the other two pots of ARRA money that haven't actually been distributed that we would have an opportunity to sort of weigh in on that. I think it would really be going beyond that.

CHAIRMAN TEUTSCH: We really need to wind up this session.

MS. ASPINALL: That was my fundamental question. I'm happy to work with Andrea as well on other issues but that was the core of mine.

DR. KHOURY: So just to clarify, the scope for this committee or this task force was the ARRA CER but ARC has already been funding many projects in CER that predate this. Some of the issues that were raised by Andrea, the analytic validity of the tests and the performance of the tests, we actually have a methods report, which I will talk about tomorrow, which discusses some of the quality issues and looking at the evidence.

So there's also other grant projects like the work on pharmacogenomics that was outside of

this funding but it’s also coming to a close. I would suggest that if we wait it might be useful to get a lay of the land, and there are other things that were not discussed here that will also be part of the discussion.

Also, it's a fast-moving field in terms of what is comparative effectiveness research and some people have already started using the term “patient-centered health research” as a part of comparative effectiveness research. So I think if we stay true to what the overall goal of our project is, regardless of the label, we will have a more long-lasting impact.

CHAIRMAN TEUTSCH: All right.

DR. WILLIAMS: Yes.

CHAIRMAN TEUTSCH: Very good. So that brings us to a break. I know we are running a little late so if we could limit it to 10 minutes so we’ll start back 10 minutes from now.

Thank you, Marc.

Thanks, everyone.

(Whereupon, at 10:00 a.m., a break was taken.)

CHAIRMAN TEUTSCH: I would like to first take a quick pulse. Given the pulse of weather that's coming our way, we could start tomorrow earlier than planned.

Would people be willing to start as early as 7:30?

All right. What we will plan to do, if people are willing to come at 7:30, we will start with some of the more informational parts that were scheduled for later in the day as best we can because the part that I know people are pining for is to hear about the patents and licensing report, and we'll leave that time-wise where it was before for those who didn't get the message.

We'll go ahead and post this on the website and on the listserv so people who want to participate will get notice that we're actually going to be starting early and, hopefully, that will give us some flexibility towards the end of the day.

Sarah will remind me to repeat this.

So we are going to return to the topic of genetics education and training, and Barbara McGrath has been chairing this task force and is going to be providing some initial remarks.

And we're going to then hear from Jana

Monaco regarding genetics education efforts by the Advisory Committee on Heritable Disorders in Children and Newborns.

And then Barbara is going to lead us through the overview of the draft report that her task force has developed which is in Tab 5 of your notebook.

At the end of the session we would really like to get to the point where we are ready for distributing the draft for public comment, so not the final version but to be able to get it out so we can begin to move this forward.

Sarah has something she wants to do.

MS. CARR: Its lunch, everybody. If you haven't filled out on the right side of you table folder, there's a little form here, please fill out if you want to have lunch this way, and put your name on it, and Marianne will come around and get it for you.

Thank you very much.

CHAIRMAN TEUTSCH: Great. So let me turn this over to Barbara.

PUBLIC CONSULTATION DRAFT REPORT ON GENETICS EDUCATION AND TRAINING AND DRAFT RECOMMENDATIONS

DR. BARBARA McGRATH: Thank you.

We have some tasks to accomplish this time with the task force so I won't delay too much. I'll start off by thanking everyone for giving me the opportunity to present this report. We've been working on it for a couple of years.

Before we launch into it, we are going to hear a presentation by Jana, who is coming up, and has been working on a similar project on the Advisory Committee on Heritable Disorders in Newborns and Children, and is going to share with us their findings.

And then, when she's finished, we will then launch into our report.

Jana?

BRIEFING ON THE SECRETARY'S ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN (ACHDNC) EDUCATION SUBCOMMITTEE

MS. JANA MONACO: Thank you.

(Slide.)

Thank you. Good morning.

It is a pleasure to be here and see some

different faces of another committee. It is a pleasure to be here today and to share with you our report as we both feel that we value the need for education and training in genetics, and especially for us in newborn screening.

(Slide.)

Our committee--our subcommittee I should say--is comprised of myself and Dr. Tracy Trotter, who is my co-chair, who is much more colorful presenting, and I wish he was here today, as well as members from other organizations to include ACOG, American Academy of Family Practitioners and American Academy of Pediatrics, Genetic Alliance, and the National Newborn Screening Center, and Genetics Resource Center, and these are some other individuals.

(Slide.)

One of our initiatives is to come up with a newborn screening clearing house and to help facilitate the discussion on that and we're happy to announce that the Genetic Alliance and the National Newborn Screening and Genetics Resource Center with HRSA is going to serve as that National Newborn Screening Clearing House. Their website is now active. The purpose of this is to increase the

awareness of newborn screening and be a good central link and a place for people to go directly to gain information from a professional and a public perspective.

(Slide.)

I won't read each slide for the purpose of time.

These are some other updates of what is going on. You're aware of the Prenatal Family Health History as an important one, which is a three year project to work with family practitioners in the prenatal period to provide a family health history tool to help, again, educate and learn what is behind these genetic issues and newborn screening and to really prepare families.

The American College of Medical Genetics has a great program that is on the horizon and that is their Medical Genetics Summer Scholars Program. And their rationale is that statistics show that about 18,500 medical school graduates each year, out of all of those, only one in 463 enters the field of medical genetics. Currently there are five states that have one or fewer medical geneticists and six states have less than two. Within the next ten years over 300 medical geneticists are expected to

retire. This addresses an important issue that we need more and so they developed this program that will be launched in 2011.

The purpose is to address this workforce issue and to capture students' interest and involving the students by practicing genetics in their work settings, to include clinics, labs, government and regulatory agencies and, hopefully, foster professional memberships and highlight the many diverse employment opportunities that the medical field has. And, hopefully, we'll initiate a stronger interest in getting more geneticists out there in the field.

You have your own educational task force here that you're working on the educational issues as well and again the collaboration of our subcommittee and your task force here together will be strong in helping to move forward with education and training.

(Slide.)

This is another list of some folks that addressing the issue of education and training and working as partners. Another quote that supports our need for education and training is that out of Pediatrics 2008 "Advances in newborn screening

service new challenges to the PCP, both educationally and in the management of affected infants. PCPs require access to information, collaboration with local, state and national partners is essential to optimize the function of the newborn screening system." Because as advanced as it is, it's not going to be as productive as it needs to be if people are not educated and trained.

(Slide.)

These are various partners that we are working with to help enhance this. The focus on the PCP role in newborn screening from all of these perspectives is to really address the response to the initial out of range result, what do the physicians do, how do they do it, how do they handle it; coordinate the complete evaluation to know what are the next steps; provide a medical home and coordinate care and educate families and health care workers from each of their perspectives because everyone plays a role in this very important aspect of newborn screening.

(Slide.)

Our Education and Training Committee serves in an advisory capacity to the current groups involved, both in the PCP and public family

education. And it has been very worthwhile to serve in that capacity to help bring everyone together to address this issue, and because we all value the fact that we just need to avoid duplication and enhance that collaboration and we will be more productive.

(Slide.)

In regards to PCP education we were able to participate in the National Institutes of Health Genetics Research Institute in their conference of developing a blueprint for primary-care physician education and genomic education. And with our committee we were able to house a roundtable session on the second day, which included about 30 participants, included the AAFP, the AAP and ACOG, and to really talk and address the issue of what are specific educational needs and barriers for them from each of their perspectives and what we can do to lift those barriers and enhance the education. A report for publication is being prepared by Alex Kemper.

(Slide.)

And some of the targeted areas are here listed as you can see. Again, from each perspective and how those agencies and organizations can address

these issues and together resolve them and provide better education and training because we feel that each organization from the time, from the prenatal time right up until the family practitioner, everybody does really play a role.

(Slide.)

We also address some of the barriers to educating the primary care providers. These are some of the comments that were made that we have to address which is lack of time. Everybody only has so much time in their daily practices to really get in depth into such an issue of genetics. The lack of geneticists to train the primary care providers including especially those that are already in practice and that is where we really value the fact of getting those medical students and educating them early on.

Lack of enthusiasm: There is poor genomics and genetics medicine literacy out there that interests people.

Lack of certainty and confidence in this area: It is very easy for people to say, “That is not my specialty, that’s not my area of expertise.”

And the concerns about relevance to child healthcare and the fact is, as Dr. Trotter always

likes to say, that everyone does genetic screening or genetic testing if they took care of a newborn in their practice that day.

(Slide.)

These are some educational interventions that are taking place that we feel will really help move things along and that is to develop educational curriculum for the residency training programs. Again, it is taking steps backward and going to the very beginning of future physicians. Assuring that board certification exams do assess basic literacy in genetics and genomic medicine and having CMEs on the practical aspects of incorporating the genetics and genomic medicine into primary care as well as promoting the participation in genetics and genomics related educational activities through the maintenance of these board certification processes. And to create a web site that will be a tool for everyone.

(Slide.)

Genetics and the Primary Care Training Institute are working on a learning collaborative that will help prepare physicians with busy primary care practices with experts in genetics and genomics medicine that together they can work and provide

that hands-on opportunity to be educated in genetics and newborn screening and at the end, meaning at the end of the year, to share their results and to institute to formally evaluate a project impact.

(Slide.)

Our next steps, as we look on the horizon, are residency training materials through our regional activities, partnership again with our organizations, such as AAP, AAFP, ACOG and the American Board of Pediatrics. And the development of genetics and a primary care institute and to continue following up with your committee's educational taskforce as we strongly value the need for education and training both on the professional level and the public level. And as technology advances and the awareness and the newborn screening programs continue to develop and progress, the need for this kind of education and training is far more important than ever has been and I think, with the hockey puck analogy, we really have to look ahead to where it's going, especially with the other disorders that are on the horizon that are being addressed and looked at to add to our panel and all our screenable disorders.

(Slide.)

So with that, I thank you for the opportunity to be here again and share our initiatives and work, and look forward to further working with you.

COMMITTEE DISCUSSION

DR. McGRATH: Thank you so much, Jana. Great minds think alike. I think you're finding spring much articulate with ours and it is nice to see that we come up with the same barriers as well as some o the same solutions so it makes logical sense that we would be able to continue to work together and we will talk more about how to be able to do that.

We have a lot to do in a short period of time and the most important part for me is to have the discretion and receive your comments on our recommendations. But before we launch into that, I want to give a quick overview of this committee.

I actually am familiar with the report as one might assume but last night on the airplane I read it from beginning to end in a nonstop way and came away with a couple of impressions that I hadn’t necessarily had before and I wanted to highlight those a little bit for you.

One is the report makes the case that

since the very earliest days that there even was a Secretary's Advisory Committee about genetics, education has always risen to the top. Every time we have any priority setting activities, education is there. Whenever we talk about a different topic there is always a nod to this and this has an influence on genetics. So it clearly has been on our landscape forever.

Over the years much has been written about the challenge of translating findings from the Human Genome Project and other genetics science into something that might be clinically useful. More recent attention is being paid towards looking towards chronic illnesses and how we can apply genetics in dealing with those more common diseases as well. And also the promise of personalized medicine is definitely on the horizon.

A common image that I think all of us are carrying in our heads these days is this continuum. And on one side it might be something like genome science and on the other side it might be something like genomic health care, different words, but in between inevitably on that line it’s a pretty thick line between the two.

Marc popped up one today and I looked

again and that line is fat.

And I think that reflects maybe inadvertently that it's a challenge to do that translation from one to the other. So we are kind of looking at the right-side of that in this group looking at healthcare but I think if we—but we all sort of know around here that it's a loop, that there are pushes and pulls back and forth, that healthcare pushes science and vice versa. So we do not want to be thinking about healthcare and health professionals sort of in isolation from the science.

There are a few things that are not controversial, I think, and I think overall the whole report is not controversial but two are sort of slam dunks. And one is that I think we all might agree that we are all best served if we have a knowledgeable workforce that understands appropriate use of how to use genetic information.

The other thing is that consumers are participants in this as partners in these endeavors rather than simple recipients of services. So those, I think, are probably shared values, at least for most of us.

What might be a little less obvious is that embedded and batted in this report is this

notion, of course, of the translation of science into clinical utility or clinical application but the report is also about the transformation of thinking, perhaps even in the absence of anything of any on the ground applications. That second idea is often called requiring a paradigm shift. And if we think about the original use of that word, coined by Thomas Kuhn a couple of decades ago, paradigm shifts, we use that a lot. It has been used already a couple of times this morning. They are dramatic and often cause disruptions in science when they happen. They are rare and we do not know if we are in the middle of one or not, but they do cause a big change. So I want to suggest that there may be some change in the subtext of the report that is not necessarily openly stated.

So if we are thinking about paradigm shifts in scientific revolutions, who is part of this revolution and that’s the task force group, you have seen these names before. They are really a very interesting group of people. It is a huge group of people. The expertise and richness of knowledge is very deep as well as the staff. We just keep adding and adding staff members to this so it’s a big, big group.

The structure of it we have divided into three work groups and each of them has leadership and health care professionals. David Dale is the chair of that group. He follows Greg Feero.

The Public Health Provider Group with Joseph Telfair, who actually rotated off the committee a couple of meetings ago and stayed very involved, which we appreciate, and he is here today to help us answer some of the questions. I appreciate that a lot. And Vence Bonham is the chair of the Consumer Patient Group, and he has hung in there the whole time and provided leadership to that group.

The timeline: We picked this up from the previous group that worked on it in 2004. And we are responding to that report.

We had an international roundtable. We were then tasked with forming a task group, at those early meetings, there was a decision about the boundaries and we came away with deciding that this report would cover three groups, Point of care, Health care Professionals, Public Health Providers, Consumers and Patients. Those discussions were long and hard, and it seems like—and that actually the boundaries are tighter than many people suggested,

the even larger group that was recommended. We narrowed it down to those three. Those three could also be three different reports and perhaps that is one way to approach it. What we attempted to do was to think about the notion that ideas and people moved through systems. They do not just stay in those three silos. So our intention for combining it into one report is to take a nub and appreciate that integration of services across the landscape and we'll see if we can accomplish that. 2008 and 2009 was where the bulk of the work happened and we reported at this committee each one of those so you've heard this is a lot. At the last meeting we did talk about recommendations and then there was a working session in D.C. held around December where we ironed out the recommendations and then they were heavily massaged by staff after that, and that is what we will be looking at today.

The final report will have an executive summary and recommendations. The draft one that you see here does not. It does have the ordinary background and scope which is the literature and then the three working groups have their own sections on their literature as well as the data that they collected. We have a freestanding survey

of federal activities which was intended to follow up on what has happened since the previous 2004 report and then conclusions and recommendations. Our data gathering activities included a review of all of the literature concerning those three groups that we mentioned and then each workgroup conducted their own original research.

They each administered, created and administered surveys. And then the Patient and Consumer Group also did some interviews. Each of the work groups functioned within each of those leaders—I'm sorry—they had people working with them. It wasn't just the three names you saw up there and we should—next time I'll show those people but within those workgroups they were the ones to decide what data gathering activities were to be done so they had a lot of autonomy though we coordinated a lot.

Before we talk about the discussions I'm going to highlight what we are trying to accomplish here today and where you all come involved. We do have a couple of discussion questions that we're going to ask at the end of them.

(Slide.)

And one is do the findings follow from the

literature review and survey? Do the draft recommendations target the issues and concerns identified in this report? Meaning specifically, are these recommendations specific enough? We have always talked about that we want them to be actionable. Do they rely on the appropriate degree on the public sector, the private-sector and the public-private partnership? Meaning, are we targeting it to the right places? And, overall, is this report ready for primetime?

When we go through it, you will see that the recommendations are fairly dense and we will talk about whether we think that perhaps the message gets lost in its denseness or it is required so we get our point request and there is a couple of decision points about how to phrase these.

I have talked about this report in the past as kind of an unruly teenager, partly because it is so big and we have taken on such a big task. Not to kill a metaphor but I will do it one more and then I promise no more metaphors but right now it feels like it's a young adult. It is feeling quite confident that it is ready to enter the real world and that it can handle any criticism that may come its way because how hard can that be, and

perhaps sort of optimistic that good intentions do lead to good outcomes. So part of the question that we're asking everybody here is, is it really ready for prime time? So that will be at the end of the session.

DR WILLIMAS: So we are trying to turn it into a cynical, older adult? Is that the idea?

DR. McGRATH: That is why I'm going to stop at the young adult and not keep wearing this poor metaphor out.

Findings generally: We came through both data points, review of the literature and the original data that we collected, and came up with a couple broad conclusions. One is that the integration of genetics into healthcare is limited by inadequate or ineffective genetics education. There is just not enough. There needs to be more education. The need for clinical services has increased but the workforce is insufficient. We need more numbers and healthcare professional organizations report about competing priorities. These are legitimate concerns that this is not a primary concern or obligation they have, and where do they put it in this list of very important other tasks that they do.

(Slide.)

The current public health force is not prepared to receive and assimilate genetic and genomic information in to public health and there are a number of barriers to that because the public health workforce is uniquely diverse because it covers such a range of population health issues and consumers prefer to obtain genetic information from the providers but they also turn to the media.

A couple needs were identified through themselves and through other advocates: The need to understand the concept of multiple risk factors. This is in contrast to a very deterministic view of genetics. Understand the role of the environment and the complexity of that, a need for various tools that are understandable to evaluate the veracity of the information, and then, of course, concerns about direct to consumer genetic testing. Most consumers view the government as a trusted source for information and so we have an obligation to follow through with that.

(Slide.)

There are seven recommendations so it is not a million. I went back and forth trying to decide what to do with this and I am going to read

them in case some people cannot see the screen or don't have them. I actually find them easier to follow in the book on page 110 in Tab 5, and that's sort of where I'll be following. So I will read through all of them first and pretty rapidly, and then we will discuss them. There are a few that you will see require very concrete decisions, others WE Will leave open to if you have comments about that. Okay. Here we go.

(Slide.)

Each recommendation is prefaced by what you might call a preamble or a preface, and that's just to give it the context.

So for recommendation number one the preface is a significant body of literature from the United States and abroad highlights the inadequate genetic education of healthcare professionals as a significant factor limiting the integration of genetics into healthcare. Genetics content is often minimal in health professional educational programs and focuses primarily on single gene disorders and is not associated with long-term knowledge retention for clinical application. Innovative approaches that coordinate the efforts of entities controlling health professional education and training will be

required to remedy the situation. These entities include but are not limited to healthcare professional organizations, educational institutions, specialty certification boards and academic accrediting organizations.

(Slide.)

So there are two options of recommendations that follow this preamble. We will need to choose between one of the two or combine them or throw them out entirely.

(Slide.)

The first one is HHS should form a multidisciplinary public-private advisory panel to identify and promote innovative approaches to genetics and genomics education and training in a context of healthcare. The key words in this one is "is to form a panel."

This proposed advisory panel should be composed of representatives from HHS agencies and other federal departments, for example, the VA and DOD, with established programs in genetic/genomic professional education as well as representatives of healthcare professional organizations engaged in genetics and genomics accreditation certification and continuing education efforts. This body will:

(Slide.)

1: Identify successful education and training guidelines and models that are outcomes based, identify where it works.

2: Identify current funding streams for developing and promoting genetic/genomics education, as well as gaps in funding. So this is all about funding.

3: Recommend mechanisms for expanding and enhancing the content needed to prepare healthcare professionals for personalized genomic healthcare. This is about what content needs to be included.

4: Recommend how evolving standards, certification, accreditation and continuing education activities might incorporate genomic content. That is about the whole world of certification.

5: Publish findings and recommendations and develop a plan to monitor outcomes of its work.

(Slide.)

Option B is HHS should convene a workshop to identify --the rest is the same. So the keyword there is to "convene a workshop." The purposes are just the same as the ones I just read and the choice is between forming a panel and convening a workshop.

So think about that.

(Slide.)

At the end of that there is a recommendation connected to this to act on a recommendation from a previous SACGHS report, The Oversight Report. And this relates to the notion of decision-making tools—

UNKNOWN: Clinical decision support

DR. McGRATH: I knew there was a word missing there.

UNKNOWN: Clinical decision support.

DR. McGRATH: Clinical decision support, and how that plays into the education needs of health professionals. We can decide whether we think it should be part of the recommendation or stand as part of the preamble or whatever if that is the choice. Okay.

(Slide.)

Recommendation two: Consistent findings—this is the preamble. Consistent findings in the literature and SACGHS surveys indicate that healthcare professionals and public health providers serving underserved and underrepresented groups and populations face significant challenges. Additionally, these communities have specific needs

and their involvement in the development of effective education models is imperative. This is about health disparities.

(Slide.)

So the recommendation is HHS should promote the development and implementation of innovative genetic and genomic education and training models for healthcare professionals and public healthcare providers serving underserved and underrepresented groups and populations.

Specifically, HHS should—

A: Target research funding, the key word is funding, to identify effective educational models for healthcare professionals and public health providers in underserved communities; so funding to identify models.

B: Identify and support programs to increase the diversity of the healthcare workforce in general and the genetic specific workforce. This has to do with workforce diversity.

C: Ensure that consumers and representatives of rural, minority and disadvantaged 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. This is community engagement.

(Slide.)

Draft Recommendation 3: The background is the inherent diversity of the public health workforce makes it difficult to target educational efforts to improve genetic and genomic knowledge across the workforce. A systematic effort that evaluates the composition of the public health workforce with current job responsibilities related to genetics and genomics and identify future needs has not been done. This has to do about serving the public health workforce, that group that is so diverse.

(Slide.)

Specifically, tapping the expertise of its agencies with relevant missions in public-health, HRSA, CDC, IHS and NIH, HHS should assess the workforce to determine the number of public health providers with responsibilities in genetics and genomics to ascertain current trends to sort of look forward to the public health workforce and see where we are now and where we might need to go. I'm sorry, I missed a sentence. And future needs…that’s the future part …to identify education and training

needs to promote leadership development in the field. Based on this assessment, HHS should support and encourage the incorporation of relevant genetic/genomic core competencies and the knowledge base of federal and nonfederal public health providers and specific competencies in those whose responsibilities require genetic knowledge. The key here is the core competencies; it should be based on those.

B: Fund educational programs based on these competencies that promote genetic and genomic knowledge, recognize the potential impact of affordable genomic analysis and incorporate the concept of environmental interactions in risk assessment for population based genetics.

The competencies should be based on these trends that we're seeing. Okay. That’s about public health force.

(Slide.)

Recommendation Number four: Consumers have consistently expressed the desire for genetic information that is comprehensive, accessible and trustworthy. And again, this is the second recommendation that we have two options that we should decide on today.

The first one is that HHS should endorse and ensure sufficient funding for existing government resources such as those developed by NIH and CDC to provide comprehensive, accessible, trustworthy genetic web based information for consumers. These resources should include scientifically validated information and also links to credible information regarding the topics such as genetic contribution to health and disease, gene environment interactions, genetic testing and legal protections against genetic discrimination. To reach a broad range of communities these resources should also include links to information that are not web based, such as television and radio programs and print materials, and they should--the availability of these resources should be promoted using a wide range of strategies from collaborating with developers of internet search engines to working with community leaders at local level, mechanisms to alert interested persons to adapt and new information should be developed.

The key here is the notion of working with existing government resources. We might think about things like the genetic home reference here, also various agencies have their own that each one is

unique. NHGRI, CDC, NCI, as well as the rare diseases websites might be thought of those as the models we are talking about here.

(Slide.)

The other option, Option B, is that HHS should endorse and ensure sufficient funding for a web based information resource center that builds on existing government resources. The rest is the same.

The difference between these two choices is the first one is to work with existing resources. The second recommendation is recommending that the Secretary facilitate the development of a new freestanding web based information resource perhaps that fills in the gaps that the other ones don't and is developed with what we know now.

The rest of the recommendation is the same.

(Slide.)

Recommendation five: The background is with the vast increase in scientific knowledge stemming from genetic and genomic research and new technologies and the increase in direct to consumer genetic services, consumers of all literacy levels are challenged to understand and use this

information to make appropriate health decisions.

(Slide.)

The recommendation is HHS should support research that identifies the methods that are effective for translating genetic and genomic knowledge into information that consumers and patients can use to make health decisions. HHS should also support research that identifies effective methods of patient communication. Based on this research and to reach diverse people and community needs, HHS should develop educational programs that use a wide array of media, television, radio, print and mobile phones, and provide for translation of materials into locally predominate languages. HHS should then support the dissemination of these programs.

As part of this dissemination, the Secretary of HHS should work with other relevant departments and agencies such as the Department of Education, National Science Foundation, to integrate effective educational programs into science and/or health education initiatives.

This is recommending that there be research to identify models or the best methods for patient and consumer education, patient and consumer

communication strategies and then the best ways to disseminate these programs.

(Slide.)

Recommendation Number six: The background is about family health tools were developed as one means for individuals and families to gain health literacy and take a more active role in preventing and managing disease, particularly inherited conditions. These tools are a powerful asset for consumers and healthcare professionals to use in risk assessment and health promotion but EHRs must be capable of accepting the information provided by the consumer oriented tools, and you might think of My Family Health Portrait as a consumer oriented tool, otherwise the value of family histories are diminished or omitted as a factor in risk assessment.

(Slide.)

The recommendation is that HHS should support continued efforts to educate healthcare professionals, public health providers and consumers about the importance of family health history. Specifically for health professionals, HHS should 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. Clearly we're talking here about the tools and the EHRs. For public health providers, HHS should promote research identifying the role of family history in public health. How does family history fit into population health?

(Slide.)

And for consumers, HHS should promote research on how consumers use family history to make healthcare decisions. For example, things like lifestyle changes. They should assess the effects of gathering family histories within diverse cultures and communities and among individuals where family histories are unavailable, perhaps among refugee groups; expand public health awareness programs and patient information materials on the importance of sharing family history information to primary-care providers. This is education again. And promote the embedding of educational materials in family history collection tools directed to consumers and ensure access for all by providing these tools in various formats, using those as another educational venue for consumers.

(Slide.)

And the final recommendation, number seven: Given the reality that healthcare professionals and the professional societies representing them are unlikely to invest significant resources in education and training and content areas for which services are only partially or not at all reimbursable, a critical step in promoting increased knowledge of genetics and genomics among healthcare professionals is ensuring reimbursement for time spent in direct patient care that delivers genetic and genomic services. We are here calling attention to the notion of time.

Specifically, in order to increase incentives and encourage investment by public and private organizations in education, training in genetics and genomics and to increase the willingness of healthcare professionals to participate in educational programs the secretary should: (a) ensure reimbursement for healthcare professional time spent in direct patient care delivering genetic and genomic services, such as interpreting of tests and collecting family history; (b)ensure the reimbursement for all members of interdisciplinary teams and for distance

consultation and telemedicine; and (c) act on the recommendation of the previous report on coverage and reimbursement that specifically called out to genetic counselors and reimbursement.

(Slide.)

Good reading, huh? Okay.

The next steps are what we're doing right now, review these and get some feedback and make a decision if this puppy is ready for prime time. If it is, it will go out for public comment. We will analyze those and report back in June with a final report. If it gets accepted at that point it will go to the Secretary in August.

So, I know we need to talk about one and four so maybe I'll just--since I have an urgency to settle that issue, I have the mike open so I will open that up first going back to recommendation one and again the issues.

Two proposals presented by the task force are (a) forming a multidisciplinary panel meant to be filled with maybe not your usual players looking at cutting edge ways of thinking about education and translation, and that panel would have whatever authority the secretary gives it. Another one is to form a workshop which is often considered to be a

single one time day long or couple daylong event that would come out with some things at the end of it. And we can open it up to any combination of that.

I think that Mara was first and then Paul.

Thank you.

MS. ASPINALL: Well, I think you clarified it at the end. The idea is a workshop is a one-time event, a panel as an ongoing event.

DR. McGRATH: It tends to be, yes.

MS. ASPINALL: And this may be—I don't know if it's slicing it too thin but the idea would be potentially combining the two and the idea of starting with a workshop to kick off the issues to then better inform a potential panel going forward.

DR. McGRATH: I imagine a risk with that would be if the workshop decides that getting it done in a day is enough then you wouldn't have that richness of a panel but that's certainly—you know, if the recommendation is simply for a workshop, you could end with a workshop. That might be the risk of doing it that way. But the idea of blending the two, there is some good reason for that.

MS. ASPINALL: Did the committee have a recommendation or was this--did the Committee have a

preference?

DR. McGRATH: I think there wasn't 100 percent consensus. The benefit of the panel is that it could be in greater depth. The benefit of the workshop is that it might be something that the Secretary actually does, whereas, a panel may be not one more panel.

MS. ASPINALL: I'm going to say I would go with the combined idea. Start with a workshop so it actually happens with the possibility of forming a panel thereafter and we get the best of both worlds.

DR. McGRATH: The best of both.

MS. ASPINALL: I'm into practical.

DR. McGRATH: Yes, I agree.

DR. BILLINGS: So I want to also endorse the notion of doing both and, in particular, to assess--and this may have already occurred in part of your deliberations and I may just be unaware of it but to assess the role that the private sector plays in providing education. There has been a lot of focus, of course, on marketing and the negative aspects potentially of the private sector materials linked to marketing. But there is also an enormous amount of education material produced by the private-sector which is, in fact, a substantial part

of educational activities now and it needs to be thought about. And, in fact, I would strongly encourage it being a topic and representatives of the activities being included in any ongoing panel or review.

The other point I just wanted to make was one of personal experience, which is at a community hospital that I am involved with we are trying to improve genetics' education for the medical providers at the hospital. And CME rules are actually interfering with our ability to get more genetics into the curriculum because of rules about priorities, establishing priorities of the hospital based on needs of the clientele. The fact is that genetics is not viewed as a need at this point so some attention to those issues, I think, is also important.

DR. McGRATH: Just really quickly, yes. The whole notion of the perceived need is a definite barrier to education and should not be taken lightly. It shouldn’t be dismissed. I think you’re right. The idea of using new educational models as part of this number one recommendation, get out of the old tired way of doing textbook learning and try to think about what new technologies and just in

time learning work.

Thank you.

Gwen?

MS. DARIEN: This may be a naive question, and I'm sorry I stepped out for just one second but if we say that we want to do a combination of a workshop and a panel we cannot say that the workshop is going to decide that there needs to be a panel. Then there's no reason to do a workshop. Is that correct?

DR. McGRATH: I think that's correct. I would imagine we'll get advice from staff on the wording but I would imagine part of it would be hope that the workshop would address the following issues, and one of them would be the need for a longer panel or something, a multidisciplinary panel or something.

DR. WILLIAMS: This is just to facilitate this then what I would recommend then that what we do is, given what I've heard, is to take Option B and essentially add an F to that, which is that part of the charge to the workshop would be to determine the need for and develop the—determine the need and, if necessary, develop the charge for our panel to move forward with the issues identified by the

workshop.

DR. McGRATH: Perfect. Yes, I agree. That makes total sense

And, Joseph?

CHAIRMAN TEUTSCH: You need a mike. Just come to the table, Joseph.

DR. JOSEPH TELFAIR: Okay. Thank you very much.

No, actually, Dr. Williams beat me to the point that I was going to make.

We had a discussion actually as part of our task force on this issue of the combined, too. And we were pushing in the direction, you know, of the workshop allowing for the charge to be developed.

The challenge again, as Dr. McGrath said, was we wanted to look for something that was a low-cost/no-cast opportunity that we thought would be done.

DR. McGRATH: Okay. I like our solution. I think we will go with it. Done.

DR. EVANS: I just wanted to—on a different note, one of the things I worry about is the people who are uninitiated in this will read it and see training and education all in terms of

residency and medical school, et cetera. And I know we say “in the context of clinical care.” I’m just wondering, if this isn’t wordsmithing too much at this point, to say something like "and integrated with clinical care” because I think the only way we’re ever going to educate the body of physicians out there is to integrate it with clinical care with just in time types of things.

DR. McGRATH: Right. I think it is good to add that where we have it in our heads but not on paper. Great.

Mara?

MS. ASPINALL: I completely agree with Jim's comment and what Paul had said. I was wondering if we—again it may be awkward at this point but, you know, this is in many ways process and philosophical but I’m intrigued by the area of domestic violence, which has been a very important and key area for physicians to be the gatekeepers to recognize domestic violence.

My understanding is that after a workshop of sorts and a panel, I believe, convened by the AMA but I’m not sure, it was a recommendation that it became a required piece of CME education in the 47 or 48 states that have CME. It is probably

premature to recommend that but my understanding of that process on domestic violence from start to finish happened in about five years and now by state it differs somewhat in terms of what the actual educational component is.

But to Jim and Paul's point, as a required piece of CME, which it now is, it absolutely integrates its and keeping something as broad and its very relevant to what we talked about this morning of the affordable genome, which is putting a piece on genetics and genomics as a required piece of CME. I recognize that adding that in and of itself may be too much to put into the report as it stands now but I would ask the committee to think about it and/or bring it up as a panel discussion.

I personally have written several--a couple of articles on this exact issue and in small groups of physician associations they were quite intrigued with that because it would put some rigor and national view so that we would get in all communities a requirement so it wouldn’t be because one state physician association was interested. Those state physicians get more information than others and there are some areas of the country from a relative point of view with fewer academic

centers, potentially that's one logic, that have less focused energy on this issue.

DR. McGRATH: I think domestic violence is a terrific example because it is not only, as you mentioned, raising to the top in terms of CME and other continuing education for other health providers but is also making it into a required part of the medical chart in many healthcare practices. So it is translating from learning in that--in your conference in Hawaii when you are sitting and learning about continuing education for your field to—your clinic having it be similar to a vital sign, that it is a question that needs to be asked of all women by a certain age. So it is that translation thing that we're talking about of clinical education and just in time education.

It would be great if we kind of keep moving in that direction. So that's a good point. Thanks.

(Slide.)

Okay. Number 4: Recommendation 4 is the other one where we just couldn't decide so we decided to let you all help us with this. And this is the idea of community--of consumer resources. The data from the survey, the literature and the

interviews highlighted the fact that consumers simply have too much information out there. They don't know what's credible. There are specific sites for one thing. If they need something else, they have to go to another site, and pretty soon they're sort of very frustrated by it. A lot of those sites were developed a number of years ago and some of them are sort of looking dated.

And coupled with this is the very strong message that we heard is that consumers trust the government as a clearing house and a gatekeeper for information. So what do we do with that information? What do we do with that data that we gathered? Is there something that—a recommendation around that?

And as you see, there is two. One is to take—you know, don't throw the baby out with the bathwater. There are existing resources, maybe work with those. The other is to develop or ask for the development of one that may be unique, that might be a little more forward-looking.

COMMITTEE DISCUSSION

So those were our choices. Any thoughts on those?

Again, this is going to the Secretary of HHS, which I think is very important to remember.

DR. WILLIAMS: I think that there is a real opportunity for a one-stop shopping site, if you will, that would be a novel resource. The thing, of course, that always is incumbent on it is execution. We just need to—that's the more pragmatic perspective, which is its all well and good to say we're going to do it but if we don't do a good job of it then it's really not going to be helpful.

And I think it's also one philosophically can't try and do everything. It has to be cognizant of the other resources that are out there and direct people to those resources as appropriate but, you know, be sort of the place where people can go to have a one-stop place where it can facilitate navigation and deal with some of the frustration. It is somewhat interesting that the study results show that the public does, in fact, trust the government. There is not a lot of empiric evidence to support that point but be that as it may that is what they said.

DR. McGRATH: Gwen, and then Muin?

MS. DARIEN: Well, I think that—I mean, if you look at it, people go--the two places that people go that I know for cancer are cancer.gov or

cancer.org. So it's either ACS or the NCI. But I think there is a compromise here which is to develop a new portal within an existing system so you end up on the CDC site or the HHS site but there is actually a portal that you can--that has its own name, that has its own URL so that you can go in either way so you get everything together.

I think people are constantly trying to replicate what is out there and better it without saying, well, this—we're now picking the best of what is out there and integrating it into that place. So I do think there's actually a middle ground there.

DR. WILLIAMS: And I think I was saying that but you said it much better. The idea of the portal—and you can look at this as some of these newer search engines that are coming out where they are really trying to understand what it is exactly that you're looking for. So rather than, you know, going to cancer.gov and saying I can't find what I need here, I need to go somewhere else, where they could go in and there could be some methodology by which they say, well, you know what, based on what you've told us, here is the best resource for what it is you're trying to find, so the content doesn't

have to be extensive but some of the thought process about how to interact with the consumer might be quite novel.

DR. McGRATH: Muin, and then—

DR. KHOURY: So part of the challenge here is, of course, communicating to a wide variety of audiences, including the providers, including the consumers, and traditionally it has been tough because even within the government—I mean there are all these resources, I mean, NCI, cancer.gov and others, and I think the consumer is really bombarded with a wide array of so-called information but there is—I mean it is hard to know what works and what doesn't work.

So as an experiment what we're doing with GAPNET right now is to try to develop this genomic applications and practice and prevention knowledge base so we are partnering with NIH, NCI and others to develop this sort of what you call information resource that actually has—is a virtual link but also has what are called distilled nuggets or topic briefs that actually capture what we know and what we don't know very quickly.

And for those of you, who watch the *Federal Register*, we just put out an RFA yesterday

or the day before calling for the creation of a Genomic Knowledge Synthesis Center that could, hopefully meet some of the needs of what you're trying to do here.

This Knowledge Synthesis Center will work with EGAP, will work with GAPNET. It can't be all things to all people but it is going to try to distill through a process of systematic reviews as well as quick topic briefs for particular applications, what we actually know and don't know and whether there are evidence-based guidelines out there that can lead the consumer to the right decision making process.

So I mean I, of course—I mean we've been thinking about these things for years and I welcome the opportunity to work with other agencies to see how best implement an information resource that is both centralized but actually virtual, it can link to other information resources because you can't have one site that fits the demands of everybody.

DR. McGRATH: Thank you.

DR. DALE: I would speak up in favor of trying to augment the existing resources. Kind of like remodeling an old house but it's a good thing to do.

And, in particular, there is so much material that has been developed that can be adapted for different audiences. And I have been a participant in the past in health literacy issues where you try to look at how do people learn and how do you get to their level, and I think adapting existing materials like gene clinics, for instance, is a way to get there in a far shorter time with far less work and cost.

DR. McGRATH: Right.

DR. ZIVANA TEZAK: So I want to go back to the consumers and where they get the information. And I think what we need to keep in mind is that this Wayne Gretzky analogy and where the puck is going, and you know we're saying we need to educate people, we need to educate people at the higher levels, but what's happening is—you know, my son goes to middle school and in middle schools in science they are now having expression microarrays, playing genetic counselors, that may be an anomaly but that may be coming all over the country. So these kids who are middle schoolers, who are 12 years old, are learning this stuff.

So maybe we need—when we are looking at stakeholders, maybe we—and the workshops, maybe we

should include somebody, middle schools, some—not middle school kids but, you know—

DR. McGRATH: Educators.

DR. TEZAK: Education.

DR. McGRATH: Right.

DR. WILLIAMS: Well, I think, you know, that is a really good point. One of the other recommendations, not the one that we're currently looking at, specifically indicates the need to connect with the Department of Education and say—because you're absolutely right. If we begin it from day one in the education then we will have a genetically knowledgeable public and workforce but it will 20 years from now.

DR. TEZAK: And, you know, genetics is right now hot apparently if they're teaching them at the middle school. So it's a good opportunity but who knows where it's going to go.

DR. McGRATH: Sylvia, and then Gwen.

DR. SYLVIA AU: So I think this portal is like the congressionally mandated Newborn Screening Clearing House from the Newborn Screening Saves Lives Act that Jana talked about where it links you to existing resources, and I think one of the things that we're doing in helping develop the clearing

house is a filtering system so that people that come in, you know, will say I am a parent living and had my baby in Hawaii, and so that filters the results so that Hawaii specific materials would come up at the top first for newborn screening.

So I think maybe something like, I am a primary care physician and I'm looking for information about whole genome sequencing because all my patients are having it and bringing the results to me, and then being able to have some of those results coming so just some filtering like that.

DR. McGRATH: I think that speaks to Marc's idea of the search engines that can be more specific, yes, and that would be the portal.

Gwen?

MS. DARIEN: I think the one—just to build on the issue of what kids are getting in school, I think that it's important to remember—I mean, we did talk about collaborating with the Department of Education but it has to go through your entire education because how many of us got A's in algebra and can't help teenagers do their algebra homework? I mean, you know—so if—

(Laughter.)

MS. DARIEN: Well, I'll raise my hand but it is—I think it is really important that it's not just a very isolated thing and that it actually goes through a longer lifespan of education.

DR. McGRATH: Right. Okay.

What I hear is a notion of a portal that would have some of the decision-making capabilities and it to help the person be more specific with the exception of David's comment of a recommendation to revise what's existing.

If we go with the portal method, the idea--and, of course it would have links to those existing ones and maybe there could be an input to improve those or update them or whatever. The way the recommendation is written, is it actionable to the Secretary of HHS? Can we picture what she might do in response to this if we are saying we would like a new portal developed that has all these features?

Yes. Okay.

David, and then Joseph, and then maybe Sara.

DR. DALE: Were I the Secretary I'd immediately ask what do we already have?

DR. McGRATH: Uh-huh. I think you're

right.

Joseph?

DR. TELFAIR: Yes, as usual. I was going to say similarly but what I was going to rec—I think one of the things that we had a lot of discussion around was to take advantage of existing resources.

What I heard actually was not a new portal but an add-on ornament or a site dif—you know, modification of a site where one already exists and all you would add would be just one more add on that would allow you to do this. So it is not the creation of a new one but just, you know the add-on and use existing resources. That would be something that--and part of what we were trying to get at, which would be actionable and you could use would be something that could be slightly modified that's out of what's already in existence.

DR. McGRATH: Okay.

Marc?

DR. WILLIAMS: So if we look at the evidence that was generated I think that you can make the case based on the studies that were done to say that, yes, we know there are a lot of existing resources out there but they are clearly not meeting the need because we're hearing from the public that

they're saying, you know, this isn't doing it. So some of that is incumbent on what David is saying about we need to modify those existing resources.

But I think it also argues for the fact that, you know, it's not just those resources are perhaps not designed as best as they could but the people are having difficulty getting to them. And I think that the—I think David's idea is very compatible with the idea of having sort of a one-stop shop that would help to direct queries to appropriate resources.

I really think that those working together to improve the existing resources and to have, if you will, a service layer on top of that that really helps get people to the right part—I mean in the electronic health record environment this is exactly the issue that we deal with all the time.

We have all of this information that's in our electronic data warehouse and people want to get at the information, and if they are just turned loose in there they will never find it. So you create service layers in there to say, well, what you are really looking for. I'm looking for this laboratory result. They can enter it in plain language and they go directly to where they need and

it saves a lot of time.

I think it is a very elegant approach.

DR. McGRATH: So a one-stop shop to me means a unique portal. Okay.

DR. WILLIAMS: Yes.

DR. McGRATH: Yes, okay. Just to clarify that.

And, Vence, I'm just going to ask if you have anything to add because this is—

DR. VENCE BONHAM: (Not at microphone.)

DR. McGRATH: I don't think it's on.

Sorry about that.

DR. BONHAM: I echo Dr. Williams' comments. Some of the comments that we received from the interviews was this issue of we have a lot of resources that are great resources, that have great data but the people don't know where to go, and identify some kind of a resource that then can lead to other resources. So that was the whole perspective about a portal—development of a portal versus just enhancing the current resources.

So my comments just echo Dr. Williams.

DR. McGRATH: I am feeling a consensus without having hands raised that suggests that maybe because it's a little bolder, a new thing is to

suggest the development of this new portal. We risk it being dismissed as too ambitious but I'm sort of feeling the tone in the room for that. Should I be corrected on that?

We will get public comment as well and we can revisit this again.

So let's go with the portal for now because it’s actually something new and we’ll get comment on that and see where we go with it. Okay.

Those are my two pressing agendas. I of course have questions on the others more generally. Are they too wordy? Are they clear? But I’d like to open it if there are specific recommendations that we would like to talk about, and we do have—we are doing all right. We’ve got about another half hour, I think.

CHAIRMAN TEUTSCH: Yes. And, also, if there are recommendations that should be included that aren’t.

DR. McGRATH: Yes, absolutely.

Scott?

I don’t think you get lunch early just because we do not talk, though.

(Laughter.)

DR. ASPINALL: I will start.

DR. McGRATH: Thank you.

DR. ASPINALL : Which is I thought it was a great report so that we may still get to lunch early but I thought it was quite comprehensive and I thought that the recommendations, as well as the report itself, was actually remarkably easy to read and flow through and did not feel terribly—you know, sort of appropriately technical. I'm not quite sure it was the best page turner but it was good and it really got to the substance of the issues without, for the most part, diving in too deep. So I am happy with the recommendations as they stand.

DR. McGRATH: Great. Okay.

So now two—

DR. WILLIAMS: It would have been a better page turner but Salinger died before we were able to take full advantage of him.

DR. ASPINALL: That's right. He wouldn't write for 30 years but he made an exception for our report.

(Laughter.)

DR. McGRATH: Yeah, I talked to him on the phone about it.

(Laughter.)

Sylvia?

DR. AU: I'm sorry if I missed it. Are there recommendations in priorities? We never voted on this. Okay.

DR. McGRATH: Do you think that they should be? I mean that's kind of sometimes there, sometimes not.

DR. AU: I just don't know what the—like does the Secretary take Recommendation 1 as the most important? I am a logical person so I would—like for me when I get a report, I think of Recommendation 1 as the highest priority and Recommendation 10 would be the lowest priority. So that's how I think but, you know—

DR. McGRATH: Uh-huh.

DR. AU: --that's me.

DR. WILLIAMS: You know, that's a good point. It's certainly something to be considered, particularly as we get the public input and see what is really resonating with the people that--part of our process in June would be, I think—before June would be to rethink the priorities of the recommendations.

DR. McGRATH: So I just missed the middle. Do you think we should try today to—

DR. WILLIAMS: No.

DR. McGRATH: Oh, after. Got it. Okay.

DR. WILLIAMS: No, let the public weigh in.

DR. McGRATH: Okay.

Andrea, did you have a—

DR. FERREIRA-GONZALEZ: Yes, I think we need to wait to prioritize.

DR. McGRATH: Okay.

DR. FERREIRA-GONZALEZ: I just wanted to move Recommendation 7 up. That's all.

DR. McGRATH: Okay.

(Laughter.)

DR. McGRATH: Let me ask that question. There are two places in here that reference to previous reports as recommendations. There's—I don't know if it's more about style or philosophical difference. One would be to leave in those free-standing recommendations to acted upon or not or the other one is to put that text either in the preamble or somewhere in the Executive Summary that there are relevant reports that came out of SACGHS that relate to this and part of our overall recommendations the Secretary is get on those.

What do we think is a better approach to take? Leave them as recommendations or take them

out or put them in the text?

DR.WILLAMS: Kathy, can you move one slide back because that's the one that's not represented in the actual hand out.

(Slide.)

DR. McGRATH: Right.

DR. WILLIAMS: So that's the oversight report and the other one is the coverage and reimbursement report are the two reports.

DR. McGRATH: Yes. Are people familiar with this one? Okay. Some people are—

UNKNOWN: We know that you are.

DR. McGRATH: If you aren't, Kathy has the text if you want it. Just pop up a hand and we'll read it. It looks like people are okay with it. All right. Good enough.

So that's the question on the table.

David?

DR. DALE: When I picked up the report again I looked for the recommendations and I had to turn back to page whatever to find them so I would put them in the front. I think that readers will like that and then they can see why did you say that?

DR. McGRATH: Yes, there will be in the

big—the Executive Summary is the very first page. It's not here in this draft.

DR. DALE: Right.

DR. McGRATH: But it will be and that is like a page of background and then the recommendations. Exactly.

What about keeping these references to previous reports as recommendations? What do we think?

Sylvia is kind of nodding leaving them as kind of separate.

UNKNOWN: It's consistent with what we're doing.

DR. McGRATH: Okay. And it's consistent with other reports. Okay. Done. I'm just checking off the decisions.

So you can see that there are seven reports. We would try to be fairly equal on ones that address the needs for the healthcare providers, which are clinical providers, public health providers, their educational needs. We tried to address the need of just to consumers. We tried to address the needs for seeing that education tries to help eliminate health disparities. That's one of the major missions of SACGHS and we brought it in

for that reason. And we are highlighting family history because that is an easy portal for Education.

Did we cover what you would think, you know, if you had to take away your big messages?

Okay.

Well, I don't—

: I think you've done great.

DR. McGRATH: I'm just going to say we don't need to beat this horse to death, do we?

CHAIRMAN TEUTSCH: No, let's not.

DR. McGRATH: Just an--there is plenty of editing to be done. Please send your comments to Kathy either as changes or whatever issue—the method. We have a couple weeks to make it just a little prettier. It will go out to public comment pretty—you know, with the content basically as we see it and then we will revisit this in June.

CHAIRMAN TEUTSCH: All right. So you will not see this again.

We will get your edits. We'll get any changes that you think really need to be here but I'm hearing good consensus.

DR. McGRATH: Yes.

CHAIRMAN TEUTSCH: And so we will let the

committee do the final adjustments and we'll get it out and, hopefully, we will be in good shape to review in June and get it finalized. So I think this consensus is testimony to the fine work that you and your colleagues have done on this. So, many thanks. Great. And we can move it forward.

All right. So we are going to get a little bit of a jump on our public comments, which is a good thing, to allow plenty of time to hear from the public. We do this at all of our meetings and we appreciate the input that we do get.

So I do not know all of the speakers but, hopefully, at least some of them I can see are here.

So, let's begin with Mark Sobel.

Are you here? Great.

Who is speaking on behalf of the Association of Pathology Chairs.

And I remind the committee that the written testimony from all of the folks is in your table folder.

So, Dr. Sobel, thank you for coming and we look forward to what you have to say.

PUBLIC COMMENTS

DR. MARK SOBEL: Good morning.

I am representing now the Association for

Molecular Pathology, which is a nonprofit medical professional association representing approximately 1,800 physicians, doctoral scientists and medical technologists who perform laboratory testing based on knowledge derived from molecular biology, genetics and genomics.

AMP has long been concerned that the U.S. Patent and Trademark Office has historically granted broad patents on genomic discoveries, including individual genes or mutations. In AMP's experience, an unintended consequence of Bayh-Dole has been the patent holders and their exclusive licensees have frequently chosen to monopolize molecular testing by restricting other healthcare providers and facilities from developing, performing and improving tests covered by those patents and licenses. AMP believes that this in many cases restricts access to healthcare and in more extreme cases may even endanger patients.

So AMP strongly endorses the SACGHS report on gene patents and licensing practices and their impact on patient access to genetic tests. We commend the committee for addressing the challenge of DNA patents, for extending its position to association patents and for taking steps to limit or

eliminate exclusive licensing practices.

If implemented, the committee's recommendations would be a significant step forward to reverse years of policy that has hindered innovation, restricted patient access to tests and constrained the widespread clinical application of biomedical research.

AMP urges the committee to finalize, unchanged, the recommendations presented last October and to encourage the Secretary and the Administration to act swiftly to implement them in their entirety.

The committee reached these conclusions after more than three years of careful analysis, sufficient public comment and the stakeholder engagement. And the report, even as released in draft last year, was written after the completion of a study initiated by the committee in 2006 to assess the positive and negative impact of licensing practices on patient access to genetic tests. We believe the research was thorough, reviewed by the full committee with many opportunities for public comment and has led to a well researched and documented report.

AMP agrees that attaching intellectual

property rights to true acts of innovation, such as new therapeutics, diagnostics or technology platforms is essential to encourage investment and reward innovation. A single gene or a sequence of the genome, however, is not only a product of nature but contains heritable information that should be not be patentable. Threats of enforcement from a patent holder and ensuing litigation costs lead to a chilling effect on the availability of genetic testing that could otherwise directly benefit patients since clinical laboratories are reluctant to develop new tests under the current restrictive environment.

We urge the committee to move expeditiously to finalize the report as presented last October so these much needed recommendations can be put into practice.

Thank you.

CHAIRMAN TEUTSCH: Thank you for your endorsement.

My apologies. I have you down as misrepresented with your affiliation so I apologize.

DR. SOBEL: I also have comments for two other societies but AMP is the lead organization so I—

CHAIRMAN TEUTSCH: AMP is the—

DR. SOBEL: Would you like me to continue with those or come back later?

CHAIRMAN TEUTSCH: Well, I have--I do not know which organizations they are because I have Shelby Melton down as well. Is he speaking on behalf of—

DR. SOBEL: No, Shelby is just here for support for AMP.

Shelby, do you have specific comments?

CHAIRMAN TEUTSCH: Are you speaking on—whichever organizations are you—so you're speaking on behalf of AMP and who else?

DR. SOBEL: Yes, Association of Pathology Chairs and the Association—the American Society for Investigative Pathology, which have a joint statement.

CHAIRMAN TEUTSCH: So is that in addition to what you said on behalf of AMP?

DR. SOBEL: Yes. They have separate comments in support of AMP's position.

CHAIRMAN TEUTSCH: Why don't you go ahead and tell us what they have to say.

DR. SOBEL: Okay. I will—

CHAIRMAN TEUTSCH: Presumably they will

be--

DR. SOBEL: You have their written comments in your folder.

CHAIRMAN TEUTSCH: Yes, we have them.

DR. SOBEL: So just to clarify, the Association of Pathology Chairs represents the academic departments that are accredited by CME in North America and represents 145 institutions and the American Society for Investigative Pathology is a nonprofit educational society representing 2,000 members that promote the discovery, advancement and dissemination of basic and transitional knowledge and experimental pathology and related disciplines.

We support the AMP report, AMP's comments on the report, and we particularly support the exemption in the SACGHS report of patent--of patient caregivers from infringement liability stemming from patent claims on genes, including anyone making, using, ordering, offering for sale or selling a test developed under the patent for patient care or in the pursuit of research.

In addition, we particularly support the call for enhanced transparency in licensing activities, public access to information about licensing actions and federal adoption of efforts to

promote broad licensing practices.

APC and ASIP view these recommendations as a call for action for policy makers to protect all patients from the detrimental effects of gene patents and exclusive licensing practices.

We support the following recommendations which we believe are in the best interests of the patients we serve and will promote better access and quality of innovative molecular testing services:

The patenting of a single gene, sequencing of the genome or correlations between genetic variations and biological state should be discontinued either as a result of judicial review or through an act of congress.

Entities, including higher educational and research institutions that currently hold gene patents, should not grant exclusive licenses to those patients.

To ensure that access to innovative molecular tests remains widely available and affordable to patients, financial terms for test licenses should be reasonable; license agreements should also be free of any terms that limit the number of tests that can be performed by a laboratory; regulating the technical performance or

clinical uses of the test should not be allowed since laboratory professionals will ensure technical performance and appropriate clinical use; license agreements should be likewise free of terms that inappropriately limit research related to testing or the public dissemination of a result in research findings.

Physicians, researchers, clinical laboratory directors, patient advocates, government officials, research funding agencies and other stakeholders should work cooperatively to develop alternative models to gene patents and explicit licenses. These innovative models should increase patient access to healthcare and achieve greater benefit from the existing body of intellectual property linked to the human genome.

CHAIRMAN TEUTSCH: Great. Well, thank you so much for those comments. We appreciate them very much.

Our next speaker is Maurine Fitzgerald. It looks like she’s here from the Disability Policy Collaboration, which is a partnership of AHRQ and United Cerebral Palsy.

Welcome and we look forward to what you have you to say.

DR. FITZGERALD: Thank you.

Good morning. I am Maureen Fitzgerald.

The Disability Policy Collaboration is a partnership of AHRQ of the United States and United Cerebral Palsy. Both of those organizations, each has represented people with disabilities for over 60 years.

My comments today are about the Genetic Information Nondiscrimination Act or GINA.

People with disabilities have experienced a long history of discrimination. And with the advent of genetic testing they have now something to look forward to but also something else to worry about.

There are three GINA related issues that I'd like to mention today. One is programs, the term "manifested", and filing a complaint under GINA.

The Disability Organization was and is a strong supporter of GINA. Through the public comments process we have commended the agencies who have written strong regulations governing the implementation of GINA. We are especially appreciative of the strong protections for wellness programs and for health risk assessments. Wellness

programs can be a real important part of an employment setting, as long as they don't discriminate against people because of a disability or risk of a disability.

From the perspective of the disability community, I am not aware of any significant problems under GINA as of yet. But I am aware of some confusion and I think it has to do with what people perceive GINA actually does.

The terms “manifested and manifestation” are very clear to all of you but they are very difficult for a layperson to understand the subtleties conveyed in GINA through the use of those terms. Let me give you an example.

A family with a member who has Down syndrome. They understand that Down syndrome is a genetically related disorder. They learn that GINA prohibits discrimination based on genetic information. When a health insurer denies that family coverage or charges them exorbitant rates, because of the person with Down syndrome, they feel they have experienced discrimination under GINA

The term “manifested” is not routinely used in the disability community. The notion of symptomatic and asymptomatic is not a common notion

among people with disabilities.

Finally, under filing a complaint, it should be readily apparent to someone how to file a complaint, how the process is going to work. In my written comments I detail trying to go online and figure out how could file a Title 1 discrimination complaint under GINA. I spent quite a bit of time trying to figure it out and in the end I couldn't. And that should be something that’s pretty available to people.

In closing, the disability community applauds GINA. We ask that this advisory committee continue in its leadership, its education and the issues that are going to challenge us all in the future.

Thank you very much.

CHAIRMAN TEUTSCH: Thank you very much.

As you know, this has been a topic that we have taken up here in the committee.

Do you have some—Sarah was asking me but a little bit about sort of the consequences of this issue with “manifest and manifested”?

DR. FITZGERALD: Yes.

CHAIRMAN TEUTSCH: What is the upshot of that?

DR. FITZGERALD: People who—for example, that explanation I gave you about a family with an individual with Down syndrome.

CHAIRMAN TEUTSCH: Right. I understand.

DR. FITZGERALD: They—to them—okay. Down syndrome is a genetically related disorder.

CHAIRMAN TEUTSCH: Right.

DR. FITZGERALD: Health insurance companies can't discriminate against us based on genetic information. When that individual can't find health insurance they then think, well, then we've been discriminated against and the breakdown is between what's genetic information that's protected, and what's a manifested disorder, which is not under GINA. So that's where the breakdown comes.

Is this clear? Okay.

So your whole discussion today about your recommendations and the education, I think, is so critical to people and a lot of the folks that I am concerned with are not sophisticated and they don't understand medical language. So being real clear about what GINA does and what GINA does not do, I think, would be part of the education process.

CHAIRMAN TEUTSCH: Right. Obviously, we

are hoping some of the health reform initiatives will deal with some of those issues.

DR. FITZGERALD: Yeah.

CHAIRMAN TEUTSCH: We will keep our fingers crossed.

DR. FITZGERALD: We'll keep our fingers crossed.

CHAIRMAN TEUTSCH: Thank you.

Our next speaker is Joanne Boughman. Joanne is here representing the American Society of Human Genetics.

Dr. Boughman?

DR. BOUGHMAN: Thank you very much.

I am the Executive Vice-president for the American Society of Human Genetics, which is a very diverse genetics organization of over 6,000 members.

We represent communities that perform basic research all the way through to clinicians that see patients. So, in fact, achieving the consensus of a statement that our board could, in fact endorse, heartily has been a challenge but one that, in fact, the process of developing this, I think, was an education in and of itself to many of our members because some of our members do not understand the patent and licensing process really

at all and others are very immersed in it.

But at this point the leadership of ASHG, which I'll refer to it, applauds this group for the enormous amount of work expended to produce the report on gene patents. The recommendations made are, in essence, consistent with the ASHG principles relevant to intellectual property and genetics.

Specifically, the human genetics community, as represented by ASHG, supports the key principles of quality, quality assurance, and accessibility in the genetic testing arena.

In the past, and continuing action, the board of the American Society of Human Genetics has taken steps to support lawsuits and positions, involving intellectual property, and our position has usually been manifest as a party to amicus briefs rather than serving as plaintiffs.

The board is of the view that the genetics community must continue to make it clear that exclusivity may, indeed, result in issues around access and cost, as well as issues regarding quality of testing and patient care. As noted by your committee, the current IP environment may play an important role in relationship to these issues.

Our scientists must comply with their own

institutional regulations regarding all disclosure of findings or inventions that might be commercialized. However, and this is one of the areas that we are trying to inform our members more fully on, they must also understand their obligations related to, beyond disclosure and protection of intellectual property, the responsibility, as well as the degree of authority that they individually have in determining the terms of any licensing agreements made based on their own intellectual property as disclosed to their institutions.

The recent recommendations of this committee suggest that there are serious issues around access and the quality of testing. Both of these concerns are of primary importance to the genetic community and the board of directors of ASHG strongly recommends the actions and guidelines noted in the recommendations that address these issues.

We all know that there are incredible and continuing challenges associated with efforts to change patent legislation and policy, including the interpretation of exclusion clauses for research and testing protocols.

However, given the rapid evolution and

relevance of the science and technology as proposed and being performed by members of our organization, a consideration of such policy change seems absolutely essential. Indeed, the technology in the field of genetics and the application to testing in human health are moving extremely rapidly, as Dr. Green stated earlier, with the trend toward the trend toward the collection of increasingly complex and complete genomic data driven by the efficiencies of the whole genome and the whole exome approach.

The advent of comprehensive data on genotype and DNA sequence alters profoundly the implications of restricting interpretation to any specific locus or the variance of that locus.

We in the scientific community, are striving to fully understand the impact of the current legal and regulatory framework while, in fact, we in our labs, are forging ahead in the development and implementation of full genome and exome sequencing.

In closing, the leadership of ASHG will continue to discuss these important issues, following and respond to activities and actions that may change the landscape, comment further on policy implications when appropriate, and I would add

continue to inform and educate our own members.

CHAIRMAN TEUTSCH: Great. Thank you very much. We appreciate that.

Our final speaker who signed up is Jeff Boyd. Mr. Boyd is a medical device consultant with Medical Device Consultants of Ridgewood.

MR. BOYD: Thank you.

I would like to thank the committee for the opportunity to speak today.

I have spoken before you in public comments back in June 2009 as it relates to the issue of clinical utility. It's actually very encouraging to see that this particular initiative is moving forward.

However, I would suggest the clinical utility is one issue that's important, as well as evidence is another issue that needs to be dealt with and there are two separate issues that really need to be addressed and sometimes they get lumped together.

I have some prepared comments and I am going to be as brief as possible. I had the opportunity to present and actually participate in the January 2010 MEDCAC meeting on pharmacoeconomics or pharmacogenetic testing, and the question—it was

interesting. The question posed to the panel as to what they thought the most important takeaway was from the meeting and the vast majority of them stated that clinical utility for these types of genetic tests is extremely important. However, the issue was that the understanding of clinical utility was very different to almost every single person on that panel.

They really had totally different definitions of what it meant. It was all over the map. It ranged from a change in patient management that may occur from the result of a test to the benefits accrued to the patient in knowing the information, to improved survival based on the therapies that are provided.

As well, the panel started talking about another issue. They started talking about let's gather evidence, let’s gather enough evidence to prove out clinical utility, and they started talking about Cadillac evidence and they started talking about different endpoints that needed to be looked at, as well as the types of studies that they needed to engage in, ranging from—anywhere from a registry to a prospective randomized trial.

Those particular issues obviously have

ramifications for people who do these tests or actually are involved in developing these tests and can ratchet up the time, effort, money associated with proving out clinical utility and also going down a path of developing evidence.

So it's unfortunate that the issue of clinical utility has really not been adequately addressed by policymakers and since there really is no clear definition of what clinical utility means, many policymakers are taking it upon themselves, especially those of payers, and I happen to work with a number of the private payers and with Medicare, and they have taken it upon themselves to define clinical utility with many defaulting to the most conservative definition, which typically means improved patient outcomes in some form or another, as well as Cadillac evidence looking at prospective randomized trials. These can be very onerous to answer those endpoints and sometimes may be really unfeasible or infeasible to be able to answer the question.

Frankly, no one should blame them for coming up with that definition because they don't have a definition but the problem is it's a one size fits all mentality, which is really--it's really

seen in the issue of evidence based medicine, which is characterized by the value of treatments which has also resulted obviously in a one size fits all assessment.

A one-size-fits-all perspective ignores the technology type, its applications, its intended use, and other practical factors involved in evidence development. This evidence-based mentality unfortunately is further reflected in the criteria that are developed—that has been developed by Blue Cross/Blue Shield for tech assessment, which is useful for therapeutics but, unfortunately, it can be inappropriate for diagnostic tests.

As I have mentioned, not only is the issue of clinical utility important but the quality of evidence and the study design is also very important. And Dr. Teutsch hit on this a bit this morning when he talked about the contextual factors that are involved in putting evidence together, where and when the test is used, what happens besides health outcomes, those kind of things need to be considered and sometimes they can be ignored by payers when they are looking for this type of Cadillac evidence.

Now it's encouraging to see that the

Clinical Utility Task Force is moving forward with a roadmap. I highly encourage that to be facilitated as quickly as possible because without this definition of clinical utility in looking at the evidence, the concern is that payers will continue to fall back on the most conservative view of what it means for appropriate level of evidence.

CHAIRMAN TEUTSCH: Jeff, we have your comments, which are great, can you sort of come to-- wrap up with a few of the other final thoughts that you have for us?

DR. BOYD: Yes, I'm going to do that.

CHAIRMAN TEUTSCH: Thank you.

DR. BOYD: So it relates to the definition that's ultimately arrived at with evidence gathering. And CMS has been at the forefront of this, I think, and have put together such tools as coverage with evidence development, which I think are very important, but the process as it's defined right now can still be very onerous, I think, for people to really meet those particular criteria.

And the way it's set up right now, coverage with evidence development, is a non--first of all, you have to go through the NCD, and then CMS basically says, "Okay. It's not covered but we will

potentially go with coverage with evidence development." And the problem is that, I think, a lot of companies are really reluctant to want to go through that process because the end result is you end up with a non-coverage determination, which is in turn picked up by private payers, and it's kind of a roll of the dice, especially if they do not know whether or not coverage with evidence development is even remotely available.

So a couple of suggestions for payers like CMS is for them to be more of an Ombudsman in this process and to facilitate those technologies which they deem to be clinically useful to them and help push those technologies through the process a bit faster rather than having to wait a long time to engage with coverage with evidence development. And, also, I think, become more transparent in the process, especially with the public as they are going through this.

I would also encourage private payers to become more involved in these flexible coverage policies, such as coverage with evidence development. Private payers—they essentially cover approximately 160 million people across the United States, which is about half of what CMS covers, yet

CMS is doing a lot of the heavy lifting. And it would be extremely helpful if they were encouraged, especially by this group, to participate in the process of more flexible coverage policies like coverage with evidence development.

Thank you.

CHAIRMAN TEUTSCH: Great. Thanks very much, Mr. Boyd. I appreciate that.

Do we have any other individuals who would like to make public comment?

If not, then I think we have come to that point in the program where we get some lunch.

I know some of you ordered sandwiches but there are also places out on Connecticut Avenue.

Why don't we plan to meet at 1:00 o'clock? It is 15 minutes earlier than it says on your schedule but it still gives you a little over an hour and so we'll plan to meet back here at 1:00 and we'll take up the session on genomic data sharing.

Mara, did you want to say something?

MS. ASPINALL: No.

CHAIRMAN TEUTSCH: Oh, I'm sorry.

MS. ASPINALL: I'm checking, 1:00 o'clock.

CHAIRMAN TEUTSCH: 1:00 p.m. Eastern time.

We'll see you back then.

Thank you all.

(Whereupon, a luncheon break was taken until 1:00 p.m.)

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

CHAIRMAN TEUTSCH: All right.

So, folks, listen carefully. Our agenda changes moment to moment. I'd first like to do a quick canvas.

How many people on the committee, just the committee members, have flights out of here or have to leave before 11:00 o'clock tomorrow? Have to leave here before 11:00.

UNKNOWN: So we're not talking about—

CHAIRMAN TEUTSCH: Leave the meeting before 11:00.

(A show of hands.)

CHAIRMAN TEUTSCH: Okay. That's what I figured.

So, folks, we will not have a quorum after—sort of early morning, midmorning.

Here's the plan: We are going to extend the session this afternoon and listen to some of the presentations primarily from our federal colleagues. So I do not know how long it will be but I think it

will probably be at least an hour beyond the scheduled time.

We will start doing the patents report at 7:30 a.m. tomorrow.

I am sorry, Mara. You thought it was early to get up at 6:00 a.m.

MS. ASPINALL: (Not at microphone).

CHAIRMAN TEUTSCH: But fortunately you're on Eastern Time.

UNKNOWN: That's nothing, Mara.

(Laughter.)

CHAIRMAN TEUTSCH: Yes, I apologize but we have got to get it done because I think after 9:30 we risk losing a quorum. So we are going to start at 7:30.

DR. ASPINALL: (Not at microphone).

(Laughter.)

CHAIRMAN TEUTSCH: I hope you stayed someplace—I don't know. Maybe you should just cancel your hotel room in Phoenix for the night and just—so we will have the patents report and, hopefully, the vote first thing in the morning.

We will have to repost that on the website and on the listserv because that's yet another change from what we talked about earlier.

We will then have several of the presentations that were scheduled later in the day moved up, some of the—we're in the middle of getting those reschedule. I think we've got most of them done. We are trying to work on the public comments, the thing that we always want to hear, and we're in the process of trying to reach those two individuals to figure out what the best plan is going forward so we are the beneficiaries of their input.

MS. CARR: (Not at microphone).

CHAIRMAN TEUTSCH: Yes, I said we are going to extend this probably at least an hour. I don't know how many of federal employees—folks—I know Sarah has been working with all of you to try and figure out who can stay. I think Muin and Gurvaneet and Jeff as well.

DR. CARR: Yes.

CHAIRMAN TEUTSCH: That's terrific. I really appreciate everybody's flexibility. I know it's a problem but it looks like if you're not out of here by mid afternoon tomorrow you're here for the weekend. So I know it's a lovely place but—

(Laughter.)

So, the order of business for today—oh! One other thing, I know that Allison wants to know

how many people are coming to dinner or need to let you know.

CHAIRMAN TEUTSCH: How many people are planning to go to dinner tonight?

MS. LEA: At 7:30 now.

CHAIRMAN TEUTSCH: And it will be at 7:30 over at—

MS. LEA: The Petit Fleur right down the street.

CHAIRMAN TEUTSCH: The Petit Fleur or something over right—a short walk from here.

MS. LEA: (Not at microphone)

CHAIRMAN TEUTSCH: And this will be at 7:30.

MS. LEA: Thank you. Okay.

CHAIRMAN TEUTSCH: Okay. All right.

So the main reason we are here this afternoon, however, is because Charmaine Royal has been working extremely hard to move us forward on genome data sharing. And, as those of you who will recall, particularly from Kevin’s input, the issue of genomic data sharing and the challenges of the clinical data research interface are becoming progressively blurred and have sort of raised this

to a high level of concern, and we have heard other issues today about just how one does this in a way that protects privacy, confidentiality, as well as human subjects.

So materials are in Tab 6 in the book and at the end of this we'd like to identify some of the best practices and gaps and decide on next steps.

So, Charmaine will introduce and run this session.

Charmaine, as you can see, we are going to be trying to run a very tight ship so if there are places to compress I think everyone would be very grateful.

DR. CHARMAINE ROYAL: Okay.

CHAIRMAN TEUTSCH: But we don't want to miss any pearls so I'll turn it over to you.

Thanks for all of this.

GENOMIC DATA SHARING-OBJECTIVES, MECHANISMS AND POLICIES

DR. ROYAL: Okay. Thank you, Steve.

Well, first I must say thanks to Sarah and Cathy, who are the ones who have really been working hard on this but we're going to—

(Slide.)

I'm just going to give a very brief

overview because we have a wonderful lineup of speakers this afternoon. And in starting out I just want to remind us about why we are even talking about this and sharing of genomic data is important for advancing the agenda of science but the sharing of this data has the potential to have all kinds of ethical implications that are associated with it.

(Slide.)

Another issue that is raised is the potential blurring. We are not saying that this blurring is being caused by genomic data sharing. Certainly the blurring of the line between research and clinical practice has been happening for a while and the question is whether genomic data sharing is going to increase this even more.

And then the questions about informed consent: Are we going to need to think about new approaches to informed consent as we move ahead with widespread genomic data sharing?

So what have we been doing so far?

(Slide.)

In December of 2008 it was decided by this group that genomic data sharing was an area of priority. In March of ‘09 there were briefings on the IOM report and from some other advisory

committees. In September of last year, the Lewin Group got a contract to draft a report on genomic data sharing and to work along with SACGHS to do that. The project is a yearlong project that the Lewin Group is working on.

(Slide.)

And in our meeting in October we discussed this and we formed a steering group and some volunteered, some were volunteered, and the group, as you see here, and we met and talked about what we were going to be doing today. And in our meeting in October we did decide that it might be great to have a session at this meeting and on our conference call we sort of fine-tuned that session in terms of what shape it was going to take.

(Slide.)

The Lewin group has actually started working on the project and they have been doing the background work and done some lit. searches. And the questions that this report is going to explore are whether there are new issues regarding privacy and discrimination that we need to address, issues about consent, how can the process be improved? What are the benefits and risks of population based registries and how can researchers and policy makers

address the issues related to indigenous groups and what we tend to call sometimes special populations who participate in this research?

(Slide.)

So what are we going to do today? We're going to have a group of speakers who are going to really talk to us about the models of genomic data sharing. We are going to gather some information from them and we're going to figure out--the next thing we're going to do is talk about the information that they give us, what issues are raised, and try to think about where we might go with this.

(Slide.)

The presentations: We're going to start out with an overview by Laura Rodriquez from the Genome Institute and she's going to give us an overview of federal policies on genomic data sharing; then Joyce Mitchell is going to talk about future directions in terms of health information technology; and then we have speakers who are going to talk from different sectors about governmental, healthcare system, academic, commercial and consumer controlled policies for genomic data sharing.

(Slide.)

As we listen to those talks, the things we want to think about are what—as we listen to the models that are present, think about what are the implications for informed consent and what are the things that are common and what are the things that are different in terms of consent, in terms of the storage of data, issues regarding access and secondary uses of data, privacy, confidentiality, protection in terms of re-identification and de-identification of genomic data. How do we handle sensitive data and then the incorporation into electronic health records?

(Slide.)

And at the end of the talk we are going to have a discussion and the key things we're going to focus on in that discussion are what are the elements that have worked well in these models that have been presented and what are the ones that haven't, and are there issues that could benefit from more policy discussion and development?

And then we'll try to think about what a next step should be? Will there be a need for us after we hear all this information? Will there be a need to identify best practices? Could SACGHS contribute to this? Or should we wait until the

Lewin Group's report is done? The report already is generating some information about what is happening out there in terms of the literature that they are gathering. Should we wait until the report is complete before we decide what we should do? Or in the interim should we just plan some additional individual sessions to try to explore this a little bit more?

(Slide.)

So we're going to ahead and move right into the discussions because, as Steve said, we are going to run a tight ship this afternoon.

So, Laura, please come and give us a talk about the federal policy.

REVIEW OF FEDERAL ACTIVITIES RELATED TO GENOMIC DATA SHARING

DR. LAURA RODRIGUEZ: Okay.

Well, I would like to thank the committee for having me come and speak today on behalf of all the Ex Officios and then just clarify pretty quickly here that I'm just reporting on what is going on from all of the different Ex Officios. I'm not an expert on many of the things that I'm going to talk about today so I'm very happy to see them all sitting around the table so that they can answer

questions that you might have as we go through this information.

(Slide.)

Charmaine has already gone over some of the information in terms of why we're having this conversation this afternoon and the goals from the committee but just to reiterate some of the rationale that I understood from the committee's discussion in terms of why they wanted to look at genomic data sharing was, in fact, the potential for this kind of data sharing to facilitate very important research and things that were going forward at the moment in a very rapid way and in a way that raised questions that we wanted to be very deliberate about in how we handle them going—as we moved.

Additionally, too, something that Steve mentioned already is the fact that these kinds of data are blurring the line between research findings and clinical care, and so that's something that we also wanted to think carefully about. And, in doing so, the number of different ethical questions that are raised by not only the potential applications of these data but also how we manage them and what are different protections we have put into place for the

individuals whose data we are looking at that is generated in large volumes around some different and new areas are the kinds of data that we are gathering.

And also again something that Charmaine mentioned is the fact that genomic data by its nature is challenging the traditional paradigm of what was de-identified or autonomous and how is that going to change the way that we needed to think about managing the data in terms of providing appropriate balance between wanting the research to go forward and also maintaining and protecting the interest of the participants from whom these data are derived.

(Slide.)

Again so we're—in terms of what I—what I understand you all wanted to do in hearing from all of the different feds and what we were doing in this area was largely because of the amount of money clearly that the federal government is putting into this in terms of the national investment in genomics research and, in fact, in building resources for the data sharing going forward.

And in doing this, the government is not only playing a role in the research as a funder but

also is providing some leadership to the community in thinking about how to go into these new domains and, hopefully, after today you'll have a little bit better sense of what kinds of things that the different agencies are thinking about as they are doing this.

(Slide.)

So the survey that was put together by SACGHS staff included ten questions that focused around the issues listed here trying to find out what research programs, if any, existed within the various Ex Officio agencies. And if they did have research programs or did not, did they see genomic data sharing as relating to their agency mission in any way, and how so?

And, again, assuming that they had programs for genomics research and some expectations of data sharing, how had they developed policies to try and implement these expectations and how did they incorporate elements concerning the different ethics questions into those policies.

And then, finally, again going back to the concept that these data are blurring a line between research and clinical information, was there any allowance within the policies or expectations within

the policies to provide interconnectivity between the research data and electronic health records?

(Slide.)

So this survey was sent to all of the Ex Officios, as well as separately to USDA and NSF since we knew that they included some genomic information, just to find out what kinds of policies, again, they were putting forward.

(Slide.)

We had responses from 12 of the Ex Officios, plus NSF. And as you will see, we had a range of feedback in terms of how this related. So there were four of the groups that had no genomic data sharing activities and they did not see it being relevant to their mission at all in terms of the purpose of the agency. And I think from looking at who these different groups are it is not surprising in some regards how they were doing it.

(Laughter.)

I am just reporting. I am not going to take—

Then there were also several others that reported that they didn’t have any genomic data sharing activities and weren’t conducting any research in this area but they did see it as being

relevant to their agency mission in some way.

(Slide.)

And, again, this is OHRP and this is in a general way. As we'll talk about later, they have some policies that overlap in the realm of general research protections and then the specific considerations around how genomic data sharing is done; OCR with their responsibilities for implementing HIPAA and also involvement in GINA, et cetera. We can see where these come from.

And then there were five other of the respondents who did have genomic data activities—data sharing activities and research programs and they did see it as directly relevant to their mission and, not surprisingly, these were the ones that were more research based and would be—as the dominant activity for what they did.

(Slide.)

Looking at those five even, they are still very different across the board. Of course, NSF and DOE, not surprisingly, largely deal with plant genomic activities. So that wasn't something that was particularly close to what this committee was thinking about but, even just looking at the VA, CDC and NIH, there were still very different states in

terms of their thinking and activities in this regard and how they were approaching it.

So the VA at this point is still--they have an expectation for data sharing within their research programs but as they are an intramurally based research program, the expectation for sharing is within their own system.

The CDC has several different programs included in their genomics portfolio and the policies for data sharing vary among those programs but they tend to be based on how they have set up their traditional sharing structures and how they have interpreted looking at the genomic data and other systems that they have. Their sharing tends to work through direct collaborations or through coming to particular CDC research sites and doing research at those sites.

And then, of course, the NIH has invested significant time and energy in building database repositories and in having the broad sharing take place in a way that is much more indirect and through central resources.

(Slide.)

So I have tried to provide throughout the rest of these slides links. Actually I—Symma has

provided links to many of these programs.

(Slide.)

Going forward, and just to highlight again one that CDC--the N-HANES program is a large cohort study that has had multiple different visits. They are—in the last few years one of the—they did a genomic data collection and they have thought a lot about how to move forward in the area of genomic data sharing. They've hosted several meetings and workshops to think about that going forward what would be appropriate within the particular structures for N-HANES, whether there is actually legislative language that structures how they can move forward and how they can share their data.

The VA has a large genomic medicine program that they have been moving forward again within their intramural program and they have been very proactive in thinking about this. They formed an advisory committee in 2006, which has met on a regular basis to think about the different questions regarding how to appropriately share genomic data and how that relates to the particular participant population that they would have at the VA, including commissioning a study to look at participant attitudes specifically from the veteran's community

and asking how those veterans felt about different aspects of data sharing. Again, what would they want to get out of the data sharing in terms of return of results and other things.

So, the policies themselves at the VA are still under development but they have been very active in thinking through the issues and imposing the questions and serving as a forum, too, for discussion in a broader way than just their own agency.

(Slide.)

NIH, as is listed here, has been very active in putting forth policies. We have multiple different policies at the NIH level. One which I'll talk about later this afternoon focused specifically around genome-wide association studies but we also have specific policies for other projects that involve sequence data. We have roadmap projects for the microbiome, for instance, that have a genomics program. All of them have their own policies for what the expectations are for sharing of genomic data.

(Slide.)

At the IC level for the different institutes we have some more policies and I haven't

listed them all. So we have been very prolific at putting together different ideas of how they apply to our specific programs and what the expectations are for genomic data sharing. Ideally these are all consistent from one to the other. We have tried to work very hard at doing that but we, of course, are still working on that.

(Slide.)

Coming back again to the agencies I mentioned where they have policies or areas that touched on their mission that did not directly involve genomic data sharing, if we look at OHRP, the policies that they mentioned, not surprisingly, have to do with coded specimens, again, which pertains directly as to how the genomic data sharing is conducted in terms of is it human subjects research or is it not considered human subjects research and what are the regulatory implications then of that kind of determination, engagement in human subjects research. And so clearly these are very relevant to what is going on in the research programs themselves.

(Slide.)

Several other—the Ex Officio agencies, the EEOC, and OCR, in addition to OHRP noted that they

have overlap in this area with regard to GINA and as there are regulations for GINA developed and are implemented.

And then, lastly, I really just wanted to mention that NIH is now going forward and extending our existing policies to putting together a trans-NIH policy for sequence data and related genomic data, such as epigenomic data going forward. And we see this as extending what we have done in the past for GWAS and all of these different individual project by project policy development activities but, hopefully, will provide a way that will be consistent for investigators, institutions, those investigators that want to use the data, as well as those that are submitting the data and, of course, the public so there is a common expectation of what the NIH is doing and being a steward of all of these data that come into our resources.

(Slide.)

The themes that came forward, I think, through looking at all of the information from the different agencies that responded are clearly that genomic data coming from many different individuals will include sensitive information. I don’t think there was really any question about that from

anyone.

And, also, that broad sharing of the data does enable an acceleration, the potential for acceleration of scientific research.

So with those two principles accepted, then the consequences are that policies that are developed must ensure privacy and confidentiality of research subjects, and this was mentioned even by those agencies that said they had no activities and no relation to their mission. They were still concerned about the ethics of this kind of activity going forward. That protection mechanisms were needed against unauthorized access and that there needed to be careful attention to the distribution and use of genomic data.

And, of course, that the LC issues regarding their management, their distribution and their collection needed to be very carefully considered, and that they must remain relevant and timely to the technologies that are being used as well as to the public conversation that is taking place around this kind of information and how we are using it within research and within society more broadly.

(Slide.)

Potential gaps that were identified through the survey: Informed consent was the most frequently mentioned place where more guidance was needed or best practices were needed.

Again, not surprising, I do not think but it was again something that was mentioned even by those groups that didn't have any activity in the area so something that is really permeating the discussions.

Additional consideration around what access participants may have to the data itself, either through the databases or to results, their own results, from their participation, and return of results is something again that's a very hotly contested issue with strong opinions on both sides of it in the community at the moment.

And, again, there was a recognition that while policies at the moment don't preclude any incorporation of this kind of data into electronic health records as those initiatives go forward, there really aren't at the moment any clear structures that will make the inclusion of the data into EHRs something that is easy to see how it will happen or feasible and so more attention to that area was another place identified as a gap.

(Slide.)

And with that I'll just, I think, come back to some of the same questions that Charmaine put up again in terms of questions for you all to consider. So whether there is a need for additional policies for genomic data sharing in this area and, if so, from a federal perspective, does the committee have thoughts about whether or not an agency specific initiative or the way it should go or if they should be coordinated in some way?

And, also, is there a need to try and deliberately raise public awareness around the importance of sharing genomic data and the inclusion of these kinds of the data in their electronic health record in a targeted way?

With that, I will, again, thank Symma, Cathy and Sarah for all of the work that they did to put the survey together and to pull these slides together as well, and take any questions.

Yes?

COMMITTEE DISCUSSION

DR. WILLIAMS: So this is a question for you but probably more broadly to Charmaine in terms of the task force. Was--how much time was spent looking at not so much issues of privacy and

confidentiality related to sharing but to actual physical aspects of sharing data like use of standards across different organizations? Is that in scope, out of scope of the task force? Is that something that you addressed in your surveys to the various groups?

DR. RODRIGUEZ: So I can say it came up minimally in the survey and again the questions weren't structured to draw it out but I think only one or so of the answers that I saw come back in mentioned the standards for that kind of thing and with regard to the scope of the task force that is definitely a question for Charmaine.

DR. ROYAL: Marc, I think we sort of put that under the HIT umbrella and so that wasn't part of our—yes.

DR. RODRIGUEZ: Any other questions?

Okay.

DR. DALE: I'll raise a question then.

In the data sharing area there is the—you talked about mostly data sharing within the government agencies but there is--when the NIH or a government agency sponsors a study then it is really governed by the IRB and usually governed by the local IRB. My experience has been there is huge

differences between the IRBs and how they look at this issue. So we have this morass of different feelings, let's call them, about data sharing.

No one has corralled the wild horses in a way and it is very confusing if you are a researcher in this area. You spend a huge amount of time trying to share data.

DR. RODRIGUEZ: So I will agree with all of those statements. I am not sure what to do in terms of solving them. I think as we'll talk about, at least I will talk about more in my talk later about the GWAS policy that NIH developed, while the decisions for whether or not data sharing is appropriate still resides with the local institution. NIH has tried to put forward an infrastructure for some consistent protections to be in place and mechanisms to be in place for how the data are shared and what the considerations are in making decisions about sharing data to try and bring a little bit more ease, I guess, to the process of doing it both for investigators, again trying to access the data, and those submitting the data.

And, ideally we have tried to provide some help to the community in thinking about these issues but obviously this is moving very quickly and we are

not anywhere near a consensus on how to do it.

DR. ASPINALL: Can I ask along those same lines, are there standards that either cross the various agencies—standards or guidelines that each of the institutions, at least NIH or NCI grantees, have to use in any of these key issues, let's say informed consent?

DR. RODRIGUEZ: So across NIH with the GWAS policy, that is a trans-NIH policy so there is a consistent threshold that is supposed to be used. We are a very large agency and sort of interpreting that policy, of course, is always somewhat subjective. So we have done a lot of work since the policy came out in terms of trying to develop rubrics and SOPs and other informational material for our staff to try to bring them up to a consistent level but that is taking time as we are all learning to go about this and, you know, everyone has different ways of doing things. So, ideally, there is consistency within NIH but I am sure it is not perfect.

And in terms of other agencies, you know, I think every agency again is trying to do this on their own and we're talking to each other, and there are some general consistencies and principles but I

think how each of us are deciding to do it is still evolving.

DR. GURVANEET RANDHAWA: So a clarification and a comment. AHRP does not have any activity on genomic data sharing but we do think it's relevant as is any patient specific clinical information is to our agency.

Going to the point that David had raised, this issue has been discussed in many different settings in terms of coordinating the different IRBs, which is a bigger problem not just in genomics but whenever we have any consortium of research in different centers, and there are different policies, how do we coordinate this.

So there has been some talk about coming up with new policies for multiple IRB or a blanket IRB or a minimum threshold, but I do not know if that has led to any conclusion or activity within the NIH. As I said, we're discussing with AHRQ of how to approach this area.

DR. RODRIGUEZ: And we are discussing it, too, but, no, I wouldn't say that we are at a conclusive point.

Okay.

DR. ROYAL: Thank you, Laura.

Now we'll have Joyce Mitchell, who is going to talk about the future for HIT.

FUTURE DIRECTIONS IN HEALTH INFORMATION TECHNOLOGY

DR. JOCYE MITCHELL: Thank you.

I am assuming that you will get it so it shows up here?

(Slide.)

Oh, there it is. It wasn't there a second ago.

I'm delighted to be here to talk to you about existing and emerging technologies affecting the genomic data sharing. It is a very large topic to cover in a short period of time. And the tactic that I have taken is to be more broad in terms of general areas and some trends that I see that are emerging.

(Slide.)

This group clearly knows a lot about genomics but I felt like it was useful to give a very broad brush overview. There has been huge progress made in the last decade or two decades certainly. And the broad overview of the whole thing is here at the bottom. There are 5,000 genomes available online, incredible information

available online, and public data repositories are routine, and that is different than the situation would have been even 20 years ago or 10 years ago.

(Slide.)

There are lots of genetic tests which are available today to anybody in the physician community who wishes to order them. There are almost 1,900 SNP chips that are routine GWAS studies, expanding gene expression studies are impacting clinical care today, and next generation sequencing has arrived and has taken all of our small-scale single gene experiments into some things which are enormous as we try to do with the average variant trial for a human sequence from 3 to 4.5 million SNPs and if you had insertions and deletions you end up with 10 percent larger than that. So it is a fairly large data problem.

UNKNOWN: (Not at microphone.)

DR. MITCHELL: Yes.

UNKNOWN: G2P is what?

DR. MITCHELL: G2P is genotype to phenotype. Sorry for the jargon.

UNKNOWN: (Not at microphone.)

DR. MITCHELL: Genotype to phenotype.

(Slide.)

So at the same time that all of that information is out there and available and expanding, then consumer demand for genetics is exploding. And I take you first to the genetics home reference. This is a site that I have a particular—it's particularly dear to my heart. I was a senior scientific advisor on this site from 2001 to 2009. It was the first site which actually targeted the public and said that the public would like to know how to bridge their consumer health questions with the bioinformatics data coming out of the genome experiments. And we started out—when people were saying, you know, how are you going to do that.

(Slide.)

Here is our website, which you could go certainly explore at your leisure. It sits at the National Library of Medicine as part of the National Institutes of Health and currently it has about 500 health conditions and about 700 curated gene summaries, and another 1,800 automated gene summaries. And what I would like to point out is it has 215 million hits per year. It is never advertised because they can't advertise it, and that's 215 million hits per year from the public and

from clinicians who go there a lot when the public hits them with questions about diseases and disorders that they don't deal with on a routine basis.

(Slide.)

And then, of course, the interesting phenomenon of direct to consumer genetic testing—I know it's controversial and I do understand the issues behind that but it is a huge force and it is there and it is happening daily. It's changing the pace and the standards for data exchange in genomic medicine and doing it in some interesting ways.

(Slide.)

First of all, it ends up in the fashion and style section instead of the scientific section in the middle of the *New York Times*.

(Slide.)

There are three major companies and a lot of other companies that deal in direct to consumer testing, and this one is 23 & Me. Just to show you a few things, and I'm sure you have all seen it before; this is a clinical report, which over here is the clinical report. There are other research reports. Disease risks, there are 11 of them; carrier test, there's 21 of them; 10 traits; and 7

drug responses.

(Slide.)

Let me just show you very briefly cystic fibrosis as an example of a carrier trait and down here the Warfarin/Coumadin sensitivity as an example of a drug response.

(Slide.)

And there is lots to say about all of these various tabs. Tell me about your data, how it works, the timeline, et cetera, but I am just taking you in this room to the technical report of cystic fibrosis carrier testing. It tells you a lot, and this is data sharing. This is for the person who paid for the test giving them complete information on the test. It has not only the 23 & Me name. It has other names. There's deltaF508 as the most common variant certainly that you would be looking for in cystic fibrosis. It tells you what you're looking for. It tells you your genotype.

And down here at the bottom it does not have any of 31 CFTR mutations. So it tells you the gene and has a reference where you could find more out about the gene. It most likely has no disease, not a carrier, may still be a carrier due to other mutations in the CFTR gene not recorded here. And I

would say that that's a pretty sophisticated kind of report and a direct sharing of data in that particular regard.

(Slide.)

And then here's another one where they actually tell you some clinical information for pharmacogenetics. This one, in fact, is looking at the results of two genes, the CYP2C9, where this particular person is a *2/*2 homozygous for that allele and the vitamin K regulator gene, VKORC1, with promoter mutation.

(Slide.)

And here is the result saying increased Warfarin sensitivity may require decreased Warfarin dose. Now, there are lots of folks who are dealing with patients who have questions about all of this but, on the other hand, I have said before and I say again, it is out there and it is ours to deal with as the profession and there is a lot of data sharing that's going on with this and a lot of curiosity and willingness to get these results and to investigate more.

(Slide.)

And the most telling thing about the data sharing is that you can actually download your

entire set of results and go investigate them yourself if you're so inclined. So now, its large files and you have to do some learning in order to have to figure out how to deal with it but that is what the public is doing at this point.

(Slide.)

Now let's talk about genetics, genomics and the EMR.

(Slide.)

This is the growth of laboratory tests. Now these are single gene tests for specific syndromes and specific mutations that are known to cause disease or be associated with diseases. This takes you to 2008. If you go to the end of 2009 that is where you get the 1,900 of these tests available and the purple is the laboratories, 600 laboratories around the world.

(Slide.)

But in addition to those single gene tests there is also a number of gene expression tests which are growing rapidly. I give you two examples.

(Slide.)

The first one is the Mammaprint. It is used to do a gene expression profile on the tumor and it is for prognostic purposes so that in 2007

the FDA cleared for marketing this test. It determines the likelihood of breast cancer returning within five to ten years after the woman's initial cancer. The first cleared a molecular test profiling genetic activity so it is a gene expression microarray test. It's a 70 gene profile and it is patented and available commercially, and you can send off a sample and get the results back. It is used routinely in some places.

(Slide.)

Here is another example of a gene expression test. It is called AlloMap. It is a molecular expression profiling, it's a little hard to read there in the back but that is for heart transplant patient management. This is a test that is an 11 gene profile. They look at the expression changes related to the immune system. It is used to alleviate morbidity associated with intra-cardiac biopsies. So when you get a heart transplant you have to go in regularly to get an evaluation to see whether or not you are rejecting your transplant or not, and the standard way for doing that is a cardiac biopsy, an intra-cardiac biopsy, which is somewhat invasive in my mind. I've heard surgeons say they are routine but they are not on the

receiving end. You have to go in once a week in the initial stages.

What they're doing now with the AlloMap is to take a blood sample and run your leucocytes through an expression analysis microarray. If it looks like you are not rejecting then, in fact, you don’t need the biopsy. If it looks like you have signs that you’re starting to have rejection then you need the biopsy and further tests.

So those are two examples and they are coming fast.

(Slide.)

So if you look at genetic testing in the electronic medical record you’ve got tests being done in all of these laboratories throughout the world and private laboratories. You have got a lot of test interpretations which are faxed back as opposed to being sent electronically. Tests are not stored in a structured form; not generally available for decision support. If your own laboratory does the test you have a much better chance of making that happen. The interpretation does not give too many details.

A MammaPrint doesn’t tell you the expression of each and every one of those 70 genes.

It gives you an interpretation overall and clinicians are struggling to explain these tests. And I would suggest that the rest of us are trying to figure out how to interpret them as well and explain them to the patients.

(Slide.)

And the business models of most of the laboratories doing the testing include the gene patents in many cases or the patents on these expression profile tests. They don't necessarily have a business model that promotes data sharing. They make money on doing the test and not on sharing the data. And to compare and contrast this with this direct to consumer data sharing policy where they say we do a test, we give you the test, we give you the raw data, we give you the interpretation and it's yours. So comparing that is a fairly major deal.

(Slide.)

For electronic medical records, its got implications for all of the component systems of electronic medical records. Certainly the laboratory exams are the ones that are impacted first and foremost but the rest of them as well.

(Slide.)

And one of the big things in standards and data sharing is messaging and vocabulary standards. There is HL7 as one of the standard methods by which you exchange data between systems. There is a clinical genomic standard which has been approved and has been started to be used or tested, and that is a big step.

(Slide.)

Here is a screen shot of Intermountain Healthcare, LDS Hospital, saying scientists clear major hurdle in genetic medicine. Dr. Williams was involved in that along the way sharing genetic data using the HL7 clinical genomic standard.

(Slide.)

At the same time genomic data is in all of these other information systems, especially public health systems. It certainly is represented in some form in newborn screening, tissue and organ banks. Department of Defense requires DNA samples of all new recruits and the identification of World Trade Center victims was a hallmark in the tools, methodologies, and techniques by which you could identify or re-identify people based upon small bits of tissue which you find after a bombing or a Trade Center collapse. And those tools/techniques are

used on a routine basis daily throughout the world with the suicide bombings and the terrorist attacks that happen.

(Slide.)

And at the same time you'll hear a little later today about some use of this genomic data looking at infective agent identification and the origin and spread. This year of H1N1 is big; SARS before, but the data is clearly there. It is not necessarily represented in a way which is standardized yet.

(Slide.)

There are definitely strategic information issues which have not been solved and they are being discussed. How to represent this data in electronic medical records is a large question. There are some systems that do that already. I'll point to the Helix Molecular Biology Subsystem within Cerner. How to send structured genetic data between systems is still being worked out, although the HL7 clinical genomics standard has started to solve that problem.

(Slide.)

How do you make this understandable to providers and patients, I think, is going to be a problem for some time because it keeps emerging as

more and more information comes along. It's not a settled issue and we learn more all the time so that's an ongoing issue to be dealt with.

And then how do you keep all of this knowledge up to date is a problem for all of us. This is all emerging and what are the implications for healthcare and providers and patients, and how is it that you notify people of appropriate information and in all places in the world.

(Slide.)

You can have once again some examples. Here is an example of a genetic test, the CYP2C9 test, which can be represented in a pharmacogenomic decision support system but these are examples in single cases and not generally available throughout the world.

(Slide.)

What is coming? All of this stuff is coming. You cannot just settle in and think that you can deal with what is there today when tomorrow the world changes. Certainly next generation sequence is interesting and here and now. The environmental variables have to be correlated in order to figure out what is the appropriate interpretation on many genetic tests. I think one

that is interesting is the microbiome so that not only do I need to know what is my DNA, I need to know all the little critters' DNA that live with me in my life and help determine how I metabolize my food and react to various situations.

(Slide.)

Nanoparticles will then be interacting at the molecular level for therapeutic purposes and all of these things are coming and in some way or another will be part of our electronic medical record as we go forward.

(Slide.)

HIT standards, of course, are hot news today. There was a Technology Standard Panel established in 2005, a public-private partnership enabling the Bush first and now the Obama's vision of this nationwide system of electronic health record sharing by 2014. I think that's amazingly close to figure all of that out but things are going along rather rapidly.

(Slide.)

There is an interim final rule on standards specifically, which was issued the last day of '09 and goes into effect next week. It is a final rule so it goes into effect at the same time

it’s still being discussed and can still be altered as things go forward but things obviously are happening at a national level.

(Slide.)

I would say effective data sharing requires standards for data representation and transmission, and all of that is emerging in the genomics world. There are standard that are being discussed and developed. The clinical genomics standard is one. You’ve got a CDA clinical document architecture which is part of the RIM, the Reference Information Model, for test results. That is being worked out.

You have got representation of how to share the data and the gene expression data for the microarrays. You’ve got MIAME. That’s a way to represent the data. Here is a way to exchange the data.

The same way for proteomics, which, of course, is the standard, which is at the base of tandem mass spec in all newborn screening. You have a ways to represent the data and a week to exchange the data being worked out.

You have vocabularies within the healthcare system, which are—SNOMED has been named

as one of the standard vocabularies in the HTSB standards. You have got other vocabularies and representation of relationship between entities that are coming through these various ontologies. If you can't represent the data and talk about it on a conceptual level then you don't go too very far.

But I would say all of these are emerging and immature at the present time, promising for the future but not quite there yet.

Thank you.

Any questions?

COMMITTEE DISCUSSION

DR. ROYAL: Any questions for Dr. Mitchell?

DR. ROYAL: I have a question.

DR. MITCHELL: Yes.

DR. ROYAL: You talk about of 23 & Me and you used that as an example.

DR. MITCHELL: Yes.

DR. ROYAL: Are there significant differences in how 23 & Me decode Navigenics and share their data with the consumers? Do you know?

DR. MITCHELL: I have not looked into the details of all of them. I do know that both Navigenics and 23 & Me will allow you to download

your complete dataset if you request it.

There are some software packages which are available to an open source, which will allow you to accept that data and manipulate it.

Some of—I'm not sure which one. I think Navigenics says if you are going to do that they would like to talk to you first. So it requires not just an email saying, you know, send me my file. It requires, you know, let's set up a time to talk on the phone. Do you know what you're getting and it's pretty technical stuff.

But that's a complete data file and there is a community of people who, of course, are doing that and who have their little Facebook pages and are sharing it and sharing interpretation, and 23 & Me, in particular, suggests that you might wish to share your data with the research community and other entities, you know.

It is very possible that 23 & Me may be making money off of various contracts that they have with companies that would like to have this data on people but I am not sure of the details of that.

Yes?

DR. ASPINALL: A very helpful report appeared. A couple of comments: I believe several

of the firms have said that they are not sharing any data with any companies or any commercial interests in the midst of any of the genome because that's part—having done my genome and all of them, that's part of the agreement going forward that when you do that they have no other commercial relationships in doing that. So one of—oh, I don't know—

DR. MITCHELL: Unless you agree, unless you agree to share.

MS. ASPINALL: Yes, not with commercial entities. They have a number of agreements that they have talked about with some of the patient groups that then do it. And that may be another interesting piece about this is the patient groups. Things like—

DR. MITCHELL: Patients Like Me is one that—

MS. ASPINALL: Exactly.

DR. MITCHELL: Yes, looking for people who are like you, yes.

MS. ASPINALL: Yes, so that's another—just one of the aspects and it was very comprehensive but one of the aspects that's interesting that I think could be something that is increasing.

The Alzheimer's Patient Family Group has

been very active in saying share full genomes. How do we, as a patient group or families of patients group, want to take this and then bring that to researchers who have agreed to deal with that so that is sort of one additional model there.

DR. MITCHELL: Yes.

MS. ASPINALL: I think the only comment that I would have when you talk about the company piece for some of the companies that have products that are currently on the market, several of them don't have products that are currently on the market, the amount of information you are able to share really depends on whether you are CLIA approved or FDA approved now, and the ability to give that additional information has been deemed on occasion not possible because the regulatory authorities won't let a lab release the additional information if their approval is on a composite that you cannot do that but the genomics companies, the patient genomics, until very recently have been regulated differently and, therefore, have been able to give more information as they so choose.

DR. MITCHELL: Yes?

DR. TEZAK: So maybe just a comment on what Mara just said.

I think that companies that have FDA approval, they can--it depends on what kind of information you are talking about because if you have FDA approval then you can say that your test is just for whatever you have validated studies for and what you have approval or clearance for. You cannot say, well, you know, there is all of this other stuff that my test can do but I don't know what it means.

DR. ASPINALL: Or it is approved for this and it is the combination of these mutations. There are some data that says this one mutation alone is relevant to this other disease. You are not allowed to give that out because it hasn't been approved and—

DR. TEZAK: Unless you validated it.

DR. ASPINALL: Right, yes.

DR. TEZAK: But, you know, just to clarify. For instance, if you have 70 genes, it's their prerogative to say which 70 genes there are or not.

DR. ASPINALL: Yes.

DR. TEZAK: So that's, you know—

DR. ASPIANLL: Mm-hum.

DR. TEZAK: --we are not telling them, no,

you can’t say—

DR. MITCHELL: Well, it definitely makes a difference if you are providing a test for a medical purpose as opposed to for the curiosity of the person who wishes to pay for it.

DR. TEZAK: I’m sorry, just another point. That is very relevant. It's also interesting because many of these companies are saying we are doing this just for educational purposes but take your data to your medical provider and then it's a question of, well, what can that medical provider—what they have to do with it—

DR. MITCHELL: That’s right. That’s right.

Yes, I have a story on that, which is I have a colleague who is an emergency room physician, who said that he actually had a patient come in for an ED visit bringing his Navigenics report with him and being very anxious about the whole thing. And so my colleague said, “You know, I could treat you for your anxiety and that would be an appropriate emergency room visit but you coming in to want to talk to me about being anxious about this direct to customer test is not an appropriate emergency room visit. I will refer you to a genetic counselor and

a geneticist but, you know, it kind of has to stop there."

So it is true that you get folks who are starting with these test results out of curiosity and then it does make them anxious and then what do you do about the whole thing? It is a phenomenon and it is impacting the care providers.

Thank you.

DR. ROYAL: Thank you, Dr. Mitchell.

We are going to open up for a little discussion, if we have any, on the two talks and then we're just going to move—we're not going to take a break as we have in our program, we're just going to move in to talking about the different models. So if there's any other comment related to those two talks by Dr. Rodriguez and Mitchell, and then we're going to move on to the next talk.

Any comments?

All right.

Okay. We'll, we'll go ahead.

Steve, where is my program? I'm all confused here. This one. Okay.

The next talk we're going to have is from Dr. Catherine Schaefer, who is going to talk about healthcare systems.

CHAIRMAN TEUTSCH: These are the five models, right?

DR. ROYAL: Mm-hum. Yes, this is our five models that we're going to hear about.

HEALTH CARE SYSTEMS MODEL

DR. CATHERINE SCHAEFER: Thanks very much for inviting me here today to be part of this discussion of these—may we say topics rather than one topic of genomic data sharing. It is a very important set issues and an important series of discussions to have. We appreciate very much being able to be a part of this.

(Slide.)

You asked me here today to represent the perspective of the healthcare delivery system, and I should just point out that being part of Kaiser Permanente, particularly in Northern California, that this is a healthcare delivery system with a very large and active research division that is creating a very large and comprehensive resource for research on genetic and environmental influences on health and, therefore, may not be typical of all healthcare delivery systems or even those that do research.

But this is the perspective that I am

going to be talking about today as the issues that arise in any integrated healthcare delivery system with an electronic medical record that is preparing a very large resource to facilitate research on genetic and environmental influences on health.

The resource that we are developing will link together data on 500,000 members of Kaiser Permanente in Northern California, including comprehensive continuously updated clinical data from electronic medical records, data from participant surveys, data on environmental exposures, including social determinants and built environment, based in a geographic information system database, and genetic biomarker and environmental data from collected biospecimens.

(Slide.)

The purpose of developing this resource is really to enable scientists, including scientists within Kaiser Permanente, but also the broader scientific community to conduct research on genetic and environmental influences on disease susceptibility, disease course, prognosis and outcomes, and response to treatment as in pharmacogenetics. Our aim is also to enable or facilitate, conduct research to translate findings

into improvements in medical care and public health. And from the beginning we have also had the aim of conducting research on the ethical, legal and social implications of genetic research, and the use of genomic information in medical care.

(Slide.)

I thought it would be helpful if I gave you a little bit of background about this resource.

With initial funding that we received in 2005 and 2006 we developed a lot of time and effort to engaging the membership of Kaiser Permanente in Northern California and the sort of broader organization, providers, staff and so forth, through focus groups, internal communications and media about what we were planning.

And to sample concerns and values and better understand the perspective of our organization, its membership, about development of this sort of resource, we organized separate community scientific and bioethics advisory panels and we spent a lot of time organizing our electronic medical record data by disease groups to facilitate research, creating over ten registries creating over 1,000, sorry, 100 diseases and conditions.

(Slide.)

In 2007, we started with enrollment of a general cohort and collection of survey data through a mail survey to 1.9 million people in Northern California, Northern California members. That is virtually our entire adult membership was mailed the survey, which sought information about demographic and background factors not included in the electronic medical record, health behavior information and so forth.

(Slide.)

About 400,000 people completed the survey over the course of about a year and then beginning in late 2008 we again contacted survey respondents and asked them to provide written and informed consent, and the saliva sample. As of last month, about 130,000 individuals have provided written consent and a saliva sample.

(Slide.)

Our current activities include continuing efforts to enroll the planned participant sample. We plan to enroll a total of 200,000 individuals by the end of this year and reaching the goal of 500,000 participants by the end of 2013. We are beginning the collection of blood samples, phasing out the collection of saliva, using the clinical

infrastructure, and we are continuing work on several funded genome-wide association studies, including a multi ethic study of bipolar disorder that involves 6,000 cases and 6,000 controls, and a study of prostate cancer among African Americans that involves 3,000 individuals.

(Slide.)

We have also developed a collaboration's portal and an access review committee that will be ready to receive applications later in 2010.

(Slide.)

And, importantly, we recently received a GO grant funded by the National Institutes of Health that supports genome-wide genotyping of the first 100,000 or so individuals/participants in our resource by year end 2011. This study was designed to be a resource for the study of age-related diseases, healthy aging and longevity. The average age of this first 100,000 participants in our resource is 65. So we have a large number of aged individuals and a large number of people in middle age whom are perfect for beginning to study factors that affect aging. We will be genotyping 650,000 SNPs as a part of this process and the resulting genomic data will be linked to data from the

electronic medical record survey and environmental databases to create this resource.

It will be accessible through dbGaP and through collaborations, direct collaborations with us, and we believe that it will require reconsent for deposit of data in dbGAP.

(Slide.)

So considerations for data sharing in this environment, in this sort of a resource:

First of all, this is a very rich resource that would be difficult and extremely expensive to replicate in another environment or de novo. It is large. It is diverse ethnically and socioeconomically and it's generally representative of the population. The comprehensive continuously updated EMR enables excellent phenotypic characterization and follow up.

(Slide.)

Kaiser Permanente recognizes that the RPGH can make an important contribution and wants to ensure that the best and broadest use is made of this research consistent with its commitment to its members. So our perspective on data sharing is shaped by this commitment to our members. We are invested in them and they determine the future of

this organization. So our situation is a little different than may exist in academic models. With this genotyping of 100,000 individuals and deposit of data into dbGAP, we clearly are going to have a lot of skin in the game, so to speak, with respect to genomic data sharing.

(Slide.)

So we are the very interested in and focused on these issues even as we are extremely committed to the data sharing, to the advances that we all hope this will bring.

Over 50 percent of our first 100,000 participants have been members of this organization and received healthcare for over 20 years. So both is a very rich—researchers can appreciate this is a very rich source of data since we have data on these individuals, comprehensive data going back to 1995 in an electronic format, and then data going forward as well.

(Slide.)

Trust in Kaiser Permanente by our members enables us to do research and so we are very—it's very important and we're very committed to maintaining that trust.

(Slide.)

In terms of factors that affect data sharing, and certainly informed consent and the nature of that informed consent is quite central, we use written informed consent that is broad and includes no restrictions on any kinds of health problems that could be studied. Health information can be updated from the electronic medical record going forward in time. It contains a stipulation that all studies must be approved by an institutional review board and data can be shared with scientists outside Kaiser Permanente who agree to protect confidentiality and follow rules for use.

(Slide.)

The informed consent stipulates that using and sharing genomic data will be for research purposes only. Research results will not be placed in the electronic medical record and participation is confidential. Genomic data will not be returned to individuals or their providers. Participants, however, may be contacted if information develops that has significance for their health. Participants may withdraw and may ask that their sample be destroyed.

So one of the questions that arises is how we ensure that these latter commitments made in the

informed consent are met when data are used through a public database where we have less information or less probable feedback from investigators who use information that way.

(Slide.)

Informed consent does not historically really address—really addresses issues of sort of individual autonomy but has less to say or has not historically been used to address issues that can arise about social harms that may arise in the process of carrying out some kinds of research.

(Slide.)

So in our environment, concern has been expressed about data sharing through a federal database such as dbGAP. Our community advisory panel focus groups that we have conducted and some survey respondents very directly have been concerned about this issue and expressed the idea that the government may “take or misuse” data.

The building of the other federal DNA databases increases the perceived vulnerability of this NIH database to re-identification or misuse at least in the individuals who are concerned.

And the use of DNA to deny treaty rights or label immigrants or other sort of forensic uses

is also a prominent community concern.

There is the concern that research may be done that could be used subsequently to stigmatize a vulnerable group, that there is—once a broad consent is signed there is actually no recourse of the individual other than withdrawing from the resource; no choice is involved about the kind of research that is undertaken then with the resulting data.

And then there is the perception on the part of our members that storage and control of data by Kaiser Permanente, by the resource, sort of local storage and control gives participants better recourse and control over events.

(Slide.)

I just want to mention--I think you are going to hear quite a bit from Dan Masys about this—a later speaker today. But the obvious fact that in most research contexts sharing genomic data means sharing phenotypic data. And so we also need to consider factors affecting the sharing of these other forms of data that may be linked to genomic data.

(Slide.)

Health plans with EMRs, which as is the case for our resource, have huge investments in the

EMR data, that is so rich, and then is linked to the genomic data.

The quality of phenotypic data that you can derive from these very high density EMRs is critical to the best use of the genomic data and the resource, and it's challenging. Let me tell you very challenging to extract high density data that will be useful to all for a whole variety of studies that can then be deposited in a database such as dbGAP.

(Slide.)

The best use of the data depend on knowledge of the system that generated the data and this is often--the meaning of this sort of clinical data, even when standard diagnostic codes are used and efforts are made to harmonize data across systems, is often--it really takes an understanding of how that data has been generated to make the best or most valid use.

(Slide.)

Partly in response to a variety of these concerns, we have begun at this point to perform a series of stakeholder interviews led by Carol Somkin, who is the head of our Ethical, Legal, and Social Implications Core, with the goal of informing

the development of our access and collaboration policies and procedures.

So we have been conducting these qualitative interviews with a variety of stakeholders, as listed here, and with the following sort of research questions, such as what are the specific data sharing, benefit sharing and governance issues inherent in a biobank that is situated in an integrated delivery system?

Well, that’s really what you wanted me to tell you about today and I regret to say that we have just begun these interviews and so I really do not have data that I can present about the outcome but the things that I talk about are the result of sort of earlier focus groups and interviews that we have conducted.

I hope there is a chance actually to come back and tell you a little bit more about the outcomes of these interview efforts at a later date.

Thanks very much for your time.

DR. ROYAL: Thank you, Dr. Schaefer.

Any questions?

Mike

DR. MICHAEL CAROME: Your institution, like many, has policies allowing subjects of this

type of research to withdraw and, by that, meaning have their samples destroyed. Are you familiar—aware of any cases where such a request has been made at your institution?

DR. SCHAEFER: Yes. Actually it happens rarely but it has happened and it has already happened with this particular resource.

But I know of only five instances out of 130,000 individuals participating where that has happened.

DR. BILLINGS: Thanks. Could you comment on how the providers in the Kaiser system understand what the heck you are doing and, also, I am curious about the uptake or the frequency of participation by your members. It seems quite high and I wonder whether--what you have done to foster such high participation.

DR. SCHAEFER: Well, I'm delighted to hear you describe it that way. It has mostly been an effort that has been—you know, the traditional ways we know how to contact people, which is essentially mailing people materials that are descriptive of the research program, the eight page—the consent form written in—consent form is eight pages long if you include the HIPAA authorization. So I think the way

we look at it is most of the participants that we have garnered so far are--and perhaps this is one reason why we have very good representation in older age groups--are people with the time and patience to basically make their way through printed material that they receive in the mail.

So our next efforts at enrollment actually are to carry out different sorts of efforts that don’t involve only essentially reaching out to our members through a mailed written material format but involve other ways of engaging people.

With respect to providers, our providers are perhaps—well, they--we have had a research division since 1966 so they are familiar with essentially having patients recruited for studies. The research division essentially operates sort of side by side with the providers but we do not typically recruit through providers. That is we do not ask physicians to obtain—to talk to their patients and ask them to participate in studies. There are certain clinical trials that are exception to that but, in general, for this sort of general research we don’t do that.

What do they think about it? They are very hopeful that in the not too distant future we

will begin to be able to do translational studies that will involve them more directly and that will fulfill the promise that is held out there that this kind of research will result in things that directly improve healthcare.

DR. MCGRATH: An interesting project. You may not know the answer to this but I am wondering whether there has been any—it may be obvious why I'm asking this question--training to the healthcare providers, the physicians or nurse practitioners who are the primary providers, not the researchers, to address issues if their patients come maybe having read something in the press about a genetic study or maybe knowing more about this study. Who do they go—who do your participants go to for sort of small questions? Not informed consent kind of questions but health related questions? Do you know what I mean?

DR. SCHAEFER: About this study you mean?

DR. MCGRATH: About genetics in general. I would assume that just being—reading through the consent form, the eight page consent form would make the participants a little more alert to things in the press about genetic research in general, that they might then go to their providers with general

questions and is there any training for those providers within Kaiser for this?

DR. SCHAEFER: I don't think as yet that there actually has been any provider training in how to respond to sort of general questions about this kind of data in particular or these kinds of large scale genomic studies.

The providers have what we have provided to them and that as yet is not a great deal of information.

We do have a strong medical genetics department that is distributed across the region. And those providers, themselves, for example, have organized, about the time that, for example, BRCA-1 testing became available, we anticipated that there would be a lot of general interest in this even though the test was really not in the appropriate for women who by virtue of family history might have a low to moderate risk of inherited susceptibility.

So the genetics providers actually pioneered a class that any woman could come to and that would sort of explain what BRCA-1 is, the sort of role of family history and the risk of breast cancer, and then women could self refer then for genetics counseling if they thought that—and then

subsequently for the test if they thought that this was something they really needed.

So we have a little bit of a model of how to handle a situation with--where there is sort of general interest in something but, in fact, there may be—and that’s a case where the test is really only appropriate for a relatively small number of people.

DR. WILLIAMS: So a couple of brief questions. One is a follow up to Michael's question, which is if somebody leaves Kaiser to go to another payer, how do you handle people that leave the system in terms of participation in the study?

And then the second question is just to resolve what, to me, is an apparent contradiction but probably just represents a lack of information, which is given the age distribution and the membership length, how representative is your sample actually compared to the rest of the Kaiser membership specifically and maybe the population of California, in general?

DR. SCHAEFER: Let's see.

We actually do not have a good solution in terms of continuing someone’s participation if they

leave Kaiser Permanente and go to another system.

Essentially, we have then no way to really follow up in the same sort of way their medical history at the point at which they leave us. So the informed consent gives us permission to use the data that we do have the system or died, for example, but right now, at least, we don't really have agreements with other systems for sort of continuation of observation.

And with respect to—

DR. ROYAL: Okay.

DR. SCHAEFER: I'm sorry. Can I answer his question about representativeness or are we—

Okay.

DR. ROYAL: We were going to take one last one but—

DR. WILLIAMS: Well, she had a second part I had asked.

DR. ROYAL: Oh. Okay. Yes. Okay. And then we will move on to the next speaker.

DR. SCHAEFER: Well, the answer is that while we have good representation of different groups, it is actually—I would not say that it's exactly representative of the population of Kaiser Permanente, which is generally representative of the

population of Northern California. So we have--now the way that we have been enrolling people, for example, it's older, more female, more White, and better educated than our general membership is.

DR. ROYAL: Thank you, Dr. Schaefer.

We'll hear from Daniel Masys from Vanderbilt.

Dr. Masys is going to talk about the academic model and then we're going to take a break.

ACADEMIC MODEL

DR.DANIEL MASYS: Thank you. And since I stand between you and a break, I will move with all due expediency through a presentation that shares a lot of the elements you've just heard from Cathy in the sense that these are phenotypes derived from electronic medical records combined with genome-wide scan. And I'm doing that in my capacity as the principal investigator for the National Coordination Center for a consortium called eMERGE, the Electronic Medical Records and Genomics Consortium.

(Slide.)

Three topics in the next 15 minutes:

First, what eMERGE is; lessons that we are learning about data sharing; and then I'll focus, in particular, on where we are with respect to the

science, the emerging science of data de-identification and re-identification.

(Slide.)

This consortium grew out of a request for applications by the Genome Research Institute in 2007. The key element of which is highlighted here in red that, in essence, was support for investigative groups affiliated with--you had to have an existing biorepository and then you had to have the ability to extract phenotypes from electronic medical records.

The consortium: Members of the awardee institutions are five that you see listed on this slide and they have both a geographic distribution and a pretty wide distribution in the differences with which they acquire both their biobanks and their clinical data.

(Slide.)

Here's a map that shows the primary phenotypes that were part of the original project submission. So as part of the grant submission you had to propose what phenotype you were going to do a GWAS on as the anchor for participation in the network but we have since expanded that with a number of cross network phenotypes.

So you see here that they range, and I will actually note as well that there is a variety of sizes of biobanks, so in the upper left hand corner then, the Pacific Northwest Group Health of Puget Sound, had essentially a dedicated Alzheimer's research cohort that was linkable to Group Health data and their biobank was about 3,000 samples.

The cataract primary phenotype for Marshfield represented probably the most mature health system based biobank, one that many have been built from, which was a prospectively consented cohort of about 22,000 individuals in Northern Wisconsin.

The Mayo Clinic one was again about 3,000 samples focused in peripheral vascular disease built from a research cohort as its anchor.

Northwestern was looking at Type 2 diabetes with a general purpose biobank built from all comers into an internal medicine environment with a prospective consented biobank participation.

And then Vanderbilt was looking at a—is looking at a continuous trait of the QRS duration as a predictor of future cardiac events and the Vanderbilt model is a non-human subjects, that is a de-identified biobank built from discarded blood

samples where the DNA is extracted unless patients have elected to opt out of that model. And Vanderbilt is also the site of the coordination center for the network. Vanderbilt started their biobank in about 2007. It is just a little north of 76,000 samples now growing at about 500 per week.

(Slide.)

So, again, the features of our network, each site having DNA linked to the corresponding electronic medical record data. An important component and requirement of the RFA was community engagement and so investigation into models of consent and re-consent. Two of the five members have had to re-consent their members because of the last condition shown on this slide that is the submission to dbGAP as a condition of NIH funding. It was part of the—already part of the model of consent for others and so it was not the case that all of the groups had to do that.

The core was a 3,000—roughly 3,000 subject GWAS study that gave us roughly 20,000 genome-wide scans that we could then not only do the primary phenotype associations but mine the associated EMR data for other opportunistic, if you will; phenotypes and I will show you a little bit more

data about that.

(Slide.)

We have since received supplemental funding for additional new genotyping for our cross network phenotypes and that work is in progress now.

(Slide.)

This is an example of conditions that were not part of the original proposal but they do represent data that because it's so commonly acquired just in the natural course of people having routine testing and electronic medical records, it gives the network the opportunity to share samples, and you see here that by and large they range for most conditions in the thousands of samples for which the genotyping is essentially already done because of a—we—the basic platform is a 600k Illumina genome scan, although the African-Americans—we have about a one million SNP chip on about 2,000 samples across the network.

So this ability to look at red cell and white cell indices, diabetic retinopathy, lipid levels, GWAS studies on height, which by and large are replication studies at this point since they’re already published dedicated research cohorts and glomerular filtration rates are emblematic of the

fact that it is a data rich environment, such as Cathy described, and it allows us to begin with a genome-wide scan and then look at various aspects of the phenotype.

Now what we have discovered along the way is—in fact, the inside joke in eMERGE is that any fool can get a genome scan and many do; the real hard part is the phenotypes. And so the informatics issues that we are engaging are essentially because we are going to pool and do meta-analysis of phenotypes, how comparable are the patient populations who walk through the doors or sign up for the cohorts in these five different health systems because if biologically there is some inherent bias in the nature of these patient populations then pooling their genomic data may mislead us with respect to statistical associations.

We have discovered that genotypes are pretty easy to share by virtue of the NIH supported genotyping centers and so sending samples and receiving datasets, not unlike the ones you can download from 23 and Me or Navigenics, is actually the easy part in terms of it but there is as yet no set of standards that represents the kind of genotype/phenotype package where you can send the

whole thing in one electronic envelope, and so we are developing in association with NCBI sort of standards for how clinical data can be put into a format that is useful for association studies.

Clinical data has a number of features that make it different than the classical cross-sectional research cohort that has been published in the GWAS literature up to the current time. One of those is we can't predict how many times some measures will be done. For example, if you have a diabetic who has blood sugar measurements, there may be thousands of them in the record so how do you decide which ones to include in a research data submission, as well as the feature of EMRs that clinicians are absolutely comfortable with the notions that they are—that are clear that some people have definite diseases, others may have probable or possible, and that notion of uncertainty that lives comfortably in the clinic is not well suited to this research environment that looks more like a case report form that has a sort of dichotomous representation that you either have a condition or you don't. So one of the things we're working with dbGAP is the assertion of whether a condition is present or absent and our level of

comfort that exists in EMR.

(Slide.)

I would like to focus on the last thing that we are making progress in the network on, and that is this re-identification potential that arises particularly out of clinical data and those phenotypes associated with the genetic samples, with a general model that we would of course like to maximize scientific value while complying with the federal privacy policies that Laura Rodriguez has mentioned and will mention in greater detail later in this session.

(Slide.)

This is the screen shot from the dbGAP data submission policy, and I've highlighted in the little red box there that says if you're a submitter to dbGAP you have to send your phenotype exposure and genotype data without identifiable information using a unique code and such.

And so the question is when you have got clinically derived phenotypes, how do you do that? It calls to mind, I think, an important set of vocabulary because IRBs always get balled up with this about the notion of, well, is it anonymous or not anonymous, or what do you mean by de-identified.

So I think in this regard, at least in the computer science and informatics community, we regard anonymous as this definition that things are not traceable to an individual and that it was a concept prevalent from about 5000 BC, the time of Hippocrates, to about ten years ago, and it was generally thought of as a dichotomous variable, that is anonymous. The data was anonymous or it wasn't, and the IRB was happy with that assessment.

But what we know now is that we had to replace that with something that looks like kind of a slider bar that it has replaced anonymous because we recognize that biologic data is so inherently rich in attributes that its re-identification potential essentially never goes to zero.

(Slide.)

And so it's a continuous variable whose properties can be calculated for some but actually not all types of health data. The primmer on re-identification is a simple one, and that is if a dataset has ostensibly been de-identified then the way--the pathway to trying to find out the identity of the individual from who it is derived requires two conditions.

The first is out of many records getting a

unique set of attributes, what computer people called a logical unit record associated with one individual. So you've got to get to uniqueness first.

And then that's necessary but not sufficient. And a lot of the U.S. population, whose understanding of genetics is mostly informed by the OJ trial and CSI, believe that DNA is inherently identifying as if you found a poly-vial of it on the carpet here you'd actually know who that person was. And so what you need in addition to the biology of uniqueness is you need a naming source. You've got to be able to intersect that with a person's demographic information.

So as a result de-identification methods basically are aimed at either preventing you from getting isolated to a unique record, that there's always more than one that satisfies any set of characteristics, or you might be able to get a unique record but what you can do is block the linkage to a naming source.

(Slide.)

This is a graphical view of this from work—and I'm going to present to you a couple of slides from Brad Mullen, who is a faculty member in

our department at Vanderbilt, who is a data privacy guy. In fact, your briefing materials have one of his recent publications.

And, in essence, it shows on the left hand side that—and actually in all of—all three of these conditions have to be satisfied. You have to be unique on the left-hand side with respect to your de-identified dataset, you have to be unique on the right side in terms of named data such as a voter list or a health and vital statistics registry, and you've got to get a firm linkage one to one between those two models.

(Slide.)

So, let's look first at uniqueness.

Well, if you take clinical data—this is our own cohort of the 2,500 Vanderbilt patients that are in our genome-wide study. One can say, well, how alike are they with one another based on common measures that are in clinical data? One of the common ones that he used is ICD9 disease coding.

(Slide.)

To cut to the chase, out of our—using it as a reference population, it's now about 1.9 million records in our EMR, about 97 percent of people are out of the box unique. It's just their--

the combination of their age, their gender and their ICD9 codes, if they have--on average we have about 12 codes per person. It only takes about five codes and all of a sudden you are in a box where *n* is one in the cell. And, so, it would seem that we are in very good condition to be able to do--sending out the entire detailed set of rich phenotypic attributes representing even ICD9 codes.

Now, we work in a world that's governed by HIPAA. And so it has two nominated standards for data sharing. The more stringent one, as you probably know, is called Safe Harbor, and it allows you to release race, gender, only year of birth, not date of birth, and only state as the smallest geographic entity in most cases. And then there is this called a limited dataset, which allows you, in addition to those two, to increase the specificity so you can release the actual date of birth and you can go down in most cases to a county level thing.

(Slide.)

And then the question is what kind of linkage does that--potential does that give you for identified data sources?

(Slide.)

So here is Brad's work on the pooled U.S.

Census data from the year 2000 that shows you the fraction of unique individuals under HIPAA safe harbor that is you're releasing only year of birth, Sex and race on the left. And the important thing here is it's not zero. The HIPAA safe harbor standard has roughly about a 10^{-4}, unique, and it still exists in that, and it depends upon the states, how sparse or densely populated your state is.

You'll notice that there is a dramatic increase in the number of records that become unique when you go to the actual date of birth, the sex, the race and the county. So now we're in the range of about 30 percent to almost 100 percent of individuals can be uniquely isolated inside of a clinically derived dataset.

Well, how about the naming sources? If the issue is that lots of things are unique in an EMR, here the story is very highly variable across the landscape, both of information resources on the Internet but, importantly, across states because a common re-identification source is to use either health and vital statistics registry or voter records. So these happen to be the state policies and the data items available for the states of the

participants in the eMERGE network. They include Illinois, Minnesota, Tennessee, Washington, and Wisconsin. And you see that authorized users include in three of the states anybody in Minnesota. You have to be a Minnesota voter. You have to be a political person in Illinois but isn't everybody.

(Laughter.)

And so you can get the stuff—we can get this stuff on a disk and it ranges from $20 to $12,500 and you get a variety of different data elements, including date of birth. You always get name and address. So, the question is what are the other things that map, for example, to those HIPAA limited dataset items?

If you then—as a result of that availability, and we've done this for all the states in eMERGE, you take—that graph on the left is exactly the one you saw before. That's not identifiability. That's just uniqueness.

(Slide.)

So what happens to uniqueness when you merge it with a naming source? And you see on the last—on the right-hand side that the number drops but it doesn't drop dramatically. So, in essence, K here is, by the way, the cell size. Because you

could say the re-identifiability doesn't begin at just a single record. Maybe it begins when it's only—when you've got a pool of five records. That's close enough where we could then use other methods to try and zero in.

So you see at even a K of one that where 30 percent were unique, it drops to about 15 percent but that means 15 percent of that entire population you have a name, address, all—you've successfully and fully re-identified the individual from the de-identified data.

(Slide.)

So as a result of that ability to do a quantitative analysis what we found in the network is that the clinical data that we are sharing with dbGAP is going to necessarily need to be a subset of those present in the full clinical record, specifically by removing uncommon codes that support elevated risk re-identification risk. And when we say "elevated," we mean elevated above the HIPAA standards so we can quantitatively say what the HIPAA standards are and then we can mathematically meet those same standards by a variety of methods.

(Slide.)

Now, between the members of the network

with respect to an academic sharing, we actually all have lawyer-approved data sharing agreements at the individual record level. So that works fine among the consortium. It took us 18 months to get, you know, n by n, and way we did that was everybody made an agreement to share with the coordination center as opposed to having to do four other agreements with four other institutions.

(Slide.)

The eMERGE coordination center in its capacity as a data quality and analysis center is providing data privacy consultation to the network members, including quantitative assessment of the re-identification risk of their datasets before they go to dbGAP because they vary on the different disease populations. You might imagine the Alzheimer's disease population is highly skewed to older individuals so it more impacts the HIPAA standards about people that are ages 90 and above.

And the good news is that we're also just about—we have a couple of manuscripts in review and I'm just about to release some tools that will be open source, usable by mere mortals for actually determining the quantitative risk of the demographics of publicly submitted datasets and how

you can, in essence, trade off for scientific purposes the granularity of one item so you can kind of smudge the zip code, if you will, if it's important to maintain age because that's an important dependent variability in the analysis.

And that's the sort of good news about the statistical standard is you can do various permutations of the data in order to meet the formal federal standards and you are losing some content but if it's content not important for the key scientific hypothesis then it's still kind of a whim.

So that's where we stand. It's a work in progress and we'll be happy and will be reporting in the literature and I'm happy to report to you as we make progress on these issues.

Like all good networks, we have a URL with the unpretentious URL of GWAS.net and so as all of our publications and our white papers for practices within the network are posted on that website.

And, with that, I'd be happy to answer any questions.

DR. ROYAL: Thank you, Dr. Masys.

Any questions?

Marc?

` DR. WILLIAMS: So on one of the first slides where you talked about the RFA, I think there was a reference in there to the use of natural language processing.

DR. MASYS: Yes.

DR. WILLIAMS: And so I am just curious how is that working out for you?

DR. MASYS: Yes. So what we discovered is that-- well, some people have said—I mean the null hypothesis for the whole network is that EMRs are so bad you couldn't use them for anything. Right? It's just a mess. So what we have discovered is that in order to get a positive predictive value of a phenotype definition, what works across multiple EMRs, you need a combination of structured items, including codes, the ICD9 codes, labs, specific lab values, and importantly medications because in a sense medication is the sincerest evidence that a clinician thinks you have a disorder. And, in addition to that, that journal gets RPVs in the range—it depends upon the condition but roughly only about 65-75 percent. We have to use natural language processing, that is teaching computers to identify concepts, diagnostic concepts, and whether they are asserted or negated in the record to get

RPVs in the 95 percent, and that's most of them are in that range.

The good news is we use experts to do that. Basically scoring how good the algorithm is.

It generally takes about five iterations to get it right. Then when one of our institutions gets it right we can actually—we found we can actually transport that across the network and, with relatively minor modifications, most of the PPVs only fall a few percent when they are re-used as selection logic in very, very heterogeneous EMRs. So that's the unexpected big win here is that if one group does the work of creating the phenotype selection logic and we're going to build public libraries of these, other institutions that want to use these to find cohorts of interest, either for administrative purposes or for research purposes, can reuse that without a lot of having to redo the wheel.

Yes?

DR. ROYAL: Questions.

Andrea?

DR. FERREIRA-GONZALEZ: It's a very impressive presentation.

I was curious to see if you can elaborate

a little bit more about the process of the informed consent of the patients. What I understood you were talking about is they use procedural specimens and they will be discarded otherwise. But you have mentioned also that unless the patients opt out of having that—so what is the process of the informed consent or there is a blanket informed consent as they come through the Vanderbilt institution that they will be enrolled in this unless they actually specifically—and how that process works.

DR. MASYS: So Vanderbilt is the one member of the network that has—that works in a de-identified space where both the records and biological samples are de-identified and we cannot construct identities to go back and contact individuals.

The general model has been published, and I would be happy to sort of provide it as the reference but the short version of OHRP-approved is that in this nonhuman subject space the federal regulations would have actually allowed us to view this as existing tissue in data without notifying anybody. Our ethics board and our IRB said, “It doesn't sound right.” And so in the conceptualization and implementation of biobank

which was preceded by a number of surveys of patient attitudes and such, we added this component of a very extensive public notification campaign. The fact that people re-signed a consent for treatment and right above the signature line the only bold-faced type in the whole thing is a big box. In bold face type it says "I understand that Vanderbilt extracts DNA from leftover blood samples and I should check this box if I don't want to have my samples used for that research."

On average, now having run for about the last 30 months, we had a predicted opt-out rate of five percent, and that's exactly what we are observing, right at about 4.9 to 5.2 percent on that. And, generally, broad acceptance of Vanderbilt patients based on what Cathy said, and that is that while our patients--they may not trust the government but basically they trust the institution that they are getting their healthcare from. So that they are willing to let Vanderbilt do this kind of research.

And, as I say, to not turn this into an hour-long discussion of this model, and we can maybe come back and give you the full soup to nuts, we have published it and I will send you the URL.

DR. ROYAL: Okay.

Any other questions?

No?

Thank you, Dr. Masys.

We'll take a 10-minute break so we'll come back at ten after 3:00.

(Whereupon, at 3:00 p.m., a break was taken.)

CHAIRMAN TEUTSCH: I'll turn it back over to Charmaine.

DR. ROYAL: We're going to hear from Laura again, Laura Rodriguez, Dr. Rodriguez from the Genome Institute, talking about the government model.

GOVERNMENT MODEL

DR. LAURA RODRIGUEZ: Okay. So I would like to thank the committee again for having me to talk to you all again, and I promise this will be the last time this afternoon.

(Slide.)

So now I'm going to switch to talking to something that I do know much more about than talking about all of the activities across the federal government, and that is—I'm not sure that I would say it is the government model for genomic

data sharing but it is one of them, and it is an NIH model that we are seeing become increasingly consistent, as we talked about before, across the NIH and across the different institutes going forward.

(Slide.)

There were several questions the task force asked the speakers to try and address in their questions, and so I'm going to do that through the course of the slides. And for that reason I will try to get down to some of the nuts and bolts about the process for how this works to try and address things like informed consent and responsibilities for different aspects of protection along the way.

(Slide.)

So as you all know, data sharing is nothing new to the NIH. There has been a longstanding tradition of sharing resources and tools, and of having large policies for all of our extramural grantees on the expectations around how they share data.

And, traditionally, this has come forward, I think, in one of the more major statements in 2003. For any grant over $500,000 to have the data shared at the time or post completion of the study

the data was to be shared broadly and made available.

So what's different--one of the things that’s different about GWAS as we move forward was that GWAS began to merge the genomic traditions of making data rapidly available prior to publication into the NIH realm of the broad data sharing.

And the reasons that we did this were partially—largely, of course, based on of scientific opportunities that were coming forward as the technology became accessible to do whole-genome scans to look at so many different points of variation across the genome and actually be able to try and tease apart the genetic underpinnings of common diseases which have been so difficult to address through standard genetic mechanisms and strategies in the past.

And so the opportunity to do this and the breadth of different institutes that were disease focused that were wanting to try and take advantage of these new strategies were something that were very—a very strong force for the leadership at NIH to say that we needed something that went across the board, across all of the institutes so that there was consistency in expectations for the

investigators, and again for the public in terms of what they would understand about the data that was out there and what would be in place for the protections for how these data would be shared.

And, of course, again, I think you are well-aware of the power that the genome-wide association data had in terms of the richness of genotype and phenotype information, and the ability to ask many different questions of the data, and thus all supporting the reasons to have as many different investigators have access to the data as possible so that they could ask as many different questions as possible.

(Slide.)

And this brings us back to the guiding principle and really the foundation upon which everything came from as we constructed the policy and all of the different elements within the policy. And that was to try to achieve maximum public benefit from the federal investment and from the wealth of information and data generated through the different studies that NIH was beginning to fund.

(Slide.)

The policy itself was broken into three primary sections. The bulk of the language focuses

around data management, and that speaks to the importance that the NIH put on both standards and expectations for data submission and data access but also for the protection of the data. And of the interest of those individuals whose data was within the resources that the NIH was creating through this policy.

(Slide.)

The way that the process works, of course, is that everything is built upon primary research studies, which take place perhaps outside the realm of an NIH funded study. It took place sometime in the past where there was a relationship between research participants and an investigator that is structured around an informed consent discussion and agreement between those two individuals about how the data will be used and whether it will be shared, et cetera.

And at the point in time that an investigator decided that they wanted to apply to the NIH for funding for the genotyping is the point--was the trigger point for the GWAS policy. And at that point then there would be an expectation and is an expectation now that the data will come in to a central repository that is housed at the NIH and

that repository is the database for genotypes and phenotypes. It was newly constructed at the time within the NCBI and there's a lot of information. These different screen shots simply portray the range of information about different studies that are available from the protocol and the survey instruments that were used to averages of the phenotype data, as well as different views of the genomic information from the genotype data so that people can zero in on where they might want to look.

(Slide.)

The other advantage to having the central resource, besides being able to make documents such as these examination procedures, which for many studies would have been in existence only in the lab's file cabinets, to now available and be searchable through open access pages on the web, is that people could find new collaborations, they could preview studies and also try to find out if they were relevant to the kinds of questions that they were going to ask before they ever attempted to request access from NIH.

(Slide.)

All of the data that come into dbGAP are de-identified and the way that we define de-

identified since, as Dan mentioned, this is a variable term, was to look to the HIPAA standards and the 18 identifiers named within the privacy rule, and use that as the basic rubric by which investigators were asked to de-identify information, to hold the key to the code within their institution and not to share it with the NIH so that when the information came to the NIH we did not have any way to link back to the code for any of the individuals within the data sets.

(Slide.)

The third and final phase, of course, is to make this data available to the secondary investigators. And this would be through a controlled access process, which I will talk about in a moment, and again they are only ever getting access to coded information, and they would be—they would request the data for a specific research purpose and project.

(Slide.)

Coming back to measures of protection, one of the things that NIH did in this policy, which departed from the basic regulatory requirements, was to attach an expectation that the informed consent of individuals, and those agreements that may have

been made in terms of how data could be used in the future or how data could be shared, would remain attached to how data were distributed through the resource. So, again, all of the data that since they are de-identified and, therefore, don't technically represent human subjects, data, once they come in to the NIH or for use by the secondary investigators, we still maintain that the informed consent was an ethical principle that we wanted to have follow the data as it went out and was used by others.

(Slide.)

In terms of implementation for the policy, the local institution, consistent with general practices where the IRB is the authority for any study that happens, is asked to provide a certification to the NIH which stipulates that the dataset and all of the data within it are appropriate to come into the data repository and to be distributed to secondary investigators.

They are specifically asked to have an IRB review elements of the informed consent and state that the consent is consistent with use coming through dbGAP.

And also, again, assertions that the PI

will remove all of the HIPAA identifiers so that it can meet that standard of de-identification set forth in the policy.

Any limitations on future data use are also requested through the certification. This can speak to issues around informed consents so that if data were collected under an agreement where the data would only ever be used for cancer research, the NIH is aware of that and can only ever release it or distribute it to secondary investigators also doing cancer research, but also for other issues where IRBs may have concerns in terms of the particular data elements or how things are going forward so that we can respect again the decisions of the local institution coming into the NIH.

(Slide.)

In order to try and find or provide some information to local institutions on these new responsibilities for the data that would be coming in to the resource, we did craft a points to consider document that discussed all of the basic elements of the policy, as well as some of the overview of the science. The audience for this points to consider document really was intended to be the IRBs who might not necessarily understand or

have the background in the science at the time they were first seeing this come through and being asked to provide the certification.

The points to consider walks through many of the elements within informed consent that the NIH felt were important for institutions to take a look at within the informed consent documents but it is not intended to serve as a checklist. And so it still leaves to the discretion of the institution what is appropriate and what would not be appropriate based on their own deliberations relative to the particular population in a given dataset or relative to the institutional policies at their research institution.

(Slide.)

Data access, as I've already mentioned, was two-tiered. So there are public access pages that are available for anyone to look at to get basic high-level information on the studies within the data set. Again, to understand whether or not the dataset might be interesting and relevant to the questions that they would like to ask but, in order to get to the individual level coded data, it had to come through a controlled access process where every investigator seeking the data will need to submit a

specific research use, proposed research use, that would be reviewed by a data access committee and the decision would then be made.

And the point of the specific use was in order to have--for the data access committee to make a determination about any limitations on data use provided by the local institution at the time of submission.

(Slide.)

To try and gain some accountability for investigator practices, once they had the data, every request for data must come in co-signed by institutional official. So that the institution at the secondary site is taking responsibility and sort of vouching for the credibility of the investigator that's coming in, and acknowledging they know this investigator has the data, they know that they are intending to use the data, and that the investigator is in compliance with any of the local policies that they have put in place for how data use of this kind of genomic data, whole genome data, is used at their institutions since, again, different institutions have different policies about how they review the conduct of research with whole genome information and coded specimens information, in general, at

their local sites.

(Slide.)

I think I have gone through some of this already.

The data access committees in terms of who they are—because all of the data reside within a government database, they represent government records and, therefore, only federal employees can make decisions about access to the data.

So DACs are consisting only of federal staff but are able to consult with anyone in the process of reviewing a document. So they can bring in an expert in a particular population if they have concerns about potential group harm, for instance, or they can bring in a scientific expert if they are not sure if the particular proposed use actually fits within the use limitations provided by the organization.

The other function that the DAC has in addition to reviewing incoming requests is to track the data use by those users that they have approved within the database. And so annual reports come in for all users where they talk about any significant findings for the work that they have had, any publications coming out of it, any IP, et cetera,

that may have been noted. And that also provides a way for the DACs to go back and make sure again that they are only working on that proposed use that they submitted for approval at the time and not doing something else with the data.

(Slide.)

The agreement between the secondary investigator, his or her institution, and the NIH comes through the form of a data use certification agreement. We have now created one common model template for all of the data access committees to use for every dataset that comes through the NIH, which was something we didn't have at the start so that is an improvement and, hopefully, it will make things easier for institutions and investigators to understand what they are agreeing to.

(Slide.)

The terms and conditions—some of them are fairly obvious in terms of being responsible for compliancy with federal and state law to only use the data for those things that they said they will use the data for. There was a promise not to attempt to identify the study participants either based on the information that they receive from the NIH or by combining that data with any other dataset

that they might have access to, public or otherwise.

(Slide.)

And, importantly, too, as a measure of transparency, everyone that requests access to the data also agrees to be identified on the dbGAP homepage so that when you look at the dbGAP homepage for any given study you can see every approved user, their institution and what their approved research use is for that data so that the public can also see what's being done with the data and how it's being used.

(Slide.)

The final two elements of the policy speak to issues of scientific publication and intellectual property. They were much more straightforward to write. They are not necessarily any less controversial.

For scientific publication, again the concept of this pre-publication broad access to data was something new for GWAS in terms of moving beyond the genomics community. And in order to respect the time and energy and intellectual contributions that these PIs will spend many times over decades to develop cohorts that they were now wanting to do GWAS on, there was a publication embargo period that

was put on to the data so data was expected to be submitted as soon as quality control was complete, and be made available for investigators to begin analyzing but there was an agreement that only the PI and their direct collaborators would be able to submit publications or any other form of public dissemination about their work for the first 12 months that the data was available.

(Slide.)

And this was implemented trying to highlight this embargo policy and the dates attached to different versions of datasets, again on the homepage for dbGAP.

(Slide.)

During those 12 months, however, anything else was appropriate to be done. So you could investigate it thoroughly, you could write your paper, you just could not submit your paper until after the 12 months had expired.

(Slide.)

In terms of intellectual property, we were a bit limited in terms of what we could do and wanted to stay within the bounds of existing NIH policies and respect the Bayh-Dole principles for this but there was a broad consensus, both

internally as well as through some consultations that we did with external experts in the area, that the basic GWAS findings that were going to come out of first round genome wide association studies really were pre-competitive and should remain in the public domain so that everyone would have freedom to develop around and innovate would have freedom to operate around and develop and innovate around those basic findings.

To try to substantiate that policy, there are automated calculations around those statistical values of the genotype analysis that are made available in the database so that again everyone can have them and they're out in the public domain to try to substantiate the fact that patents shouldn't be filed on those first round findings.

(Slide.)

This is then further emphasized within the policy statements as well as within the data use certification where investigators acknowledged this intent for the NIH and this principle that the data remain in the public domain as well as their institutions going forward.

(Slide.)

Something else that was important and I

think has proved to be vital to GWAS management, and even within discussions in the community over how to go forward with genomic data sharing and biorepositories at this point, is a governance model.

(Slide.)

This model is both simple and complicated, depending on the level that you are working at, and I think that was part of the design and has been helpful. So at its core there's a senior oversight committee which reports directly to the NIH Director, and they make all of the policy decisions in terms of changes that might need to be made, as well as managing at the highest level how the policy is implemented across the NIH.

The committee is chaired by Dr. Green at NHGRI and includes other IC directors as well as senior staff from the NIH director’s office.

But for day-to-day issues, and to help make this a manageable task for the senior oversight committee, there are two steering committees which sit under the SOC and they are made up of senior staff and focus on two specific realms of issues. The technical standards steering committee focuses on scientific and programmatic issues, as well as

technical issues around dbGAP and security standards that would be important for that, and the participant protection and data management steering committee as constituted from the various data access committee chairs, as well as other experts at NIH in human subjects' research protection and bioethics. And that is where really I think the core of the policy development and practices have developed as the DAC chairs try to learn how to do their jobs together and develop again more of the framework for how NIH is going to do this across the board.

And they definitely inform and interact with the senior oversight committee as issues arise so that we have both leadership at the highest level making decisions, as well as those staff who are on the ground trying to implement the policy on a day-to-day basis informing what the decisions are.

I will stop there and just point to our GWAS website that is under review but, hopefully, will be a place where we can have some of this information and again increase transparency on what we are doing and what the practices are going forward for everyone that needs to interact with the policy from the investigators to just members of the

general public who hear that we have this database full of genomic data o thousands of individuals.

And I will stop.

DR. ROYAL: Thank you, Dr. Rodriguez.

Any questions? Marc?

DR. WILLIAMS: I may have just missed this but based on what you were talking about in terms of the oversight and that, it sounds like that if you are an investigate that wants to use existing GWAS data and you go through the data request and approval, and all that sort of stuff, then you're able—it sounds like—to download the data on to whatever your local resource is and use it under the terms of the agreement as opposed to the data residing within dbGAP or that database then being manipulated there by investigators as opposed to—where it really wouldn't move to a local type of server.

Clearly the advantage of having it centralized is that you can develop audits and can automatically make sure that people are staying where they are supposed to be staying. But presumably there was a decision made as to why this model versus another model was used.

Could you comment a bit on that?

DR. RODRIGUEZ: There was a great deal of debate as to what model to use going forward and the final decision was made because the statistical geneticist and many of the people that would want to analyze the data would be writing their own programs, and so it was not something that could be done effectively within NCBI space.

And so instead the decision was made to create something that could be securely transmitted to the local site and to put agreements in place in terms of what security standards should be in place at that site for the data.

And actually the IT officials for the institution are now required—one of the required signatures, though it doesn't actually get implemented that way, but then they are supposed to be aware of every request for access as well so that they're signing off again that they have the capacity to protect the data in the way that the investigator is agreeing to protect the data.

DR. WILLIAMS: So just to follow up on that. Are there—obviously, you're requiring a report to come from the institution to say, yes, we have been behaving well, we're using the data the way we're supposed to, and here is the results of

that. Is there any opportunity to—for NIH to audit or if people suspect that something has not been used the way it's supposed to, that you would have the ability to go in and say, "Could you show us exactly what you're doing?" You know, if—I guess it's sort of an IRS model, which was, yes, this is what you told me on your taxes but is that, in fact, really what your income was for this period.

DR.RODRIGUEZ: So we also talked a good deal about setting up some type of audit program and the issue at that point—we looked at several different models and the cost was quite significant and questions of who would absorb that cost and what the return—the benefit of that return would be on instituting such a policy was such that it was determined that we would not go with an audit model to start with unless, you know, we saw that we had problems and, in fact, so much of what NIH does operates on this assurance model with the organization and that we will trust that you will do what you had agreed to do and, if you don't, then there will be consequences.

DR. ROYAL: David?

DR. DALE: Yes. I'm interested in the clinical phenotyping of the subjects. Are there

standards for that? You know, one of the problems we have are diseases that predominately affect one organ system but also affects something else and where the clinical phenotyping may be partial the cause of the observer who originally created the dataset. How are you addressing that issue?

DR. RODRIGUEZ: So dbGAP set itself up so that they could accept any measure and however it was reported to be open because there was such a variability across the measures.

DR. DALE: Right.

DR. RODRIGUEZ: What we have done is, again, by putting the protocols on line for every study, you can see exactly how the blood pressure, for instance, was measured in one study and know whether that's going to be comparable to a blood measurement and another study.

And, in terms of going beyond that for standards development, NHGRI has a program, the Phoenix Program, which is looking at building some standards for phenotypic measures across the board but there are no requirements for that at this point within dbGAP for GWAS data.

DR. ROYAL: Jim?

DR. EVANS: I was just wondering how your

deliberations, your model and all was affected by the Jacobs' *Nature Genetics* paper about inferring genotype and phenotype, and inclusion, and GWAS. Is that—

DR. RODRIGUEZ: So—

DR. EVANS: The fact that it's possible to analyze the aggregate data and infer phenotype.

DR. RODRIGUEZ: Right, the Nils Homer and David Craig paper from 2008 or Kevin Jacobs' had a paper recently.

DR. EVANS: Right, the subsequent one. Yes.

DR. RODRIGUEZ: So our policy hasn't been changed at all relative to Kevin's paper from this fall. We are having ongoing internal discussions about at what point do we re-address the situation and is there any level of data that might be possible to be made public that we haven't yet come back to have the formal discussion with Kevin or his group that we've—you know, we've definitely looked at the papers and the groups.

DR. ROYAL: All right.

I have a question, Laura.

So you guys are in the process of changing or modifying the GWAS policies for sequencing data,

right? You're still in the process or you've done it?

DR. RODRIGUEZ: We are just starting to actually do that. We did some internal data collection to go out to our extramural program staff and get information on what policies already existed for sequence data, how they would describe a sequencing project that would or would not be subject to such a policy. The sequence projects are a lot more complex with GWAS but it's pretty straightforward what it is when you have it. And so we have that information now and we are beginning to look at the different policy scenarios that we might put together around that, as well as some of the technical issues because it's a lot harder to transmit all of that sequence data and decide when is an appropriate point to release that because the sequence data again comes in, in a very different format and different timeline than the GWAS data does.

DR. ROYAL: Do you have an idea in terms of when you might roll that out?

DR. RODRIGUEZ: Not officially. So we're working on it right now and we hope to have a draft ready for leadership to consider by the spring but I

would never predict what the leadership will say about the draft.

DR. DALE: Can I ask another question, and that is use of genetics and genomics for prediction necessitates having information over time. Have you planned for that in this database, that is, observational data that shows what happens?

DR. RODRIGUEZ: That was again another reason why having coded data was thought to be so useful, because there can and there have been updates to different datasets. Framingham, for instance, has had several updates and there are different versions of the data that are available for the Framingham so that when there's a large cohort that has another round of visits, and another round of data collection, you can go back in, and associate that with the data that you already had so it can be a dynamic resource.

DR. ROYAL: No more questions?

Thank you, Dr. Rodriguez.

Now we'll hear from Dr. Hoffman from Cerner, who is going to talk about a commercial model.

Dr. Hoffman?

COMMERCIAL MODEL

DR. MARK HOFFMAN: Just as there's no single academic or government model, there is no single commercial model for data sharing.

(Slide.)

My intent today is to provide a few examples of things that we are doing in the commercial electronic health record environment to set the scene for the more effective exchange of genomic data and then some examples from other domains outside of genetics that I think will serve as relevant examples of future trends for how to facilitate data sharing.

(Slide.)

We will begin with a comment that might seem out of center field at first and then, hopefully, when I come back to it you will see why I am saying it. There are more virtual farmers in Facebook Farmville than there are real farmers in the United States. So I'm just going to leave that out there and then come back to it. It is a little bit provocative though.

(Slide.)

The topics that I want to really hit on in my conversation today is that, first of all, how can you generate high quality data during patient care

to facilitate both data sharing and decision support?

Then, secondly, we will talk about a few examples of what I call the data sharing ecosystem. There is no single model for how you go implement data sharing and there's actually strengths and weaknesses to a couple of the models that are out there. So I'm going to share a couple of efforts in each of those.

(Slide.)

Within Cerner we are working on both sides of this puzzle. We're working on the patient care provider side in terms of how can we enable genetic testing laboratories to capture data discreetly but then we're also working to facilitate research using our deep knowledge and understanding of clinical processes and of clinical data architecture.

(Slide.)

So to summarize at a very high level some of the key attributes of the electronic health record, and I should also point out there is no single electronic health record. There are multiple implementations. You can go to some of the organizations that are very prominently represented that have homegrown EMRs, then there are the

multiple commercial electronic health records, each of which were designed around different principles but, I think, most would agree that capturing information during clinical processes is fundamental. Simplifying data retrieval, queries and analysis is a key goal of moving to electronic health records. Automating processes so you reduce the opportunities for error, providing decision support capabilities, create efficiencies, and generating a body of data that can then be analyzed, whether for administrative, operational, clinical or scientific insights.

(Slide.)

There's often some blurring between the electronic health record or electronic medical record, and the personal health record, which to me, the medical record is a legally binding system. So if a physician is part of a malpractice suit, the assumption is that there will be high-quality data in the system that can be extracted and then utilized in the discovery process. Whereas, the personal health record, there's probably quite a bit more blurriness around the obligation there. There's often the expectation that the two should be one. I think, likewise, the expectation that you

can have one system that's an EMR or PHR and a research system is something that needs to be scrutinized much more carefully. It's not a perspective that we try to promote. We do think there should believe there should be fire-walling between the systems.

(Slide.)

In informatics, I think, sometimes we want people to think that you couldn't do research in this model where information is stored on paper but, the fact of the matter is, that there is still a large amount of research that's done through manual chart abstraction, and the privacy issues there are very similar to those in the electronic world where you have--in many ways they are even more challenging because you have human beings pulling the paper charts out, they see the names, and then re-enter that information into other systems.

What we are trying to move towards is to a fully automated digital system where clinical information and eventually genetic information is stored discreetly in a mineable fashion.

(Slide.)

A couple of the other presentations have referred to standardized vocabularies and

ontologies. We have been very active in developing and deploying what we call the clinical bioinformatics ontology. This is a vocabulary that’s available through an open content model and can be downloaded, and creates standardized concepts that can be used to codify findings whether for molecular diagnostics or cytogenetics or other testing methodologies.

(Slide.)

Just to give one example of probably the orphan topic in genetics discussions, and that’s cytogenetics. If there's anything that would put fear into the heart of an informaticist I think it would be a karyotype. And we have actually put quite a bit of effort into making the karyotype a mineable resource because let's say that you are interested in a condition that’s tied to band 21.2 in this example. If you were to do a purely text-based mining of that karyotype you would never find this patient's result. We drop out discreet concepts into the database from that, one of which is a concept related to 21.2 because the beginning and the end positions of the abnormality documented here, and that creates a mineable resource, whether for research or decision support.

(Slide.)

So these are just some very high-level examples to show that within diagnostic labs we are working towards systems that create that granular body of information so that as you get into data sharing your data is ready from the point of capture and you don't have to re-enter into another system.

(Slide.)

The second theme that I want to cover is some representative data sharing models. One model that’s very familiar is what I would call the centralized data warehouse model. Increasingly, things are moving towards distributed models. From the electronic health record supplier perspective, we have a common architecture that’s in use at thousands of healthcare delivery facilities and believe that architecture alone positions things to be used creatively for collaborative work and so I will share an example of a project based data warehouse.

(Slide.)

We also have brought in technology to provide a consent-based—a web-based consent-driven system, and I will show that briefly, and then I will return to my social media comment.

(Slide.)

So the data architecture that--there's a couple of options embedded within this picture. Within an organization, the clinical care data is embedded into a database or the EMR, and that information can then be used by the physician or the CIO or CFO to make observations about how they are running the organization and so forth.

It's also very feasible to migrate that information into a larger meta-data warehouse, and usually that process involves scrubbing the data of all HIPAA regulated identifiers.

It's also normalized, so a key part of any data merging activity, especially among non-affiliated organizations, is mapping to a common vocabulary. And so that is a key part of what many aggregate data warehouses offer.

(Slide.)

Moving to distributed models. The—so if I—if I just summarized the data warehouse model, the distributed model is that instead of pulling data in, you push queries out to the user—to the sites. So in IT systems we think of operations jobs that run at midnight. So the impact is minimized. And those will be routine processing but there can also

be queries that evaluate the data within that site. And then summaries of the findings of those queries, instead of the actual body of data, can be sent to the organization that's managing the distributed project.

(Slide.)

So we at Cerner are deploying what we are calling our research network where throughout our client base we can push packets of queries. So if you are interested in cystic fibrosis patients, we can—and you work with us to sponsor a project and push these queries, the data remains at the local site. We don't really want the data from these types of initiatives in our hands under this model.

And then the--I really don't like to make the comparison but helps it click. The analogy that resonates is Matchmaker.com where we see our role as matching a trial sponsor to sites that have a candidate group of patients and that that has value to the process so that if you are looking for trial candidates you are not mining in territory where you are never likely to actually find candidates.

(Slide.)

Then more recently in the public health domain we have taken that model a step further and

worked with the CDC, state and local health departments, on an influenza surveillance initiative where we reached out to the entire client base and said that we'd like to work with you. You will get a daily view that's updated every day showing how your organization compares to your state and national peers in terms of positive flu results, influenza-like indicators, and so forth.

We, in three months, rolled this out to 780 facilities throughout the U.S. so it's present in almost every state. We had, I think, 23 million records that have passed through the system for surveillance. The CDC gets updated information every day with state and local stakeholders. It provides GIS level mapping and trending. It's very feasible to use this push model in a very rapid approach and I think that a commercial company has the agility to do this type of thing very quickly.

(Slide.)

As an adjunct derived benefit, there's also a lot of healthcare information that comes out of this so one of the parameters that's tracked is emergency department utilization. So I don't know if there's—I think there are some people from Tennessee here but if we compare Tennessee to the

national norm of emergency department utilization, every day we can see that, even on week days, 50 percent of healthcare is delivered in the emergency department in Tennessee. So there's a lot of insights that can be gained from this.

(Slide.)

I'll also mention that we recognize that prospective research is an important model. I think you will be hearing about a consumer approach in the second talk but our stance is that we want to let scientists do the science and provide the enabling technology so that they can get to the science as quickly as possible. There is a company called First Genetic Trust, so we brought in source code or patents to the technology, and it enables patient controlled disclosure of genetic information through this model—through this web-based model.

(Slide.)

The second to the last slide just is an example that we participated in that pulls many of these topics together. Cerner does the data and project management for CDC for their HIV outpatient study, which is a prospective study. Patients are consented and enrolled and then tracked longitudinally. When the study was launched they

had the insight to capture the HIV genotype data, as well as the prescriptions and the lab data.

So one of our questions as we looked at personalized medicine, how--when armed with genetic data, how well are physicians utilizing that information?

(Slide.)

And so we did an analysis of the data and found using just one scenario that--using antiviral resistance that if you mine the data as an analogy of physician behavior, we found that for the patients who were found to have—the 441 patients with the resistant HIV genotype, 59 had contraindicated genotype therapy initiated six months after that result was determined. So I think that's evidence of the need for decision support.

(Slide.)

So I promised that I would come back to the Farmville comment. The data sharing in the social media world is really completely, maybe it doesn't--I haven't heard it on the Table yet but if any of you are in Facebook and have used a single Facebook application, I actually found one from the NIH, when you sign up for a Facebook application, you are giving data from your profile and your

friend's profile to anybody, to the organization launching that application.

So if you are signing up for Farmville and your friends are in the retinoblastoma perineal support group, you are sharing their status, their status with that organizer.

So I think that often technology quickly gets ahead of policy. I think one of the things GINA has going for it is instead of defining the technology, it defines how we protect the patients from harm. And so I think that should be some consideration as we think through how rapidly evolving these various models are.

(Slide.)

So I think that the aggregate data warehouse has both strengths and challenges in terms of there are some highlights—you can't—if you haven't pulled the data, you can't go back and add it later so you have to either pull a lot of data or sacrifice on data quality.

Distributed models are much more agile but they involve a much more limited amount of data.

Social media, I think, as yet untouched, but again it's getting way ahead of things but things are moving faster there than anywhere else.

And in my opinion the role of healthcare information technology is to serve as enabler and to help any of the stakeholders in the process.

So, with that, I will stop and address any questions.

DR. ROYAL: Thank you.

Any questions from anyone? No one?

Okay. Thank you, Dr. Hoffman.

Now we will have our last speaker, who is Mr. Shelton, Robert Shelton, from Private Access, talking about the consumer-controlled--a consumer-controlled model.

CONSUMER-CONTROLLED MODEL

MR. ROBERT SHELTON: First I want to thank the committee for inviting me to make this presentation and Symma and the staff for making it possible to be here.

(Slide.)

So when I received the topic I thought maybe the best thing to do was to modify the first slide so I would like to submit that instead of thinking what I'm going to talk about as consumer-controlled, I'd like to talk about it as being consumer-empowered. And in the context of this committee, I would like to think about consumer-

empowerment not as just empowering the consumer but, also, the consumer empowering the researcher. And so a lot of what you're going to see in this presentation is about ways that the consumer properly empowered can, in fact, empower the researcher to go a lot further than the researcher is otherwise able to do.

(Slide.)

So I think I decided, as I was sitting in the audience, that I am perhaps the only person who doesn't have an M.D. or Ph.D. behind their name so I thought I'd start with talking about why I'm here, what's Private Access.

And, number one, I start as the parent of a prenatally diagnosed child with a rare genetic condition.

(Slide.)

This is a picture of him when he was about four-and-a-half years old. I selected that for a specific reason which I'll get to in a second. He was diagnosed with 47 XXY, which is a proclivity towards Klinefelter's Syndrome. It's a one in 600 incidence in live birth and roughly 75 percent of the people who have this diagnosis are never diagnosed from birth to death. And so one would

assume, as in his case that it's a pretty mild condition. According to the most recent statistics, a 2007 study done in California, roughly 70 percent of the parents who receive a prenatal diagnosis of Klinefelter's Syndrome will terminate that pregnancy in utero.

So when this committee thinks--I added this slide set as I was sitting in the audience because I would really like to bring the individual perception and the perspective of individual patients to this committee, and say that the kinds of subjects that we are talking about in macro in millions, and tens of millions of people, really boil down to individuals and parents make bad decisions based on limited data sets and fear and lots of things that you all know very well.

(Slide.)

So that led me to basically taking off from work for—my day job—for about three years to become first the director and then chairman of the board of a national disease organization that supports Klinefelter's Syndrome and also Trisomy X and XYY.

And the reason I selected this particular image is because the organization had been in

existence for 15 years. In 15 years we had never had a picture of a person with Kleinfelter's Syndrome on the website because a lot of the people with the condition are afraid of being recognized as having the condition, and so there's a tremendous privacy concern among that population. It's not one of the protected populations in many state laws but it has very high privacy concern, in part, because it's so mild and, in part, because there's significant stigmas.

(Slide.)

So this picture actually now appears on our website because someone called up our organization and said, you know, "I have decided I am going to terminate the pregnancy because I assume since you go to the Down syndrome site you see pictures of Down Syndrome children, you go to the Klinefelter's Syndrome site and you don't see any pictures of people with the condition." So I decided to go ahead and make this picture available so that people would actually connect with a person who has this condition. So information is power.

(Slide.)

The other thing that has happened is you will see that I am also an entrepreneur and have

founded a privacy technology company called Private Access. When we got started we focused the technology in Private Access on serving some of the needs that we recognized through the disease advocacy area. Today, with roughly $5 million invested, a few hundred--almost 500,000 lines of code, to make possible what I'm going to show you.

So we also think of the world through partnerships. No one would recognize our company unless they have heard us at a conference or met us person to person but we partner with organizations that are already trusted organizations. So we think of trust as being an extension from human being to human being; not based on technology but based on human relationships. So partnerships are really vital to us.

(Slide.)

Our mission is that we focus on creating an environment of trust. And we talked about how we do that. So if I started this slide over in the upper right hand corner, I remember going to a conference at the Health 2.0 conference three years ago, Esther Dyson was speaking and she referred to privacy as the giant hairball that was clogging the drain for data liquidity, and that we need to blow

that hairball apart.

So, privacy can be viewed as a speed bump that is keeping data apart and hurting liquidity. It can also be viewed as something that through technology is an achievable goal that actually will help enable health information sharing. And so I think that what we are really talking about is how to create an environment of trust because inside of an environment of trust you get speed and there's books that are written on this topic and borrowing the fast company quote, the new economy begins with technology, it ends with trust. So we have to build trust in the system.

(Slide.)

So our particular way that we focus on this is we're looking at creating what we call the perfect balance between privacy and access or accessibility to information. So you see one patient on the side that has got the ability to leverage their words to a consortium of people that are really out to help them to achieve their health goals.

(Slide.)

And the need for speed is something that, as a disease advocate and coming from that

perspective, is something that is just, you know, really critical. When you look at the internet, and I presented at the Electronic Patient Record Conference, TPR, earlier this year or mid-last year actually, and I used an example, and actually did it live of searching for a person based upon attributes. It was a public person through Google and in a minute and 27 seconds, without knowing the person's name, just knowing some things about them, we found the person. We located how to get in contact with them and we actually booked them for a speaking engagement. So in a minute and a half in Google we can locate people.

In Match.com, which the previous speaker mentioned, or Monster.com we can do the same thing and so I went through an example, and in under three minutes I was able to locate a person that matched the demographics, the location, the characteristics that I was interested in finding for either a date or for a job.

(Slide.)

So, in healthcare, however, we have got challenges. We take six months to a year to recruit people for clinical trials. We have terrible accrual rates in trials. We also take an average of

15 years to develop drugs for diseases. Time is actually more critical in the healthcare area than it is in those other two domains, and yet we have the worst ability to move things quickly in healthcare. And I would like to submit that part of the reason is because of the trust factor we need to replace.

(Slide.)

So there was a study done by Case Western Reserve focusing on dried blood spots from newborn screening. The question that was posed was how willing are you to have your child's blood spot sample used for newborn screening for future research studies; and it was done with permission and without permission. And the choices were simple. It was very willing, somewhat wiling, somewhat unwilling and very unwilling.

Over 75 percent of the people that were asked would they give permission for this granted permission to their information being used for research. But when you change the equation to denying them permission, what happens is all of those positives around granting permission changed dramatically and the opposition to using the information for research increases dramatically. So

to me that's what happens if consumers are not asked about sharing their data. And so a lot of the technology we have proposed is set up to focus on that.

(Slide.)

That study is not discrepant with the secondary literature. In fact, it is very consistent with the secondary literature and I am just going to slide through these because you all probably know this data but the one that is the most compelling to me is from the Institute of Medicine study at the end that 57 percent of people would permit their personal health information to be used for research only if various privacy conditions are met and 38 percent of the total, which is the largest share of the 57, want to get information and notice on a case-by-case consent basis.

(Slide.)

So how does that happen? So if we think of the world as data seekers and data holders, a data seeker can get in contact with a data holder, a data seeker can also put out a query for data around who has got my data, who has got data that I would be interested in, and a data holder could raise their hand and say, “Hey, I’ve got some information

you're interested in." And if the conditions are right—if the terms are right, I'm willing to share it with you.

The challenge is that for that data holder to act quickly that data holder needs to know do I have the right to share this data with that seeker, that particular seeker? And that entails a determination of what's permissible under federal law, what's permissible under state laws, what's permissible under the institution's policies that the data holder is encumbered by? Are there any special considerations that are entailed for this particular record? What would my patient think? So there are legal and reputational risks that are entailed in that and those answers—particularly where they answer a search query like a Google or a Match.com, particularly for that level and speed, those answers have to be answered fast. They have to be answered reliably and they have to be answered containing the information about what that record-holder will be compensated for the information, and so even if the compensation is in millicents or pursuant to some sort of a contractual relationship between them.

(Slide.)

And so what are doing in Private Access is replacing those questions with an automated transaction-based system that is programmed with an ontology of privacy that looks at each of those issues, the institutional law, the federal law, the state laws, and the personal privacy preferences expressed by the individuals to give that record holder, that data holder, back that information in under a second or two. So that would allow them to know red light, green light, yellow light, do I have the right to move that data to that particular seeker who is looking for it.

(Slide.)

And then in order to power that--remember the title, consumer empowered--we look at tying the patient in through the ability to dynamically consent or decline access to the sharing, the proposed sharing, if their voice is permitted under the prevailing law of their state or federal law.

(Slide.)

We also allow them at any time to view the audit trail associated with the data sharing activity. So the data then can be pushed. It doesn’t have to be electronically. It could be pushed in the form of a Fed Ex pouch. It could be

pushed by U.S. mail. It doesn't have to be electronic but what is conveyed back to the system is an audit trail of the actions taken and any dollars, any amounts of money that are charged between the data holder and the data seeker.

(Slide.)

So that little fundamental architecture is what we have spent all the money building and time developing over the last three years. So to date we focused our solutions directed to registries and biobanks, and to allow all or selected parts of the confidential personal information to be moved based upon the particular needs or interest of the patient.

So our first focus is to set up a consumer-centric site, which in most cases we have co-branded with the trusted intermediary, so with the disease organization as being a co-branded indication. So in each case thus far we're working with a trusted intermediary.

The second thing is we use a system of trusted guides to help the individuals set their privacy preferences. If we get down in to the level of granularity that really creates this ability for speed and accessibility, it's incredibly granular.

That means someone has got to do a lot of reading and clicking of on and off buttons.

The patients that I am familiar with do not have either the patience and in many cases the proclivity to actually spend that time. And so the way that we focused on it is to set up a spectrum of people's perspectives. We call them Trusted Guides and we select three at least in each case. Those guides reflect a perspective of the spectrum from I am in favor of a lot of sharing of data to I am in favor of very little sharing of data. I am very privacy concerned. I'm very accessibility oriented.

And then we ask each of those guides to pretend that they are talking to a person across the table from them who says, "You know, I've got high privacy concerns. What would you tell me about what I should consider doing?"

Or "I have low privacy concerns. What would you tell me?"

So from that we get a broad spectrum of perspectives on the issues of what should the data—what should the subtitles be and we boil those down to—in effect, permitting access, permitting access on a de-identified basis, permitting access on a pseudo-anonymized basis, permitting access with a

prior consent, permitting access with a dynamic consent, and so we set a series of stops along the way for each of those perspectives on each of the factors involved.

And then we, as I said before, have a comprehensive audit log for each access to the data and when the IHE standards are adopted in HTSB and included the minimally—in the standards required for C-chip certification, hopefully, those will permit the audit trail to touch any EHR, any PHR that is standards compliant so that the patient can go to one place and see the accessibility to their data.

And then the last piece here on this particular element is we--identity verification is vital. We have identity verification up front in the system. We have written this privacy directed language, which is a robust ontology. We have the dynamic consent management, the audit tracking, and then we've integrated the commerce features.

(Slide.)

The initial applications that we have built are focused on clinical research. So we are using these to help people locate--help researchers locate patients for clinical trials who wish to be found. So we call this application that we have

built a recruit source and it's based upon a researcher-centric site where a researcher can go in and enter a natural language inquiry that is searched based upon either text match or based upon UMLS language for their particular query. So if they're looking for Tylenol they would find acetaminophen hit in the database.

That then results in either—depending upon the privacy preferences, a fully anonymized or a fully personal identified record for them to see and they can search based upon the demographics or the locations of the patient. They can say I went 10-miles within a radius of a specific spot where I've got a research cohort that I'm trying to put together. And if the patient has said I want to be in a de-identified forum, if the HIPAA de-identification rule says there needs to be less than 50,000 people within that radius and we have less than 50,000, according to SMSA data, we can't show them that data. So we use that switch to turn that off in accordance with the federal laws.

(Slide.)

Finally, we have the dynamic consent tools that are built in from privacy layer so that if a researcher says, you know, "I saw you in a de-

identified forum. I saw you in an anonymous form. I'm interested in you and you've indicated that you don't want me to know who you are, you don't want me to know your address until you—until I tell you dress, until I tell you about my research project." Then the researcher can push that information through the switch back to the consumer who can, in turn, decide to push the green button to permit the data for their contact information to be sent back to the researcher; push the red button to say, "No, I read about it. It's not something I want to do and I talked to my doctor, and we've decided this is not something I want to do"; or push the yellow button in order to snooze and say, "I'm going to wait for this answer for a while."

(Slide.)

The first project replied to was on the organization that I chair, Klinefelter Syndrome and Associates, which is renamed now Support in Action because people didn't want Klinefelter's Syndrome on their return envelopes. And so we have looked at 1,200 patients with five researchers. The persons who have actually completed a survey, 90 percent have indicated that the system is easy to use and they like the experience; 75 percent have indicated

they would recommend it to family and friends, and our experience would be that partnering with that trusted source was overwhelmingly what drove the patients to have an interest.

(Slide.)

And so we have a number of research projects under way. One of them that is in the packet of materials that I believe you have been given is a project that we're doing with the University of Michigan focused on the newborn screening blood spots. It was a challenge grant award for 200 or so of the challenge grants that were awarded. It is presently ongoing and is looking at facilitating a state sponsored population birth cohort to use the information for genetics testing, and looking at the use of consent for that purpose.

(Slide.)

This is the steps of the process. We are presently at the stage of creating systems and environments. And early in the summer we will begin with the pilots and recruitment for that study. So we are very early in the study but excited about it because all of our prior work has come through working with disease organizations, and this is

actually a general population as opposed to a specific disease organization.

(Slide.)

We are pleased that we have strong support from some industry stakeholders. At the end of last year we announced a collaboration with Pfizer and Greg Simon, the senior vice-president of Worldwide Policy was quoted in the release announcing it and saying that patients are the most important stakeholders in medical research. By merging respect for their privacy and access to relevant actionable medical information, we are giving patients more control over their destinies. And this collaboration has the potential to accelerate medical progress by putting patients' needs front and center.

(Slide.)

This was echoed in December by the CEO of Pfizer who in front of 650 people at the Partnering for Cures Conference said when he was answering Mike Milliken about what he was excited about in terms of accelerating treatments for patients to come through their organization, he said, "Focusing on patient privacy and a technology that would accelerate the ability for us to get in touch with patients who

want us to get in touch with them." So I think that we're finding support for this.

(Slide.)

And, as I said earlier, we focused on collaborations. Our first round, the one that we're perhaps most proud of is with Genetic Alliance, who is—we're in a public-private partnership with and advisory to University of Michigan. We have a number of other projects that have not yet been announced yet with some significant disease organizations working with a couple of government agencies on using this for their informatics grid type computing. And so--and several HIE, Health Information Exchange, Regional Health Information Organizations for their applications, and then we were pleased to be on two sharp proposals for the recently announced IT initiative from the Office of National Coordinator where we—one is with Harvard-MIT for—in talking about de-identification of data earlier. It's the Tanya Sweeney's proposal. And the other is with C-DISC, which is the clinical Data Interchange Standards Coalition, where we're on their proposal as well.

So, hopefully, we can maybe in a year from now come back and give you a lot more data on how

this work.

DR. ROYAL: Thank you very much, Robert.

MR. SHELTON: Thank you.

DR. ROYAL: And thanks for sharing your personal story. It helps remind us why we are here.

Any questions?

Paul?

COMMITTEE DISCUSSION

DR. BILLINGS: So I understand your kind of roll out is limited and maybe you don't have any data on this yet but do you have a sense of when you put your processes in place--do you have more uptake? I mean there's—I know how you do the comparison but do you have a sense you are going to foster more research participation?

MR. SHELTON: Absolutely. There's no question. There's a lot of secondary literature on this. The Harris Western Poll has been done for a decade. The most recent was done for the Institute of Medicine in 2009. Alan Weston happens to be an advisory board member of our organization so we've seen his polling results and the raw data. And his polling results mirror pretty closely what we are finding in the disease advocacy world.

DR. BILLINGS: He's a character in

privacy, I believe.

MR. SHELTON: He's certainly the dean of it. So I think he wrote the definitive textbook in 1967 on the subject, privacy in a free society.

Thanks, you all.

COMMITTEE DISCUSSION OF NEXT STEPS

DR. ROYAL: Thank you.

We are going to open up for discussion now, general discussion about all the topics.

I am just going to put up a couple of slides.

(Slide.)

Yes, let's go to the next one.

(Slide.)

So we heard a lot of information today, a lot of interesting information, and just to really move our discussion along I just wanted us to go back to these two questions.

The first one—I think I'd change that to what have we learned, what are the lessons learned?

And then the second question is, are there issues that warrant further policy considerations, and issues that SACGHS might consider?

So we may want to talk a bit about what we've learned, what we heard, what stood out for us

in terms of all those presentations, those different models that we heard.

CHAIRMAN TEUTSCH: So, Charmaine, let's see if we can flesh this out. So we've heard a lot of presentations. We know that we're trying to aim towards best practices. Have we heard some best practices? Things that we can say, gee, they are already underway, we really don't have a further role. Or are there some gaps here, some issues that could really benefit from what we're—from this committee actually weighing in. So we've heard several models, right?

DR. ROYAL: Right.

CHAIRMAN TEUTSCH: And I think we saw them—you know, none of them are very old but some of them are—you know, were very—have been thought out but they're in place. So where are we on this trajectory and where are the gaps where we might weigh in? Or do we say these groups are doing a great job, we should move on?

So I think if we can talk about what we heard and, as Charmaine said, what is already there and working well, and what are those needs going forward and, if there are those needs, is there a role for us to weigh in?

Yes, you can. Yes, go ahead.

DR. ROYAL: No, go ahead.

CHAIRMAN TEUTSCH: She was asking—

UNKNOWN: No, she didn't—

DR. ROYAL: No, you can go ahead. But you need a mike.

CHAIRMAN TEUTSCH: You need mike. I'm not sure if it's on.

DR. SCHAEFER: Thanks.

DR. ROYAL: So can we have all the speakers come up front? Sorry about that.

DR. SCHAEFER: I will just finish my question. So I am sort of struck by the fact that people like me, who are trying to develop these large resources, are also very focused--part of what makes them valuable is that they are epidemiologically sophisticated, or epidemiologically known sort of populations. So there are a lot of issues about, possibly, even though obviously everybody involved is a volunteer in one sense, nevertheless, there are issues about being able to conduct research just with people who happen to see the information and volunteer and so forth. And yet—which is sort of the—in some ways the private access—more the private access model and

yet the situation that I confront is one where I— it's very expensive for me to update information about what people in my cohort think about different research projects that we might do or about different new emerging issues regarding privacy and confidentiality that come up.

So I guess what I am trying to get to here is it would be very helpful if within the context of these sort of epidemiologically defined populations we had technology that allowed us to have the kind of communication that in some ways your system envisions would be possible between researchers and participants.

Right now that's prohibitive for us.

DR. HOFFMAN: So when I mentioned a couple of government agencies that we're working with, it's based upon exactly that concern. When you were speaking earlier you talked about your definition of de-identification that you used to establish the policy. Well, one thing I know about politics is politics is 50 percent plus one vote equals a change of policy.

What happens if the change of policy on de-identification is different than you set up the database? Is the database dead? Does the database

have to be reconsented? So there's tremendous challenges that I think cause the need for de-aggregating the switch from the store of data.

I think that the metaphor I would use is in a baseball game you have an umpire. The umpire does not care about the score of the game. The umpire does not care about what the batting average of the batter is, does not care about the pitcher or no-hitters. The umpire is calling the balls and strikes, and that's all their job is.

There's a role for that in this system, I believe, and I don't think it ends up being one company. I think it ends up—we're in a capital society. I think it ends up being multiple entities that play that role, and the ones that play it best will end up prevailing.

Our ambition is to be one of those parties playing that role. And the reason we focused on this around the federal, state and institutional policies in addition to patient-privacy preference, is there's a tremendous thicket that exists by virtue of these policies that is mind-numbingly complex. And so in order to address that, we—there's two things that are necessary. One is somehow or another to develop an ontology for

processing it. I think we've got a long way towards that but most of the processing—I had—in discussion last night with a top privacy advocacy. I said, Most of the private—most of the resolution, adjudication would yield amber lights, not green, not red, somewhere in between and then you'd say, you know, it's just ambiguous. The law is ambiguous here.

So the architecture we are putting in place actually pushes the issue of ambiguity back to the policy makers, back to the legislature if that's where the issue exists,; back to the institution if that's where the instrument exists, with the question. We're the umpire. We're not trying to set the policy. What we are trying to do is to say there's a challenge and process in these policies that presently address from a robust ontology.

You as the policy maker need to decide do you believe that the law should be permissive? Do you believe the law should be preclusive? Are there rules associated with that based upon various conditions? We can model all of those but once you make that decision then adopt it, and if it changes next legislature, fine, then the rules will change the next legislation, and how the system processes.

So I think that there is a way to play, whether it's private access or it's Cerner that does it, I think there's a role to play for that type of technology inside the architecture that reflects not just patients but also each of the persons that are stakeholders in this in the moving of data.

DR. WILLIAMS: So one of the things I heard from many speakers were a number of very elegant solutions to some of these vexing problems.

And the other thing that I was struck by was how under some of these efforts things are going to be put out into the public domain where things could be used for others. I was particularly struck by the idea that you could quantify the level of de-identification in a robust and repeatable way.

I mean, I can think about those of us that deal with IRBs and this issue of the privacy and de-identification. If we could—you know, there's something about a repeatable quantitative way of assessing research projects that are coming over and over that I think would be highly attractive. I can't imagine that people wouldn't be interested in that.

So the point of that is that clearly there are innovative people that are coming up with

innovative solutions to these issues, and some of them are being put out into a public space.

Is there a role for DHHS, the Secretary, to aggregate some of these solutions in a space that people could access and use, and try them out, and contribute their data? I mean, in some ways it resembles what's being done on the GWAS side, which is we think the data is important data and we think that people can do interesting things with it, and we're going to recontribute it and we keep learning new things. That to me was the most important thing that I took out of the discussion.

DR. PAUL WISE: I have a question.

People aren't born 55 years old and I know you've thought a lot about the developmental precursors of many of the diseases you are concerned about. How are you going to integrate the developmental aspects of etiologic cascades into your analyses over time given that you are starting with older, consenting patients? How do you see the developmental processes entering into the database as it grows and matures? Like adding children, reproductive outcomes, maternal histories, things like that that could be attached to the progression or the emergence of disease as people grow and

develop.

DR. ROYAL: That's for Catherine, for Dr. Schaefer?

DR. SCHAEFER: Well, we are actually beginning to build a pregnancy cohort now. I have been very fortunate in working with an established cohort, the Child Health and Development Study Cohort of some close to 20,000 live births that occurred in 1959 to 1967, who were part of an NIH funded study then where they had the foresight to store maternal serum samples from each trimester of pregnancy that are still available for analysis now.

We have used those samples in follow-up studies of schizophrenia, for example, to investigate the role of maternal exposure to influenza and other viruses and show that maternal exposure to influenza, for example, in the first half of pregnancy is associated with a significantly increased risk of schizophrenia in the offspring.

So just sort of--I am definitely a believer in the importance of a better understanding of developmental contributions to adult diseases and have benefited directly--I have seen very directly the importance of this. The prenatal period may be

extremely important and unusual, unique in terms of the interaction of genes and environment and playing a role in adult health. And so if we neglect that, we really won't have a full picture of the origins of adult health.

So I don't know that I have a complete answer to your question. We would like to be able to add children. We didn’t originally. In part, there was a resource issue. We had actually a very limited amount of money to initially survey our population. And in part it was the complications of asking parents to consent for children about being part of a very long-term study but we are now initiating a pregnancy cohort where we will get samples during pregnancy and then intend to follow the children born of those pregnancies, and enroll them, and get samples from them as well.

Sorry, that's about as well as I can do right now.

DR. FERREIRA-GONZALEZ: Initially it caught my attention about the two speakers, the Kaiser Permanente and the Vanderbilt, is the different ways to do the informed consent to recruit patents in these. Your system mails an eight page document and I guess a spit cup for them to send

their DNA back. And the Vanderbilt system is an opt-out system.

I'm just wondering if at the NIH level or the federal government development or starting to develop best practices of what actually constitute informed consent for these type of studies and where there is all these de-identification and re-identification of data, do the individuals fully understand what they are actually consenting to?

DR. RODRIGUEZ: I think that was for me.

So we are not to the point, I don't think, in the evolution of the discussion around this point in terms of what is appropriate informed consent for anything, let alone for genomics where we're talking about de-identified to understand exactly what the right way is to do that because concepts are changing so much around sharing of our data and what we're doing.

So, I mean, we're certainly trying to think about it for genomics. We have a resource on our website which has some suggested language which actually—we have some example language. It's not even suggested language. Where people have IRB approved consent forms for different types of genomic studies and we are just trying to make them

available at this point for other people to see how it works. And we are hoping that will be a dynamic resource that we can get comments on and that we can build from to have ongoing conversations with the community but at this point I am not sure that we have a best practices, and I know it's something the community wants a lot because they would like to know what the right way is to do it but I don't know that there is one right way to do it because it will always vary for the patient and subject population that you are talking to.

It's hard to quantify the risks right now so it’s hard to know what to tell them.

DR. FERREIRA-GONZALEZ: But I think that's concerning because we are collecting or recruiting patients that we don’t really know.

CHAIRMAN TEUTSCH: I’d like to put Laura on the spot because you looked at it from a variety of federal agencies and in the beginning Charmaine put up sort of different things that we are concerned about. Informed consent, storage, access and secondary uses, privacy, confidentiality, re-identification, handling sensitive data, the whole ball of wax and then how it all fits into EHRs.

And I guess the question we have is to

what extent do you think we are already close to having, you know, good practices, if not best practices, and where do you see the real gaps and where do you think a committee like this could help shape the--what are the key issues that we could actually help in moving the field forward on or if there aren't any that would be fine, too.

DR. RODRIGUEZ: I mean that's not fair to do. So part of the first question is, you asked if we were close to good practices and my response is on which one of those many issues that you mentioned because I don't—

CHAIRMAN TEUTSCH: Why don't you--tell us which ones you think we are close on, which ones you think that are—where we still have a lot of work to do.

DR. RODRIGUEZ: I think that there's work to do on all of them because I think that the technology is still moving and we're still trying to understand what participants think about all of this. I mean there's private access and we don't have research data to know what is the risk tolerance for people or do they care if we are sharing their data this way. They may not think that it's a problem. If they're truly altruistic

about wanting to contribute data then we may be worrying a lot about how we are managing the data and how we are sharing it, and it's not a concern to them. So there are some studies going on right now to try to collect some of that information.

But I think that, you know, informed consent needs—it needs some work. It needs some hard data to understand what people understand in consent and what's the best way to communicate risk to them. But that's at a much more granular level than what this committee can do. So it's hard to say. I'm not--things are moving in such an amorphous direction at this point, I'm not sure if I could really come together and say this is the one thing that this committee should definitely do because I think, again, that there's value in having different approaches go forward and learning from them.

So I'm not sure I have an answer to your question.

CHAIRMAN TEUTSCH: Is there a role then to sort of look at the different approaches to, as Charmaine said earlier, identify what these different elements—what's sort of the different options and which ones look most promising?

DR. RODRIGUEZ: I think there's some of that. One thing that could be useful would be to try and articulate principles. That could be useful to the group, and trying any of the different solutions. If there is some common principles that should be present in any different—any model that went forward. That would be something that I think is at a high-enough level and that will be common and important in terms of providing leadership to the field as they continue to try and experiment and modulate what is going forward now.

MS. DARIEN: I think one of the issues, and Robert actually started to bring it up but you didn't bring up the entire context, is that sharing patient data is very different depending on what you have been diagnosed with. So, you know, I'm a long-term cancer survivor but I had non-Hodgkins lymphoma. That doesn't really have a stigma. Breast cancer had a stigma. All cancers had a stigma. Your son's disease still had a stigma attached to it. So you can't really say that this is the way patients feel about sharing their data.

I don't—I mean people know because I am a cancer advocate that I'm a cancer survivor, but it is—the disease is de-stigmatized. So I think that

it’s very difficult to make any kind of blanket statements about privacy and sharing of anything when you’re talking about a very large universe of diseases.

MR. SHELTON: I couldn't agree more and I would add another vector to that, which is the stage of the disease. It's not just the disease; it's also the disease state. And you are trying to say something so let you talk.

MS. DARIEN: Sorry, but I—yes, that’s absolutely true. I think that—I mean I work with more in the cancer field but that’s absolutely true. And I think the other issue is that people are often less concerned about themselves than they are about their family members and what the impact is of their family members because we already—I mean we assume if you’re a survivor of a serious disease that everybody knows you have it but you care about what happens to people that are close to you.

So, yes, it’s stage, its family member. I mean there are so—it’s very, very nuanced. It’s not something that you can just sort of make a blanket generalization about.

MR. SHELTON: I was going to go to the same place that you just went. So to build on it I

would say before I came here, I always talk about my son because I think of my first role as dad and he is now 11. So before I came out here I asked him whether he minded if I mentioned his having this condition because when he was five it was my decision. He is now 11 and he is still not at the age of consent legally but I'd like to know if he has a sensitivity about me even mentioning he has this condition because it's starting to become his decision, not mine.`

So there's a lot of nuances to all of this and the irony that I see, again from a patient advocate perspective, the irony in our organization is--I talked about this high termination rate. Well, there's not a single person who ever met our son who has terminated—that I know of—that has terminated the pregnancy that they were carrying.

So we have in our organization a hotline for patient or parents that want to meet other parents or children of other parents. One of these people that decided to go forward with their pregnancy were scheduled for a termination on Tuesday morning—

We met them on a Sunday and they changed their mind--has become a long-time friend, and they live close

to us, and we're invited to their birthday parties and their family events. We are always invited to come there 15 minutes early before anybody else gets there and they use that time to remind us that no one in their family knows that their child has this condition so not a single family member knows. Their primary care physician does not know. They changed primary care physicians because they didn't want the primary care physician to know. They—none of their educators know.

Now compare this to this exact same person comes to every national conference, is tremendously outspoken, is participating in two NIH sponsored clinical trials, and so they are tremendously active in a research context and in a context of advocating for the condition, and at the same time parents, primary care physicians, educators don't know because that's not who they believe the knowledge will help them. They're going to focus on the use of the knowledge in a way that will accelerate their child's development and they think that the stigma of the condition is enough that—and I don't mean stigma like a bad thing but a stigma in terms of in their case they don't want their son to be treated like he couldn't do something in baseball. They

want the baseball coach to throw it just as hard to this child as he would throw it to any child and not say, “Oh, well, he has got a syndrome so I’ll throw it to him softer.”

So that’s their particular concern because they’re athletic. They’re into athletics.

But every single person that I’ve met in this role as—you know, as patient advocate and chairman of this organization is just a little bit different, and one person has got this little thing and someone else has got something else. Policy-wise, you know, which is—as I understand this committee—what you’re here for, policy-wise I think there are some fundamentally policies that could be developed to empower that tremendous granularity in the society to take place and to take power.

And what I believe—just to the gentleman's question asked me as I was standing up at the podium, what I believe would be the result of those policies and I think that it is a testable hypothesis if the agency wanted to find out. But what I believe would be the result is that more data would be shared.

The paradox here, I believe, is the Marco Foundation has done research that says the number

one privacy protected behavior is failure to disclosure, nondisclosure. Number two privacy protected behavior is distortion of fact; lying. So if those are the two privacy protected behaviors without technology, maybe there's a way to encourage people to have greater trust in the system so they don't fail to disclose and they don't lie about their circumstances but they direct the data to go to the places where they want the data to be to help them or to help a family member or for altruistic purposes as someone said in their remarks.

That's--the empowerment of that I believe will result in a proliferation of data, not a repression of data but that is a testable hypothesis and, hopefully, that could be something that could be tested and demonstrated as true.

DR.MCGRATH: I think what I am going to do is state the obvious. You know, you were asking about what elements work or any common themes, and it seems the common theme we're hearing is that—the whole notion of community engagement or informed consumers or participation. If people feel that they--if people do, not just feel, really that strongly, if people are involved in the decision making and have some say and have a reason to

participate then we know the research about altruism is out there but when it's a feeling of lack of control and things going into the ozone is when—at least the research I've seen is when there is a lack of trust. So if we're going to come in anywhere I would say that that would be a very easy thing that I saw across all the speakers today.

DR. ROYAL: Anyone else?

I think going back--because the question that we have up there about best practices, are there best practices, and I think going back to what Laura said is--and sort of what Barbara is saying, I think, is the need for principles as opposed to best practices per se because these are—these models were quite different. I think it was probably hard to assimilate all of this information because there are some similarities in It was kind of hard to assimilate all of this information because there are some similarities and there are so many differences but there are principles that seem to kind of—is a common thread in terms of trust and engagement, and privacy.

I don't know whether we think as a committee that is something that we may want to tackle in terms of coming up with principles. That

probably could be applied across the board or the next question though is should we wait for the Lewin Report? They just started the work in terms of getting some background on what's going on in data sharing, genomic data sharing, and theirs is a year long process and they are going to do interviews with various stakeholders, and then do a report. Do we want to wait? Do we think it's best to wait for that report to decide if SACGHS should do something or do we think there are things that we could do now or should do now?

DR.KHOURY: I think this is probably the worst time to come up with an answer to this question. If you want to rush the committee you might get an answer today that may be different tomorrow morning at 8:00 when people are fresh.

SUMMARY OF SESSION

DR. ROYAL: Everybody looks tired.

All right. Well, I think we'll just go ahead and just close out this session, and then we'll I guess figure out—maybe the steering group can come together to think about how we may want to proceed.

CHAIRMAN TEUTSCH: Yes, I think we started with the premise in the early discussions of the

fact that we have all this clinical data. We clearly have research needs and pretty soon the boundary between what constitutes research and what constitutes clinical information systems are going to break down. And how do we look at it with the systems that Marc talked about what some of those are and how one can build into it the appropriate protections, and still allow research to move forward. I still think that those are some of the compelling issues that we're facing and I'm hearing some of the attempts to try and deal with it in terms of the technologies and information out there.

But it strikes me still there are some policy issues and you sort of said we're still getting focus groups, getting people's impressions, finding out where the boundaries are.

So I think there still are some very compelling issues in all of this. I'm having a hard time putting my finger exactly on what the next steps would be for us and I also feel sort of some lethargy here that is keeping us from actually articulating this very well. At least a couple of people seem to have awoken to that comment.

So I think it is worthwhile that we ask you to sort of take it back and begin to articulate

what it might be based and what you have heard here or you think we need to go. Actually, the champion for this was Kevin before he got off the committee and maybe we should re-engage him.

DR. CARR: He's still on it.

CHAIRMAN TEUTSCH: He's still on this task force, right? To engage him to help us articulate some next steps.

I guess the real question is are we going to have enough that comes out of the Lewin Report—Cliff is here or was here.

Cliff, maybe you could reflect for us do you think that--I know your reports are always brilliant. That's a given. But given where we are in this discussion, do you think that we are well advised to wait until you complete your work or do you think there are some things—I think Sheila wants to comment.

DR. CARR: Well, Cliff before you get started, I do want the group to know that you're still in the initial kind of literature. I mean you've done an initial scan of the literature. So it's a little early to ask Cliff to address this but I'm glad Steve called on you because I think you can be helpful. Even so—even though you're only in the

beginning stages but I did want to let the committee know that it's just underway.

CHAIRMAN TEUTSCH: Yes.

DR.CLIFF GOODMAN: Thank you, Sarah.

First of all, I'm eternally grateful for Steve setting the bar ever so higher every time. Thank you, doctor. Yes, well—what I can say is our approximately timeline which may be helpful to you.

So we have a draft literature review that's due towards the end of April. I believe it's the week of April 19th is a draft literature review. Final literature review, about the end of May, May 31st or June 1st, something like that. A drat final report at the end of August and revised final report the first week of October.

So that's our timing and I would defer—my task group officer, Sandra Howard, is here as well—if she'd like to speak up, too, but what I might say is that—Dr. Teutsch and panel, if—as you progress and this—particular issues become more clear to the SACGSH, if there are any particular areas in which you'd like us to focus more or serve or you better, we can.

I mean we'll proceed with our report on this schedule and we'll through your staff and my

boss at ASPE can communicate about how we might adapt our report to your needs within the scope of our contract.

CHAIRMAN TEUTSCH: So it sounds to me like the timing is actually pretty good. Our next meeting is mid-June.

DR. GOODMAN: Right.

CHAIRMAN TEUTSCH: By that time we should have a pretty good picture of what your finding and what the salient issues are. That could inform Charmaine and her group so that we can have a discussion about it the next meeting and find out about—maybe provide you some input but beyond that help us begin to see where there are some information gaps that we can begin to address if there are any.

DR. GOODMAN: If that is okay with Sandra Howard that is okay with us. I would say that by then we will have something that’s a literature review and not the final report.

CHAIRMAN TEUTSCH: Right, understood.

DR. GOODMAN: The main difference, by the way, between the lit review and the report itself is that the lit—the final report will include not just the main points of the literature review but a

series of interviews, multiple stakeholder interviews so that will be another chunk of input that may occur in late spring or over the summer.

CHAIRMAN TEUTSCH: But you can potentially give us an update about where you are.

DR. GOODMAN: We would be glad to but, as I stressed, we would love to keep in close contact with you.

DR WILLIAMS: So I want to make sure I heard from you correctly because it sounds to me like there may be some work that could be done in the interim between now and June. So two questions. One relates to whether or not there would be from the group now that could direct the literature review that would be useful or whether that would not be useful at this point?

And then the second thing is that clearly there is this interview process with key stakeholders and it certainly sounds like—I mean, I think a lot of them are sitting up front here it sounds like that that would be a role that the task force could presumably do would be to create a list of potential interviewees for that.

Is that a fair statement?

DR. GOODMAN: Yes, we are tasked with

actually putting together a draft of such interviews first for a review by our task force officer and others, and clearly input from you would be most welcome, yes.

DR WILLIAMS: Okay. And then how about the literature review question?

I mean are there—is there input at this point that would be useful or is this a process that is already going and we should not perturb it at this point?

DR.GOODMAN: It is already going and we do not mind slight perturbations on occasion. And I know if through Sarah Carr we might want to see the set of questions that we are to answer. If you have any particular insights on those we'd welcome them. I'll give you an example right now. If there's any stellar piece of literature that we absolutely cannot do without on any of those questions, we would like for you to let us know and we'll make sure that is included in the lit review.

DR WILLIAMS: So it sounds like, at least from my perspective, that if those questions were able to be shared that would be something that if I were running the task force I'd be really interested in seeing them based on the work that I've been

doing to say wait a second, I'm not sure that this is actually well represented or something of that nature.

DR.GOODMAN: And Dr. Royal is quite familiar with those questions, of course.

CHAIRMAN TEUTSCH: Charmaine has seen it today. I'm not sure what stage the literatures are. So it sounds—I'm hearing that we'll keep our task force active as they begin to articulate what's going on and need to work—listen closely to what is emerging from your work and your colleagues at Lewin.

And then we'll, hopefully, be in a position to have a more concrete discussion about—first of all, where you're going and; second, where we should be going when we meet in June.

Is that reasonable?

Great. Well, I'd like to—oh, I'm sorry. I'm looking right and I should be looking left.

DR. SCHAEFER: I just wanted to ask if—so we heard a lot today about different models. In some ways for collection of data also for sharing of data and also for sharing of data to some extent, and I was wondering if it would be useful to hear more at some point. It would be very helpful to me

if I could report back, for example, or incorporate information about what has the experience been to date? Is there any kind of collection somewhere of information? What has the experience been to date, for example, with dbGAP? What has their experience been like? Have there been problems? What are the successes? What are the sort of results. Are there other sort of the venues for data, genomic data sharing, and could we learn more about any of the experiences to date that would help us kind of shape—you know, we learned a lot today about the structure but less about what is actually now happened since this policy has been in place.

As I said, it would be helpful to me to be able to reflect to people more realistically about what the experience has been and, therefore, better informed people about what the issues are when I'm trying to reformulate a consensus sharing and as we learn more about any of the experiences today that would help us kind of shape, you know, I learned a lot today about the structure but less about what is actually now happening since this policy has been in place and as you said it would be helpful to me to be able to reflect to people more realistically about what the experience has Ben and therefore

better inform people about what the issues are when I am trying to reformulate a consent or something like that.

CHAIRMAN TEUTSCH: So can you be a little bit more specific about what you want? Are you looking for like adverse that's have happened as a result of it? How were they dealt with? Are you talking about sort of routine operations? How smoothly they go? What aspect of this would be of particularly help to you?

DR. SCHAEFER: I think those—you know, both of those things would be helpful. I am not aware of adverse events with respect to individual breaches and things like that. Just of the work that has been published about the increasing recognition of the potential for re-identification. So that is quite relevant from the standpoint of informing research subjects, for example. But more generally how is it going? How—what has it been like from the standpoint of the different stakeholders involved, scientists and the people whose data is deposited?

CHAIRMAN TEUTSCH: Laura, do you think that you could work with the task force to help put some of that information together?

DR. RODRIGUEZ: Yes, we could do that. We had a session that was similar to this at ASHG the year before last where we heard from institutions and investigators about their experience, interacting with it, and we could also add something, too, on putting together what the experience at NIH has been.

CHAIRMAN TEUTSCH: Yes, I think getting some of this real world practical experience.

And if you have some of that, whether it's at Cerner or at Private Access or from Kaiser, any of them would be—I think that would be highly informative.

MR. SHELTON: The reason I brought it up was to say something as Mark made some comments talking about virtual farmers in Facebook and more virtual farmers than real farmers. And I'd really like to encourage this committee to think not just about what has happened in the past but what the technology—the direction of direction of technology is moving and what is happening in the future because there is a wonderful video by Kevin Kelly talking about the fact that the Internet, as we know it today, came into existence—the world wide web came into existence in a span of ten years.

And his remarks are not about just what happened over the past ten years leading up to his speech but what the next ten years would entail and the kinds of technologies could become if the web continues on the trajectory that it's on and if the web surprises us in terms of what it does.

And it feels to me like the—you can never predict the future but I think I would just encourage the committee to think about is there's a tremendous amount of activity going on in the way the databases are connected and the way that the data can be acquired. So continuous glucose monitors, Nike tennis shoes that collect biometric data as people jog, these are things that exist today and that can feed the record in a way that has never been done and it can feed the research in a way that has never been done so that the data is continuously updated and the data is continuously entered into the record without needing to have a patient provider encounter. And that kind of that kind of information and dealing with the challenges of control of that information and how you build trust in that research system is something that I really hope and entreat upon you to take a look at.

CHAIRMAN TEUTSCH: Gwen.

MS. DARIEN: Well, I think that—I don't know if you were in the morning but the theme of the day is Mara's Gretzky hockey puck quote because that's exactly what you're talking about.

And it is true the way that kids—like the way the kids use the web. We emailed my stepdaughter to remind her about something and she said, "I was on vacation and I don't look at email did not look at my e-mail." You should have—we're not allowed on her Facebook page but they don't look at email when they're on—that's considered—that's old-fashioned. That's for work. That's for her homework. She is 13

But I mean I think that the hockey puck is—I think it's a perfect organizing metaphor where the hockey puck is going to be today.

CHAIRMAN TEUTSCH: Great. Well, that is a good way to end because clearly I've got to look forward.

So many thanks to all of our guests and for all the information they shared, and to Charmaine for leading us forward. We will engage Cliff and we look for doing that—having more discussion of this in June.

E V E N I N G S E S S I O N

CHAIRMAN TEUTSCH: So we're going to keep plowing on and I know that this gets biologically challenging so if you need to take personal breaks during things that's fine but we're going to keep going because what we will do is go through several of our federal colleagues' reports that were originally scheduled for tomorrow. And I think that shows the flexibility of the federal workforce and their ability to help us in times of need.

I appreciate that.

The first speaker will be Muin Khoury and Muin will begin.

I think your focus is primarily on Healthy People 2020.

So, Muin Khoury?

DEVELOPMENT OF GENOMICS OBJECTIVES FOR HEALTHY PEOPLE 2020

DR. KHOURY: It is 5:00 o'clock. It is biologically challenging for me to be here. Usually I am at the gym trying to get my muscles moving but its hard and having a bunch of feds at the end of day to speak to you may not be the best time to

spend. But if any chocolate next to you, grab it and eat because you'll need that energy to go by.

(Slide.)

So I was given the task of talking about the Healthy People objectives and I'm going to tell you folks something that depressed me while I was putting this talk together but before we get to the Healthy People 2020 I wanted to give you a background on why this is important.

This is where the puck is at the population level trying to figure out how genomics fits in. I want to start very quickly with this translation gap and give you a little bit—since some of you on committee are new--sort of where CDC is coming at this from both research and practice perspective, and then end up with the 2020 goals.

So I do not have to belabor this point. You have heard this. The promise of technology is amazing; two NIH Directors, Zerhouni and now Francis Collins, have said the same thing. We're about prediction, personalization and prevention. The last quote from Francis' new book on personalized medicine illustrates to you the promise of the technology but the reality—actually more famous, Francis said back in 1999 that in 2010 we will have

it all solved. And he is not here to tell us why we do not have it solved in 2010.

So there is an evidence gap, a translation gap, some people call it dilemma, some people call it gap. I'm not going to belabor the point. And that—the valley of death between discovery and population health has to be filled with data and this is not discovery data anymore. This is complicated data. You heard this morning from Mark about the translation pathway in format. It gets more and more complicated the more I draw diagrams. It is an iterative process, not linear, but you really need these other disciplines to come in and help us, including clinical research, epi research, behavioral research, communication research, health services research. And what we need to do is figure out when do we have enough to make an evidence based recommendation. And the challenge around the evidentiary threshold is sort of what you heard this morning around the discussion of CER. I'm not going to dwell on this diagram except to say that this is not as simple as it sounds and this committee is really on top of this because you are at the intersection of research, health and society.

Now a few years ago I took a look at the

amount of research done in genetics and this translation space and I was depressed because of D350,000 human genetic research articles published in the literature there was two percent or less in the T2 or beyond space. This is the space that allows us to do evidence based recommendation or outcomes.

And during that time there were two evidence based recommendations only done by the U.S. Preventive Services Task Force and you'll hear a bit from Guvarneet later on. One on BRCA1, which was done 11 years after the gene was discovered. Essentially it was a positive recommendation, meaning it's time to implement with full speed because it can save lives, the balance of benefits and harms, and another one on hemochromatosis ten years after the gene was discovered. And that I would say wait a minute, not ready for population testing because we don't know what the natural history of this condition is. Now, this is one reason why CDC started the EGAP process which I will talk about in just a minute.

(Slide.)

Since I spent so much time at NIH I wanted to figure out why we are here the way we are. So

this is a paper that just appeared in press a couple weeks ago on the investment in NCI cancer genetics research portfolio. To cut a long story short, there were about 1,000 extramural grants funded by NCI in 2007. 827 of which were through discovery research and 174, about 17 percent, are early translation, and then you see the numbers. They picked it out. There was only one funded research on outcome at the population level, T4, which was a BRCA study.

So we are not doing enough investment in this area and actually the numbers will even be more skewed now because 2007 was beginning the inflection point for GWAS so now we will be funding even more, I guess, discovery research. So this is a segue for why our office existed and why the whole enterprise of public health genomics exists, and not to bore you with too much detail it is—all these disciplines coming together to figure out an effective and responsible way of translation of these discoveries to improve population health. This is a good segue into the Healthy People 2020.

(Slide.)

And as our new director, Tom Frieden, who was the New York City Health Commissioner, said up

an interview in the Atlanta-Journal of Constitution on the beginning of the year, "The single most important thing that public health can do is to increase the degree to which decisions are made using good data."

(Slide.)

This is our boss who said that and those decisions don't have to be public health decisions. They could be clinical decisions or health services decisions.

So this is a lot of the guiding principles behind CDC's surveillance efforts and surveys. So that is what we have been trying to do for the last ten years. We have developed a portfolio of a number of projects that span research to practice and I—you know, there is no time to go into them but we are trying to figure out through—actually there are more than 60 ongoing studies at the CDC to figure out what does genetic information mean for community healthy health?

You know, not sort of a gene discovery but what does it mean to—this population or that population and what the providers know and what the consumers know, and a number of surveys in that space. And that inflection point between research

and practice is sort of what we have worked on collaboratively with The Arc and other groups through the EGAP initiative to actually begin to integrate the evidence and lead more to evidence recommendations for actions, not actually identify gaps for further research that then would lead to more research to fund the actions.

And then through a number of collaborative initiatives, the last of which is GAPNET, which I don't have time to talk about. Including the workforce issues. We and others have funded a number of translation research and programs to actually begin to more validated genetic information into practice. We fund the great state of Michigan, for example, and Janice can tell you more about what we're trying to do with implementation of cancer genetic recommendations into practice. There are a number of these translations research and program that are being done.

So this leads me to the 2020 objectives and sort of the tagline here which is really important for us to think about is that what gets measured gets done. Or, in other words, what gets measured gets funding or may get more funding, and then may be more likely to get funded because there

is—this is sort of having your pulse--your finger on the pulse of the nation's health.

This is an activity that has been going on for years, obviously led by HHS, and they had the 2010 objectives and I'll tell you where genetics faired in just a minute but this is the beginning of the planning process for Healthy People 2020 with four overarching goals. You can read them. It's about high quality, longer lives, achieving health equity, create social and physical environments that promote good health for all, promote quality of life and so on and so forth. And under that ecological model of disease they have the determinates of health and biology and genetics is one of them. So at least we have achieved a certain stature in the lingo of Healthy People, is that in prior years maybe genetics wasn't even integrated into the way we think about healthy people but now it is. So that was encouraging.

There is a federal interagency working group which has 55 members representing 24 HHS agencies and offices, and includes non-HHS federal partners that make decisions on what goes in and what gets measured.

The vision of this organizing framework is

a society in which all people live long and healthy lives, and they are—these five mission statements, which include improvements in health improvement priorities, increased public awareness, provide measureable objectives and goals. I'll get to that in a minute, which was quite depressing for me when I started thinking about genetics. Engage multiple sectors to take action to strengthen policies and improve practices, and then identify critical research evaluation and data collection needs.

You can see the parallel between sort of what I've been trying to do within the CDC framework but this is sort of a national effort that can actually help genomics in a major way.

Now, anybody who wants to propose objectives needs to fulfill these eight criteria. The condition or whatever needs to be measured—has to be important and understandable to a broad audience. It has to be prevention oriented and achievable through various interventions. It should drive action. It should be useful and reflect issues of national importance, measureable and address a range of issues, build on past interactions of healthy people, support with best available scientific evidence and then, last by not

least, address population disparities.

So I think the data expectations that each objective should have a valid, reliable nationally representative data source or potential sources—it could be state or national or some combination. You have to have baseline data and then you have to have an assurance of at least one additional data point through the decade. Remember we're in 2010.

Each objective will have to have its own target. The target setting policy or methods are currently being discussed. Each objective will be approved by the Federal Interagency Committee.

Now in 2010 there were two over arching goals. One of them was health disparities and the other was on healthy life. And 28 focus areas, 467 specific objectives, and no genomic focus areas or objectives were done, other than newborn screening. And I'm not putting newborn screening in this bag right now.

There was in the narrative some passing references to genomics and its importance but nothing was measured, nothing was done for 2010.

Now, we got depressed and we decided that we needed to have at least some proposal for 2020. So we proposed to the Federal Council that it could

be useful for Healthy People 2020 initiative to develop a work group and objectives to help assure that rapidly advancing knowledge is translated into practice to maximize the benefits and minimize the harms. So they said go ahead and do it.

So Katie Kolar, our policy aid from our office, and Gurvaneet Randhawa co-lead this genomics working group and you see the names of people on this distinguished panel. So I am representing what Katie and Gurvaneet has put together. And if you have any questions you can ask Gurvaneet since he is sitting at the table.

So the proposed four genomics objectives to promote evidence-based practice. The first one is increasing the knowledge base to support evidence based practices for genomic applications, including more translational research studies and evidence based recommendations. That was rejected by the federal panel because it was not measurable enough and did not fit the eight criteria that they put together. But they accepted the second one which is the increasing implementation of evidence based practices for genomic applications.

Now I was quite depressed there are only two things to be done by 2020. One is the Lynch

syndrome recommendation and the BRCA1—BRCA recommendations because the task force made recommendation back in 2005 and EGAP in 2009. I said to Katie and the group there must be more than that we can do by 2020. And right now we are thinking about what to do with this but at least in the space of these two conditions it's very clear what you can measure. You can measure the—increase the proportion of persons with newly diagnosed colon rectal cancer who receive genetic testing to identify syndrome and on the BRCA side you can increase the proportion of women with a family history of breast and ovarian cancer who received genetic counseling.

And so at least its clear what needs to be done in these two conditions and that could drive both the data collection and maybe implementations in national, state-wise and local-wise. So this is sort of what happened in the interim. There were comments from—on the topic areas. Six comments received and five objectives on the comments.

And I think SACGHS put together your own comments.

What happened since then was no changes to the proposed objectives but some comments will be

incorporated in the narrative of the topic area. Now, there is every intention, I think, of the group that as new evidence based recommendations come on line that they will be added to this rather meager sort of genomics and population health picking right now but you know sort of this is where we are.

This is how things are measured in terms of lives saved and practice. And, you know all this wonderful promise of genomic technology, we're still in 2010 and I'm hoping that there will be more to discuss and use by 2020.

(Slide.)

So the next steps are the final dispositions of public comments, identifying more targets, and draft some narratives of the section—of these topics but it would surely be very useful for this committee to weigh in and tell this working group, you know, where they can add more genomic objectives, if possible, and where some of these points of implementation can be.

So thank you very much.

CHAIRMAN TEUTSCH: Thanks, Muin.

As a reminder, I believe in Tab 8 are the comments that we sent in on Healthy People.

Any comments or questions?

Anything you wanted to say, Gurvaneet?

Marc?

DR. WILLIAMS: I just don't think you should be that depressed, Muin. I mean, over 2010 you've had an infinite improvement, increase, you know, so that's—I mean, how many people can claim that, right?

DR. KHOURY: One way to look at it. The promise is surely much greater than these two conditions.

CHAIRMAN TEUTSCH: Tab 9. I'm sorry.

UNKNOWN: But, Muin, when we submitted for 2010, they did not take any of them. You got one.

DR. KHOURY: We got two.

(Laughter.)

UNKNOWN: Two!

(Laughter.)

CHAIRMAN TEUTSCH: Well, let's face it, it's ain't over until it's over.

DR. KHOURY: Yes.

CHAIRMAN TEUTSCH: And these are still going to get scrubbed a fair bit over the next few months until the final set gets released presumably later this year sometime.

DR. WILLIAMS: I mean in some sense this

reflects, I think, something that all of us when we really sit down and look at Genetics in the cold, hard light of day, in comparison to a lot of the other things, I mean I was looking at this particularly from the perspective of coronary artery disease relating to a proposal that we were putting forward for a grant application. And essentially the coronary artery disease recommendations from Healthy People 2010 are moving unchanged in the 2020 because nothing has happened in the interim.

I mean that’s a frightening thought when you think about the overall progress of preventive medicine in general in this country. So in some sense, you know, while I obviously have committed my career to this area and am heavily invested in it and I think there’s a lot of promise, the reality is that a lot of the way that we deliver invested in think there is a lot of promise the reality is a lot of the way that we deliver healthcare in the system is problematic.

It’s not so much that we do not know what to do; it’s that we don't know how to do is.

DR. KHOURY: Yes. Speaking of heart disease I think, you know, one thing which we might, hopefully, integrate in these recommendations—the

NICE group in England has produced a recommendation on cascade screening for familial hypercholesterolemia in the summer of 2008.

Now, HHS here has not considered any evidence-based recommendations not sanctioned by HHS and I think NICE is a very rigorous process. So we might want to try to insert the FH recommendations or let maybe the EGAP or the Task Force to look at FH because I think we can implement that and save some lives in addition to the general preventive strategies around coronary heart disease.

CHAIRMAN TEUTSCH: Thanks, Muin.

I think it—but it does betoken the need to find those things that are effective, that can be done, that we're going to have a measurable impact. There were other objectives in there and not so much on genomics but in other things that deal with things that are pretty obscure. And they, I suspect, will fall by the wayside and I think part of our task is to not just talk about the hope of genomics but actually to begin to gather the information that Muin was talking about so that we can begin to have effective technologies that make a real difference that we can begin to move into practice and become part of the mainstream.

DR. WILLIAMS: And the other thing that I don't know, Muin—so much about how this process works but it seems to me that, you know, where we've made—granted the NIH State of the Science report isn't necessarily going to help us in this case but be that as it may, you know, there are a number of things where there is a relative underpinning of understanding that family history is at least a contributor to it.

And so as a cross cutting kind of theme, you know, the collection of that information, particularly in the area of how that affects health behaviors, you know, if something like that could be included thematically in the report, I think there would be high value to that.

DR. KHOURY: I think that is what Marc is alluding to as was recent NIH state for the science conference on the utility of family history for improving health. And if you want to talk about being depressed, the conclusion of that report was there was insufficient evidence that family history can improve health.

Now they have excluded the single gene conditions from that assessment so that ties together BRCA and Lynch syndrome and familial

hypercholesterolemia, is that they are all autosomal dominate conditions for which family history is very important and it's part of the cascade testing of relatives but I think they were evaluating the role of family history in general as a tool for, you know, health promotion and deisease prevention, and they called for more research of the type that CDC has sponsored. We're actually doing a randomized clinical trial to evaluate whether or not if you give people personalized recommendations based on their history that they will do something to improve it their health. Believe it or not, there are really no clinical trials that look at family history in an evidentiary basis.

So I think we will try to insert family history any number of ways in the report but to have measurable things by 2010 I'm afraid—and stick at least with the single gene disorders for now unless there are some wonderful gene expression profiles or pharmacogenomic applications that mature quickly over the—in the next couple of years for which measurable things can be done at a population level.

CHAIRMAN TEUTSCH: The last comment, David?

DR. DALE: I also want to comment in that

sphere, that is the single gene disorders. You could have a measurable outcome of time to diagnosis for even the more common single gene ever because we talk to people like we had at this meeting about rare diseases here two or three weeks ago, and that's a great frustration. It takes too long and there's so much anxiety created in disease caused by the delay in diagnosis. And that gets at the unevenness of health care in our country.

DR. KHOURY: Yes, I think that is a very good point because there are thousands of genetic conditions for which this may apply and sort of the diagnostic odyssey.

I wonder if, Gurvaneet, maybe your group has tackled this. I wonder if there is a genetic way to add something along the lines of earlier detection or earlier diagnosis for any genetic condition. They might come back and say; sure, I said this will actually improve outcomes. So I don't know if you have any comments on that but that's a great suggestion.

DR.GURVANEET RANDHAWA: Yes, I think that's a process, Muin that makes sense. The challenge is how do you define it? How much time would be ideal time and how would it vary across

diseases and conditions? So I think its useful thing to explore and we'll get some standardization on.

The challenge of putting this in Healthy People 2020 is even if we come up with a definition is there a way to extract the information from the current healthcare delivery system infrastructure, and that would be another challenge.

DR.DALE: May I just respond. I think there is. That is, the simplest way, of course, is to have a survey of people who had diagnosis made and how long it takes. There are population ways that you could approach it, too.

Anyway, it is measurable.

And there probably are some others, too.

CHAIRMAN TEUTSCH: Great. Thanks.

Thanks, Muin, for leading that discussion.

Well, let's turn to CMS and Jeff Roche. CMS has been highly responsive to a number of our recommendations and moving forward with some evidentiary work on genomics. Last week there was a MEDCAC meeting on pharmacogenomic testing for anticancer therapies. And that was the third, I think, of series of meetings over the past year that deal with genomics.

So, Jeff, thanks for being here.

MEDCAC MEETING ON PHARMACOGENOMIC TESTING FOR ANTICANCER

DR.JEF ROCHE: Hi. Thank you very much, Steve.

(Slide.)

First, let me mention that there are actually two relevant advisory committee meetings and I thank my colleague Penny Keller, who is sitting back in the audience today, from the CLIA group at CMS.

In January, just last month, the CLIAC proficiency testing working group met to explore some of the issues around making sure that for genetic testing, in particular, not only the appropriate reference materials and challenge samples but also the survey infrastructure and data collection tools were available so that genetic assays can take advantage of the same type of external proficiency testing validation that so many other laboratory studies get. I just wanted to check and see if Penny, who is still here, might be willing or wish to comment further on that.

DR. PENNY KELLER: I just kind of wanted to update. We just initiated it. We had actually gotten the approval from the CLIAC workgroup last year but because of the H1N1 epidemic, the agencies were busy so it was delayed. So we had the initial meeting in January and another one is scheduled for March. I'm sure there will be a series of them.

Except for the cytology proficiency, which has been in the works for five years, and there is a notice of proposed rulemaking that went out and we got some public comments back. So that was done. That kind of opened the door to look at the proficiency program overall for all testing and, of course, genetic testing will be an issue but we just initiated it but I thought that we would share that.

DR. ROCHE: Thank you.

Also just about a week ago yesterday we were kind enough to have Dr. Goodman, who is sitting in the audience, and Dr. Teutsch, who is one of our distinguished panel members, be part of a MEDCAC panel about pharmacogenomic testing and cancer therapy. And in the interest of time I'm going to go through this very quickly.

(Slide.)

We were very lucky at the MEDCAC meeting

to have two distinguished people help us with us understanding some of the issues about whether the quality of evidence about pharmacogenomic testing when used to guide treatment for cancer actually improve outcomes, Because as Muin and Guvarneet have mentioned, we're kind of interest in outcomes.

And we were very fortunate when Dr. Friedman actually proposed not only a great many very valuable lessons about some of the potential in this area but also gave us a vision of the future where someone could bring in the sequence to the pharmacy and get the appropriate drug.

Also, Dr. Friedman was kind enough to point out that this area has received some interesting attention from some fairly high place elected officials, at least in the past.

We also were grateful to Dr. Trikalinos and his group at Tufts for an evidence-based practice review about specific tests that can be used for patients with certain cancers or are candidates for certain anti-cancer agents.

And in the interest of time, again, I am going to ask you to look potentially at the materials which I believe are or will be available on the Table tomorrow and focus just for a little

bit on some of the public comments that the committee heard before they actually voted.

The first was echoed earlier today by the need by some of the parts, especially the testing community, to clarify what their responsibility is and what really CMS is interested in when we call for clinical utility studies.

Second, we are very much aware from many public comments that there are significant barriers to clinical utility studies, especially those which may turn out to be somewhat negative in terms of the potential role of these tests in outcomes.

But we also heard very clearly that some of these studies have been used for years and they are now considered standard of care. They are part of many clinical guidelines for the cure—for the treatment of cancer, forgive me, and in fact that these are now being integrated by some of the larger organizations like pharmacy benefit managers to make sure that patients for whom such drugs are prescribed have the appropriate testing to make sure that the drugs are going to make sense.

In addition, we had a very interesting public comment from Dr. Novak, representing the Association for Molecular Pathology and the College

of American Pathologists, in which he revealed to the committee that there are, indeed, about 1,200 laboratories who subscribe to CAP proficiency testing studies who have signed up for HER2 challenge studies. In other words, they are part of an external clinical validation program for the testing they do.

A somewhat smaller number, perhaps because it's a new program, are signed up for KRAS testing where smaller numbers are signed up for BCR-ABL testing or CYP2D6 or UG21A1 testing.

Again, this reflects the fact that laboratories are looking at this as an important area that they want to make sure about their accuracy and validity of testing.

Finally Dr. Novak revealed that a majority of laboratories in the United States are, indeed, interested in, especially those who are members of both CAP and AMP, are interested in the first three tests but not quite as interested in CYP2D6 or UGT1A1.

(Slide.)

The MEDCAC panel, as those of you know who have read some of our accounts of it, essentially tells CMS what level of evidence we should have

about the value of these tests in terms of determining clinical outcome benefit to patients. Now, we use a five point scale with one reflecting a relatively low degree of confidence that such tests have such value in terms of improving outcomes and a five which reflects high confidence.

The first question that we asked, a week ago Wednesday, we asked the panel to tell us about their impressions about the level of confidence that pharmacogenomic testing affects healthcare outcomes. I hope that showed up on this slide. I guess it did. In these five situations--five particular situations in which we know there is testing out there and it does affect some of cancer treatment. We set a barrier of 2.5, which is a little bit less than some confidence to distinguish those tests with relatively larger amount of confidence from those with less.

And this was about the question to the effect health outcomes. Clearly HER2/neu, BCR-ABL-1, and KRAS testing is clearly thought by the panel to be supported by sufficient evidence to say with some confidence, in fact, with a high degree of confidence that there is an effect on patient outcome. The second question was a follow up to the

first.

Does the panel believe that based on the evidence, and as I say this was presented by several groups, as well as a packet of information which was prepared for the panel ahead of time, that such pharmacogenomic tests improves healthcare outcomes. And, in fact, for these three specific agents, and let me mention that for BCR-ABL this particular question was for diagnosis and monitoring of the type of patients who would benefit from not another tyrosine kinase inhibitors, that indeed HER2/neu, BCR-ABL for diagnosis and monitoring, and finally KRAS testing were inspiring high confidence based on the evidence presented, whereas BCR-ABL, which was used to detect treatment failure mutations which would make a patient more liable to be unresponsive to TKIs was not felt at least at this time to be at the same level of confidence.

The panel was also asked to suggest whether they had a level of confidence about the generalizability of these findings to patients in community based settings as opposed to tertiary cancer centers and there was a fair degree of confidence—a fairly high degree of confidence there, as well as for generalizability to the Medicare

patient population.

Finally, the panel was asked to talk about evidence gaps that they felt could improve the evidence that CMS would consider in looking at possible future covered stations. Let me mention that we are not currently looking at any coverage decisions for any of these tests, individually or as a group. And, in fact, the concerns about comorbidities, especially things like polypharmacy and nutritional status, which become very important issues for the elderly in terms of how they would respond to medication, to standardize genotype or phenotype assignments, especially in the area of 2D6, which was felt to be an area where that assignment is not something that’s comparable among different studies.

The importance of being able to maintain tissue in DNA source banks and finally studies representing more diverse patient groups were all mentioned.

But as I think was mentioned earlier today the final question that was place to the panel by Dr. Goodman was whether there were any particular high points or points they would like to emphasis and almost unanimously the panel said that evidence

providing additional information about clinical utility of these tests, including information about functional outcomes, quality of life outcomes, would be welcome.

Thank you very much to all of the panel members, including the two who are present today, who have helped CMS understand this issue better.

CHAIRMAN TEUTSCH: Great. Thanks, Jeff.

Cliff, did you want to add anything as you were the chair of this panel.

Cliff does many things.

DR.GOODMAN: Thanks, Steve. I wasn't expecting to but one, I guess, hopeful and revealing bit of the discourse had to do with the concern about many of the speakers, the presenters, about whether someone is going to always demand RCTs linking the test to outcomes. And I think it was fortunate that we were looking at KRAS for example and as I think all of you know and I think Marc may have addressed this in some of his earlier comments, the evidence impressed to the panel about KRAS were it was based on retrospective subgroup analyses of RCT data, several RCTs. So what we probed was do you need more evidence or not and, if you do, what kind is it?

And just to get to the very end of it, the answer the panel sort of gave was, yes, we do need more evidence. It should be prospective but it need not be RCTs was kind of the place where they arrived and that was kind of a useful insight as far as the discussion you had earlier about what comprises clinical utility in some of these instances.

CHAIRMAN TEUTSCH: I would say having sat through that, one of the reasons they could do that with KRAS is because the evidence was zero for harms so there could only be a benefit.

Marc?

DR. WILLIAMS: So two points. One would be I'm just curious in terms of that list of evidence gaps. One that wasn't represented there that I think has been a recurring problem in evaluation of some of the pharmacogenetic studies is the idea that we focus on prevention of adverse events to the neglect of efficacy and the UGT1A1 is a great example of that where in the EGAP report it really showed that while, yes, if you have this polymorphism that you are more likely to have an adverse event. However, your cancer responded a hell of a lot better, too, which is not a bad thing. And if I was a patient I'd be more willing to risk

an adverse event if my likelihood of cure was higher. And yet we haven't really developed strategies by which we can develop evidence to say where do we identify the balance between adverse events and potential efficacy, at least in certain circumstances.

So that was one comment/question.

The other question I had is related to the CLIAC information that you presented at the beginning.

Could you give us a sense, for those of us who worked hard on the overset report, whether or not that was actually used as part of the decision to go more into the proficiency testing or on genetic testing?

DR. KELLER: When I came aboard I read the oversight report. The whole thing. And it was—we considered it a good idea but it wasn't in the process of being presented to CLIAC.

Like I mentioned before, what is—well, it was a matter of timing in that the work that we had been putting into the cytology proficiency testing actually moved on and they actually approved the proposed rulemaking, and that allowed us to move on and propose anD coordinate another workgroup for the

other proficiency tests.

And the fact that the committee's report stressed the importance of considering genetic testing because it is very unique in the parameters and such. All of that will be discussed and probably be re-introduced in the work group. But those are preliminary right now. The workgroup will determine what the issues are and what the criteria are and such. We just kind of coordinate at this point.

CHAIRMAN TEUTSCH: Great. Well, thanks a lot, Jeff. I think we're going to move on because I know we're beginning to lose folks. I appreciate all of that.

Gurvaneet, do you want to talk—you can do it from wherever you wish. I guess you have slides. You can move up to give us an update on AHRQ activities.

AHRQ EVIDENCE-BASED REPORTS

RELEVANT TO GENETIC TESTING

DR. RANDHAWA: I can make it a five minute from here on.

(Slide.)

So all of you have the slide set in front of you. It's a fairly short slide set.

I have two kinds of the updates. One, I'll focus on the EPC report, primarily on a methods project that we are doing right now. And, second, I'll give you just a little bit of update on the BRCA clinical support tool.

(Slide.)

So the EPC methods project that we are working on has two different areas of focus. One is on evaluation frameworks. What are the ways that we look at genetic tests? What are the harms? What are the benefits? What's the accuracy? There have been several different frameworks proposed and we wanted to try and synthesize what these are and what the strengths and limitations are.

The other part of this project was just on the analytic validity, which Andrea had raised earlier. So, hopefully, this report will help address some of those questions. If you are doing an evidence report, how do you search for analytic validity? What is the quality rating criteria? How do you look at the evidence and how did we fill the gaps?

So the initial conclusions, we have a draft report which should be finalized by next week but I can give you some highlights of what we have

found so far.

There are several different evaluation frameworks. Frybeck Thornberry had been proposed about 15 years ago, the Preventive Services Task Force uses one, and we have been modifying that over the last 25 years, and the more recent frameworks were from the CDC, the ACCE project which was started in 2000, and the EGAP working group, which was started about four years ago.

Each framework has different strengths and limitations and some of it is driven by who the ultimate audience of the framework and assessment is. Is it the patients and providers? Is it the payers? Is it the regulators and the test developers? Our report is not focusing too much on the last two categories, the regulators and the test developers.

(Slide.)

One of the conclusions is one single framework to meet everybody's needs and for all clinical scenarios is implausible. We are trying to come up with maybe a small set of frameworks that may be useful for most situations. We will see what the peer reviewers say about that approach.

The suggestion that came up in the

workgroup and in the review was the EGAP working group approaches comes closest but it probably needs some enhancements with some specific questions that they have not dealt with before.

(Slide.)

A different part of this project was on the analytic validity, which for those who have followed this field, no real surprise, there is very little published data on analytic validity and it's often found in the gray literature which is data we find from websites, conference reports, symposia, talking to experts, materials sent by test developers. So there are different credible sources of information, some from federal websites or from credential organizations like GAP.

There are also several different quality rating tools, although there is only one that was proposed EGAP that comes closest for specifically genetic tests but for diagnostic tests there are quite a few tools or instruments which rated the quality and the reporting, the QUADAS, STARD, REMARK, which focuses on cancer, and of course the task force and AHRQ have published their tools.

So one of the directions we're moving forward is to come up with a new tool, which is a

checklist which has right now items. We'll see whether it stands up at the review. We don't have time to comparatively test this tool but we're hoping this will move the field forward in terms of something that people can agree on.

(Slide.)

Now I'll switch gears and talk about an implementation project. So we have been working on this for about a year-and-a-half now. It's a clinical decision support tool that's moving us towards implementing the Preventive Services Task Force recommendations.

The challenge for a primary care provider is to know which women are actually at high risk for having a BRCA mutation and it is very rare to have the family history information available to make that assessment and even to take it in a systematic format that someone can assign a risk score.

So this tool is a web based tool that can be used in the primary-care practice which will have both the patient and the provider interface where once the patient fills in their family history, a risk assessment score will be generated with some guidance to the clinician what to do based on the risk score.

There were different phases of this project. The first phase was looking at the available evidence, the literature review, and talking to experts.

The second phase which is where we are finishing up now, which is where we are finishing up now, is the usability testing of the tool and modifying that before we actually roll it out in a couple clinical sites and see how useful the tool is.

(Slide.)

And you already heard about these reports so I will not talk about the family history or the EGAP report on Factor V Leiden and prothrombin testing.

(Slide.)

One thing I want to just tell the committee is we will have a workshop at AHRQ later this month on genomics from the family care perspective, which will be assembling a small group of a fairly diverse skill set, and people will come together to hopefully move the dialogue forward in terms of what are the challenges facing the primary care provider and how do we overcome this.

So we are working towards a white paper

and once we have a draft and input from this workshop we'll be happy to share it with this committee and get their feedback.

And one small update is we're finishing up a randomized control trial that we had done on Warfarin pharmacogenomics. This was done at the Marshfield clinic.

It has taken about two years now and it compared two difference dosing calculators. One, using gene-based information and clinical factors and the other one only clinical factors to see if there was any difference in some surrogate outcomes like time and therapeutic range. The report is still getting finalized but what I can say is there really is no conclusion from this project that will say we should start using this right now.

(Slide.)

And, of course, I will end on some of the funding announcements that have come up. I will be happy to answer any questions that I can on the grand opportunities we have on comparative effectiveness, some of which are also asking for pharmacogenomics and other diagnostic tests that will be part of this review.

And I will end there.

CHAIRMAN TEUTSCH: Thanks, Gurvaneet.

Comments or questions for Gurvaneet.

Lots going on. Lots of resources thrown at it. It's a nice thing.

Well, fortunately, we have one more presenter and, Alberto, you have been incredibly patient. We talked a little bit about FDA this morning in conjunction with the force in the Myriad labs, and we mentioned that FDA has been developing new mechanisms for getting reports of issues concerning lab developed tests, and we're hoping that you will be able elucidate what that is.

DEVELOPMENT OF AN ADVERSE EVENT REPORTING MECHANISM FOR LABORATORY DEVELOPED TESTS

DR. GUTIERREZ: Yes, I will go through the slides quickly. It should be fairly quick. If we can get them up.

(Slide.)

I will spend a couple minutes just giving you a background just to make sure that we are all on the same table here. Can I have the next slide? I can go up and do it.

Okay. Oh, thank you.

(Slide.)

So just to remind you, as this committee

well knows, there are few differences between what laboratory developed tests are getting looked at in terms of the regulatory oversight and what the FDA does, and one of the things that we noticed is that it's not only premarket look at the tests themselves and ability to tell whether there is clinical validity or not that is of concern to us but, in fact, there are a lot of post market or things that the FDA does that laboratory developed tests are really getting by because we're doing enforcement discretion.

So one of the controls that we have in post market is that we actually do surveillance. We do product identification and correction for tests that are regulated by the FDA. What that allows us to do is we can really pick up problems and we use this as a tool that allows us to get manufacturers to correct issues that we see. It prevents recurrence of adverse events, identifies problems, it really is a tool that we use quite frequently.

So as it stands now manufacturers are the ones responsible for reporting death, serious injury, or malfunctions to the FDA and we look at the reports. We look for data trends. Sometimes we look for issues and there have been several cases in

which the data has been quite useful.

In terms of the current surveillance of LDTs, because we apply enforcement discretion, LDTs--the the laboratories don't not actually have to report malfunctions and DRs to us. It is not being enforced. That is not the only issue.

We really have had a lack of a mechanism to really analyze and segregate the data because the way we do that now for in vitro diagnostics that actually get cleared through the agency, clear or approved, is that we give them a product code based on the analyte usually and then the data gets analyzed based on that. So we have experts that look at specific protocols and look for trends and issues in there.

Since we do not have a protocol that specifically says this would be a laboratory test, if somebody does report for some reason an issue with a laboratory developed test it actually would get lost among all of the other data that we have. So we are trying to create a mechanism where we have a protocol specific for laboratory developed tests so that--and will have an analyst assigned to that so that they will actually look for any trends and issues that we see in laboratory developed tests.

And, lastly, how will this work? Well, still we're probably—we're still not going to enforce our reporting from our laboratory developed tests but there is a mechanism for voluntary reports. So we are planning to advertise this and hope that people actually report any issues voluntarily so that we can then go ahead and take a look at what kind of adverse events we are seeing among laboratories.

The method for a voluntary report is called the MedWatch and it can be used by anybody's web base. You can go to this website and report an adverse event, you can report that it didn't work, you can report whatever you want and we will be able to actually then follow up on that.

(Slide.)

So I have here just--If you want more information on MedWatch and where you would report on MedWatch, it's in the slide.

DR WILLIAMS: So for the reporting would there be a mechanism by which somebody that say is knowledgeable about the fact that there is a laboratory developed test that has had problems would be able to report that to FDA or would all reporting have to come through the provider of that

LDT.

DR. GUTIERREZ: No, by doing it through this voluntary MedWatch you can report directly to the FDA.

DR WILLIAMS: Okay.

DR. GUTIERREZ: We have a dual mechanism for reporting. Most of our reports come through the manufacturers because they're obligated to report to the FDA. When we go and inspect them we will make sure they are reporting but we get a fair number of reports from people who are interested or who have been armored through the MedWatch and MedWatch is setup to do exactly just that.

CHAIRMAN TEUTSCH: So when do you expect the LDT part of this to be up and running with the analysts that you have?

DR. GUTIERREZ: We expect this to be fairly quick. Within the next couple weeks or so.

We already have started asking people to report. The biggest issue is, the way that MedWatch and MDR works out is there are actually contactors that take the reports and then put them in the buckets that we need to put them and we need to train them and we need to make sure they are putting them in the right bucket.

CHAIRMAN TEUTSCH: I think it would be really interesting for us to understand not only these systems but then sort of what kinds of issues do you turn out, what are the consequences? Because we talk a lot about these harms but I don't think we've been very--

DR. FERREIRA-GONZALEZ: I think also there is—

CHAIRMAN TEUTSCH: Yes, Andrea, go ahead.

DR. FERREIRA-GONZALEZ: --an immense diversity with LDTs.

DR. GUTIERREZ: There will be.

DR. FERREIRA-GONZALEZ: So I was just wondering, you know, in the process of developing these protocols are you going to seek input for end users or from the public?

DR. GUTIERREZ: We can do that. We can actually collaborate with CMS if there is an issue that we see. CMS will help us look at it. The biggest issue that we have in terms of analyzing at this point is that if we do not have a bucket that the contractor—we get a lot of MDRs. We get thousands and thousands of MDRs. If we do not have a bucket that the contractor can put that into, it really gets lost.

DR. FERREIRA-GONZALEZ: Because here for LDT you're talking about culture, you know, virology, microbiology.

DR. GUTIERREZ: We understand.

DR. FERREIRA-GONZALEZ: You are talking about immunohistochemistry and surgical pathology, and you're talking about genetic testing.

DR. GUTIERREZ: We get MDR on the other side from culture—from the manufactures themselves so we do know the range of what we're talking about here.

DR. FERREIRA-GONZALEZ: Yes. So I think maybe some input from the professional organizations in looking at some of these protocols and providing feedback might be something that you might think about.

DR. WILLIAMS: Are these data--when these are reported and assuming you can actually do an analytic on them, are these all available publicly then for review?

DR. GUTIERREZ: Yes, they are. Some of it is public, yes. Yes, some of it.

CHAIRMAN TEUTSCH: So you also have the capability once you've got these in buckets, you've done some analysis, to go back and investigate; is

that correct?

DR. GUTIERREZ: We do. I mean, I can give you an example. We have been following glucose meters for a long, long time and we have begun to see a recurrence of deaths that were due to an interference of some drugs with some of the glucose meters. And we actually have been able to analyze that. We have been able to go back to the manufacturers and we have been able to actually put a safety notice based on what we sought. So we do use these things in ways to prevent problems or to help solve problems.

CHAIRMAN TEUTSCH: Great. Well, I think this is a real step forward so thank you for that and I expect there will be more interest in talking at more length.

Closing Remarks

CHAIRMAN TEUTSCH: So all of you have displayed incredible tolerance for a very long day so thank you for that.

A couple reminders: 7:30 tomorrow we will take up the patents and licensing report.

And dinner, for those who are going tonight, is at 7:30. If you do not know where it

is, you want to meet in the lobby about 7:25 p.m. People can meet there and walk over together.

Other than that I think we will be adjourned and I will look forward to seeing you all very early tomorrow morning.

Thanks so much.

(Whereupon, the proceedings were adjourned.)