SECRETARY'S ADVISORY COMMITTEE ON GENETIC TESTING

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Conference Room 6C-10

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C O N T E N T S

P R O C E E D I N G S (8:35 a.m.)

DR. McCABE: Let's go ahead and get started. We've got a lot to do today.

Welcome back, everyone. We're going to begin the morning with progress in the development of coordinated genetic testing information systems by Muin Khoury and Tim Baker.

We spent yesterday morning discussing FDA's response to SACGT's recommendations regarding enhanced oversight. This morning, we will be briefed by CDC on the interagency efforts underway to develop voluntary integrated systems for collection and dissemination of information on genetic tests.

We will first hear from our colleague on SACGT, Dr. Khoury, who will provide an overview of the types of data needed about genetic tests. Mr. Tim Baker, Dr. Khoury's deputy, will present on interagency efforts to develop coordinated genetic testing information systems.

We anticipate that these presentations will provide us a clear picture of how HHS is implementing our recommendations on postmarket data collection. We also hope to gain an understanding of the scope and feasibility of the interagency plan and how coordination of efforts across the public and private sectors will be achieved.

Dr. Khoury?

DR. KHOURY: Good morning. Can you all hear me?

DR. McCABE: Yes.

DR. KHOURY: As we go through this presentation, two presentations, I'd like you to once in awhile refer to the many, many attachments that you have. I'm not sure which tab, but I'll be referring to some of them as we go along.

Actually, what we have here is really a huge challenge, figuratively, in all ways. You've heard me before talk so many times about data, and we live in the data domain at the CDC, and it was really very invigorating yesterday to hear and see the progress that we are making along those lines by the FDA and by others, and what I'd

like to do today is recapitulate for you very quickly what I call the phases of data development and then move on to an update on three activities at the CDC that will help you see how we're looking at this issue from the acronym ACCE.

I'll describe what that is to you, some of the activities around HuGE and HuGE Net, and then the beginnings of an information system, and I'll give you some examples for how that will work, and then I'll hand it over to Tim, and Tim will talk about some of the interagency discussion and efforts that have occurred over the last few weeks towards the beginning of a coordination of genetic testing information.

I'd like you throughout this process to keep the two challenges that we all face in mind, and we'll come back to them towards the end of Tim's presentation as well, and the first challenge is how can we improve both HHS and non-HHS data collection coordination and management, and given that many groups are collecting data that attack genetic tests from different perspectives and different angles, how can we do all this together?

I can see the beginnings perhaps of a solution to this, is by first defining what the data elements are and the empty boxes that need to be filled, and I think SACGT's contributions have gone a long way towards defining those things for us, and then the Challenge Number 2 is about access to the available information that gets collected and disseminated.

So before I start, I'd like to tell you a small story. People like me with back problems always pay attention to stories like this. This is a JAMA article, was published on April 11th, and let me read to you the quote on the left-hand side in Reuters.

"A team of researchers has identified the genetic risk factor for a debilitating lower back disorder, opening the door to new ways to prevent, diagnose and treat a disease that affects millions of people worldwide."

As one of those millions, one of the many millions, but let's look at the data. I mean, this is the data where that quote came from. It's a case-control study

in Finland, where they had 171 people with MRI-diagnosed LDD or lower disk disorder, and they had 321 "controls" without that condition, and the gene we're talking about is a Collagen IX allele, and we don't have to worry about what that is, and they found that 12 percent of cases have this TRP3 allele compared to 4.7 percent of the controls.

Now, I don't know about you, but I see this story repeated again and again week after week, and, you know, you jump from the right-hand side to the left-hand side, and I just don't see how we do it, and that same story happened a couple of years ago about the APC gene variant in colon cancer with people jumped immediately to try to offer a genetic test to Ashkenazi Jews because of that variant.

So to me, we're facing a black box here. Everything starts with sort of a relationship between a genotype and a health outcome similar to what we've seen in this paper, and how do you jump over that black box to get the genetic test, and what I'd like to do today is tease out that black box for you, and there is nothing magical about this and tell you about the CDC approach from this side and that side as we go forward.

The first thing I just want to put on the map is as we move forward with examples of these kind of associations between genotypes and diseases that are not genetic in basis but multifactorial and complicated, that relationship does depend on other factors, like environmental factors.

So for example, the relationship between Factor V Leiden and venous thrombosis is not the same in all people. Women who take oral contraceptives have a very different relationship between Factor V Leiden and the risk of venous thrombosis.

So as we move forward through this cascade of events, I'd like you to keep in mind the modifying factors, and so the first thing to open up that black box really is about epidemiology, and epidemiology is the population-based science that begins to describe to you those relationships in a population-based manner, and simple things, like the prevalence of the genotype in the population for which a genetic test might be offered, the prevalence of a health outcome, and the prevalence of the modifiers in that same population, sort of the A, B, C, where we start.

Then a description of the association between the genotype and the health outcome, both in terms of relative effects or absolute effects, and how much of the outcome is explained by the genotype, and last but not least is the importance of this modification of the relationship between the genotype and the health outcome by other genes perhaps and also by the environmental factors.

So a lot of work has to go up front before you even get to the genetic test, and many, many of these things never make it to the point of a genetic test where it's offered, but once a genotype health outcome relationship is described, and claims are made about the utility of that genetic information, data collection begins right there and then. We don't have to wait any longer for that.

Now, as we go down the line, and you're probably all sick and tired of analytic validity, clinical validity and clinical utility, but as we advance through that spectrum or the continuum of data that are needed, and people think that there may be a test that should be offered, then these things come immediately to the forefront, and the reason I put them in the same box with the epidemiology is because I think there is a direct relationship between those clinical measures and laboratory measures and some of the epidemiologic data that we have collected in the research phase.

For example, clinical validity and associations are just different terms for the same thing, and they really describe genotype-phenotype relationships, and the way we approach it from a population perspective is sometimes different from approaching it and probably more valid in terms of inferences than convenient samples of cases that are collected.

Clinical utility and interactions have a lot of relationships because the interactions between different genes and environmental factors provide you with a hypothesis of the utility of information for clinical settings.

For example, in the context of Factor V Leiden mutation and venous thrombosis, the clinical question becomes should women be screened for Factor V Leiden before they take oral contraceptives, and that clinical utility question depends on

the description of the interaction between Factor V Leiden and oral contraceptive use.

Analytic validity is pervasive. Whether you're doing research or you're offering the test to patients, you have to have an assay that tells you that the genotype you have is accurately measured, and last but not least, we put the assay data in that box because as the data comes in on the various parameters, we should not forget about the impact of the genetic information on the psychosocial issues, and this committee is fairly familiar with that.

Now, through a miraculous process of review and whatever, now there is a genetic test. Think about the FDA process as sort of the bridge to get to a genetic test that's been offered on the market.

Now, what will happen then is that genetic tests become used, and therefore we need to collect more data on the use and impact of these genetic tests. There is a big feedback loop that goes back to that black box because these parameters are never static. Prevalence, associations, interactions, analytic validity.

These parameters keep changing long after a test is used, and also the impact of the use of tests, the practice parameters, laboratory performance, et cetera, et cetera, and then the eventual effect on reducing the burden of disease in the population kick in.

So in a way, it is rather artificial to talk about premarket and postmarket data because, as you can see, the premarket data that led to the development of tests is the same as the postmarket data once the test is on the market. It gets enhanced. You fill in more boxes, and more information comes to light.

We at the CDC have approached this problem from both sides, from the right-hand side, from the use and impact of the available tests, and then from the preside, if you will, emphasizing the epidemiologic and population aspects of genotype disease relationships.

Now, I want to tell you about the three things we've done the last couple of years and to shed some light on this, and then I'll give it to Tim for further

discussion.

Last year, we funded the ACCE Project, and ACCE refers to Analytic Validity, Clinical Validity, Clinical Utility and Ethical Issues, and this is a three-year project that the Foundation for Blood Research is in charge of, and the overall aim of this project is to develop and test a model system to assess the availability and usefulness of the existing data on DNA-based tests and algorithms, which may involve other than DNA.

So the specific aims of this is for each DNA test protocol, we'd like to identify the data sources, collect, analyze and interpret results, identify the gaps in knowledge and disseminate information.

Now, you have more in-depth information in Tabs 9 and 10, Attachment 9 and 10, about this project, and I'd like to give you briefly the thinking behind this, and this is, remember now, from the postmarket side, where data has already been available and collected, and the way this group, dynamite group, has been thinking about this is through this ACCE wheel, if you will, and each one of these terms, be it clinical validity, analytic validity or utility, has well-defined implications and meanings --

DR. McCABE: These are attachments under Tab 6.

DR. KHOURY: Okay. Attachment 9 and 10 in Tab 6, I guess.

MS. CARR: Yes, that's right.

DR. KHOURY: And what the group has done was to define a set of 40 questions that cover the whole wheel. Notice that the ethical, legal and social implications is sort of the pie, slice of the pie, that goes through all the phases from the clinical utility to the validity analytic side of things, and I don't have time to go in-depth into each one of these questions, but I want to give you a sample of how they've approached this problem, and basically what we're doing this year is finish up the work that we already started on cystic fibrosis and hemochromatosis last year, and the intended use of the setting -- I mean, we discussed this at length yesterday.

Take cystic fibrosis, for example. There are three settings of use, one in the carrier testing phase, one is for newborn screening, and the third is in the diagnostic setting, and each one of these is a separate wheel. Each one of these carries its own data around clinical validity and utility, and right now, they're almost done with the carrier testing side of things on cystic fibrosis.

We're going to move to iron overload, hemochromatosis, and then Factor V Leiden, later on this summer, and the examples that you have of the 40 questions, we took one of them, which is Question 20, and I think you have that attachment, and the systematic way of approaching data is manifested.

I have a draft of the cystic fibrosis analysis, which is a very thick one, and obviously for time purposes, I'm not going to share it with you, but perhaps at the August discussions, when we have that.

Now, is this different from the FDA's template? Of course it's different a little bit, but it's sort of along the continuum of data collection from the pre to the post, and the emphasis will be increasingly on clinical validity and clinical utility, as these tests become used.

So I'll be happy to answer questions about that project, but obviously I'm not doing a good service to it by describing it to you very concisely but perhaps in some other time.

So let me switch gears to some of the HuGE Net activities, and as you will see fairly quickly how these will feed into the knowledge base that we need to fill that gap between gene discoveries and clinical utility.

The HuGE Net, for those of you who haven't heard, is sort of a collaborative project that was launched in 1998 by CDC and many, many partners, with the implicit and explicit purpose of the collection of the knowledge base on epidemiologic aspects of genes and the relationship to disease, essentially the same kinds of data that I showed you earlier in that black box, and we want to do it collaboratively. We want to build that knowledge base and disseminate it.

So far, the HuGE Net collaboration has a steering committee, an editorial board, and all kinds of little informal groups that hopefully are making it a better approach. So far, the two main activities that have been done are the HuGE reviews and the HuGE fact sheets, and there are examples of each at Tabs 1, 2, 3, 4 and 5 that you can refer to or you can read at your leisure.

But basically, the HuGE review, and I have an example of that in your packet on hemochromatosis, takes a systematic look at all these questions on data, from prevalence all the way to clinical utility, and sees what the published literature says, and admittedly this is an analysis of published literature. So it has to be enhanced with unpublished literature.

So far, it has been driven by people who want to do them. So it hasn't been systematic in the sense that we identify that we need six HuGE reviews in this area. You can see from the list of HuGE reviews that are already done, and those that will be done in the next few months, that there is a wide collection of these that will become online.

The condensed version of a HuGE review is a fact sheet. So you take the information fairly quickly and put it in a one-sheet format.

In addition to these, and since last October, as part of our weekly online update of genetic information, our HuGE Net coordinator has begun abstracting through a complicated algorithm all the abstracts from the literature that have something to do with HuGE, and the way we do it is through a very complicated Medline search algorithm that is highly sensitive but not specific. So there is a lot of hand searching that needs to be done, and I'll show you a very specific example of what that database looks like.

Now, in order to do the work, we've come to realize that it's very hard to assemble epidemiologic and clinical data from the literature. So last January, we put together an expert panel workshop that some of you have attended where the explicit goal of coming up with guidelines for how we review individual studies, and how we

can put them together towards creation of the evidence base that we need to assemble literature, and there are three papers that are being written as we speak that will provide some concrete recommendations of how we assemble that literature on (a) genetic test, (b) gene/environment interaction, and (c) the simple gene/disease relationship.

Last but not least, we've come to realize fairly quickly that in order to push the HuGE agenda forward, we're going to have to differentiate by working groups, by disease categories, because that's how the funding stream and how most investigators are driven by emphasis on certain diseases.

So later on this month, we're going to launch the first HuGE working group, which will be a HuGE Cancer Working Group, and hopefully when you leave that to the expert, then the cancer genetic information will flourish more than in an undifferentiated way. With some funding hopefully, we'll provide three of such working groups in the next year or two.

So this is to summarize where we are, and leading into this information, HuGE information system that I'll talk about very briefly, two ways we've attacked the problem. One, completely from the postmarket phase, use and impact. This is the ACCE Project, and there are some other projects we're doing.

There are some collaborative projects with the Division of Laboratory Systems, looking at the data on reporting and the different forms of how genetic test results are delivered from the labs, and there are some other things that I don't have time to talk to about this morning.

And then from the premarket side, if you will, is assembling that literature that may or may not feed into the development of genetic tests, but when it does, we'll be ready for it because that literature will have been assembled in a systematic way that can provide the base upon which one can perhaps make some informed decisions or discussions about the usefulness of these tests.

So last, I'd like to walk you through this information system that is right now in the works. There is only one part of it that is ready to go online in the next

few weeks. So it starts with something like a query. You come into the system, and you ask about HuGE-type information, and you can do it by gene, by disease or environmental factor, and then, Step Number 2, you choose the category of information you want, be it prevalence, association, interactions or genetic tests.

Then Step Number 3 gives you the data source from which each one of these informations can be given to you, either from a HuGE review or a fact sheet, from an ACCE review or a fact sheet, from the published literature database, which I'll give you a quick demo of it as we speak, from CDC reports and other reports, from the Disease Working Groups as they will begin to be developed, and then the links, the links to other online information, like GeneTests and OMIM and other things and resources, and the output can be either in a detailed format, in a tabular format or in a summary format.

I'd like to show you what this might look like. We've done this search for one disease, asthma. So we took a complex disease like asthma, and we abstracted all the information from PubMed, and this is only that abstract database I talked to you about, and Step Number 1, you choose either Genes, Health Outcomes or Environmental Factors, and in this case, asthma was highlighted, and when you highlight asthma, two things come to you.

One, all the genes that have been described in relation to asthma. You know, you have interleukin-3, interleukin-4, et cetera, all the environmental factors, like house dust, mites, smoking, et cetera, and then you go on to select which type of information you want.

In this case, I don't think we selected anything, and Step Number 3 is the tabular format of how we want to see the kind of data, and this is what this will give you. This is basically a sample of that kind of literature with the options of having abstracts, study design, study populations and methods exploded and looked at and evaluated.

Once we have an Asthma Working Group going, then that group will

actually provide the value added. This is fairly descriptive to show you what we have, and the table that I just sent around shows you what the asthma database looks like, and this is the database from 1990 and onwards, and that big table first shows you the number of articles on the extreme right-hand side.

Of course, the initial search algorithm gives you thousands more, but then after review, we end up with only a 120+ articles, and you can see most of the literature on genetics of asthma has come in the last couple of years actually. The number of articles in 2000 and 1999 is much more, and then the HuGE category, you have the number of articles, the kind of design, the kind of outcome, the kind of environmental factors, and the number of articles, and on the second page, you have the findings in relation to specific genes, and what the genes are, and we don't have to go through this fairly much in detail.

But many studies are negative, some studies are positive, and we view this as only one piece of the puzzle, if you will, around the HuGE information that we're thinking about.

So to wrap it up fairly quickly, right now, if you come to our HuGE information system, and you click on methylene tetrahydrofolate reductase, this is what you'd expect to see. You would see a HuGE review that reviews the relationship between MTHFR and birth defects with a specific focus on neural tube defects.

There is another HuGE review coming online on cardiovascular disease, which hopefully will be finished in the next few weeks. You will get the flavor of what the HuGE published literature database has, and you will see some CDC reports on prevalence, and I'll give you an example of that.

There is an international collaboration on the prevalence of the MTHFR variants out of many countries in which that information will be online soon, and then the association between MTHFR and neural tube defects through a meta-analysis that we've done a couple of years ago describing what that is, and, of course, you'll get the links to GeneTests and GeneClinics and OMIM and all the rest.

If you come and search by disease, hemochromatosis, you will see the HuGE review that is in your packet. Very soon, in the next few weeks, a few months, you will see the analysis of the ACCE Project from the Foundation for Blood Research. Of course, you will see the HuGE published literature database, and you'll see two important pieces of information that are original CDC projects.

This week in JAMA, there is an article on the prevalence of the mutations using the NHANES DNA Bank, which is a national representative sample. This is a project that Karen Steinberg from our lab is the primary author on, and it shows once and for all that the prevalence of these gene variants are X, Y and Z in different populations.

You will see some estimates of the penetrance. This is the kind of pooled analysis that Wylie did when she was at the CDC, will be highlighted, of course, with all its bells and whistles and the lack of information, and, of course, you will see the links to different values.

And now if you search on environmental factors, like lead, you will see a HuGE review that connects lead to a specific gene, the ALAD gene. You'll get the HuGE published literature, and you'll have some prevalence data on the prevalence of lead in the population again from the environmental report that our center has put out. Again, it's from the National NHANES, and you'll see a lot of links.

So in summary, before I give it to Tim to continue this discussion, we have started a long, slow process. I mean, data is not easy. We have realized that from the beginning, that there are no guidelines, no standards, and it's going to take awhile before these things come together, and to me, the hope is that when we collaboratively with the other agencies and the private sector begin to attack the problem from these different angles, and then once the data begin to be filled by these various groups, that there will be a concerted effort to coordinate the dissemination of that information, so that everybody can be helped by that information.

There is one of the attachments, Attachment Number 12, which is sort

of a Qs and As by three different kinds of audiences, policymakers, professionals and the public, who might come to, let's say, a coordinated information test system and ask of that system different questions that may be different.

So the emphasis is not necessarily only on health providers but also on the general public and on researchers because we think identifying the research gaps and showing the empty boxes, to me, at this early phase of the translation of the Human Genome Project, is as crucial as having a box filled with bad data and bad information.

So I think we'll answer the questions after Tim is finished with his presentation.

Tim?

MR. BAKER: Good morning. If anybody's got any question about Muin's excitement about data, you can clearly see any time he talks, he gets this fever, and when you stay with him every day, it's very infectious.

As Ed introduced this, one of the things that we attempted to undertake is a response to this committee's recommendations to the Department and the Department's subsequent action in asking CDC to take a lead in a coordinated genetic testing information system.

The challenge, of course, is defining what that is and being fully inclusive in that process, and it's being started by HHS, but it is intended to be fully inclusive of all other agencies and non-agencies as well.

First of all, let me clarify what we're not talking about. What we're not talking about in this part of the presentation is a CDC system. This is not going to be something the CDC does, not even CDC leading, but it's something that CDC is going to try to initiate and try to get started and find out the best way of getting that accomplished.

Secondly, it's not even probably going to be an HHS system. It's certainly going to be a coordinated effort amongst a lot of organizations.

Third, it is not going to be any kind of a single system. There's not

going to be a database ever of all this information. There's not going to be a single access or one monolithic mainframe somewhere that captures and keeps everything, and, finally, this certainly isn't anything we're going to do in a year or maybe two years.

This is going to be a very long-term challenge for all the things you're struggling with, and then how do we effectively include that in a process that increasingly makes information available.

Now, going back to ED, as we always do, we're adding to that equation of what we know and don't know, and what we don't know that we don't know, not who's going to know what we know. That's one of the challenges we're trying to address, is helping people figure out who has what we do know in such a way they can come and get it until we know more.

Now, what I've tried to capture here is the problem, and the problem is the errors. What your committee is struggling with, and we have been struggling with with you, is there are a number of sources of data on the left that are going in a number of forms to a number of organizations that's being transformed into a number of different kinds of information that may or may not be available to users on the far right, and actually on this slide, I probably should be starting with frowns instead of smiles.

Perhaps the goal of this will be to take frowny faces and make them smiley faces in the future because a number of people are complaining about the access to information, but the clear problem here that we're trying to address is simply how do we improve user access to available information?

You see in the center, we've made a shift from data on the left to information. That distinction is very important because a lot of data, and then how do we transform that into something that says something that's useful, and then how do people come and fetch that in the various forms that meet Barbara's question about how is it met in a form that addresses consumers' needs while it meets Wylie's concern about it having a certain structure of response that the providers need. Perhaps the same information, but extracted in a way that it's responsive to everybody's needs. That's the

challenge.

Now, what we're trying to focus on here is reducing the number of errors on the left, increasing the -- and this is really building off of everything you're talking about here. How do you structure the data in such a way that you reduce the number of places it needs to go to create the information types you see in the middle in red because it's various information types we keep talking about that exist in various organizations.

So the focus here is not on whose organization has it. It's a method of defining what is the kind of information we're all trying to capture collectively? Who is best positioned to do that? Who is already doing it? In what way can we characterize that more effectively and consistently, so that as you see at the top of that, information being made available.

Now, the focus here, the challenge we're trying to address is not information an agency has or an organization has, but information they're attempting to make available. The notion of this is how do we collect it and disseminate it? Okay.

So we're trying to make that shift beyond the work of capturing and organizing it so that we can answer some internal questions into how do we ensure that people can come and get it in a way they can use it? Much of the discussion has been going on, so I'm not going to belabor those points.

Now, we come to the two challenges that Muin was talking about, and this is really taking that slide and focusing in on two sides of this equation, and this side of the equation is really part and parcel of what Wylie's Data Committee is going to be doing and has been doing and will continue to do, and what Steve talked about yesterday in terms of defining the data templates, the data constructs, the structure necessary to enable whoever produces data, whoever the source of data may be, to efficiently provide that in a way that increases its compatibility, increases consistency, so it can be assembled into information more effectively in fewer places.

These are grand terms. I mean, those are so easy to say, and anybody

that's done that knows that, you know, it's kind of naive to even make a statement like that with the complexity of data here, but the fact is that's the challenge we're trying to meet. Otherwise, there's not going to be any purpose of trying to simplify the data and make it more integratable, to make it more functional, to make it more useful.

We have to meet this challenge of making it fit through a common core framework, common data templates, where it's relevant, increase efficiency of that at the beginning of this process, not after we are any further into it, at the beginning, so that we know the extent to which you can accomplish the goals in the Data Committee, and those template processes and initial data collection and make that data collection as seamless as possible throughout postmarketing data collection.

You will make so much easier everybody's lives as far as reducing the duplication in the center of all the organizations that should have it and certainly increasing the efficiency of all the organizations on the right side, individuals on the right side, that are trying to come and fetch it.

Now, I've gotten gray dealing with information systems through the years, and I know that this is a very painful process, but we're consciously focusing on both sides of this equation at the same time because one informs the other. You can't just do the data side on the left, this challenge of integrating data collection and management, and frankly I left the HHS data collection up on the top of this because, as Dr. McCabe said, this is the response to the Department's challenge to us to get the agencies working together, to coordinate its data collection, and then to be inclusive with all other organizations as well, such as GeneTests that Dr. Gutman mentioned, and others, that clearly have a high volume of the data, most of the data in some cases, and how do we make sure that's available, so that when Dr. Atkins starts doing evidence-based review for the Preventive Services Task Force, there's a common consistent way of getting to not only published literature but some of the unpublished data that is fragmented in various places because of the fairly early nature of this data.

Now, the process on the right is really the harder challenge, and that

certainly has to be met, and this is really more the challenge that I think our discussions are leading us to.

Muin touched on some of those earlier when he was using some of the examples that clearly worked together on this. Some of the tests and some of the questions that will come from different users that will be accessing the information in the center, the kinds of questions that might need different sources.

Remember, a lot of these users don't know what a gene test is. They don't live in the genetics world. They don't know what these acronyms mean in the middle. Probably some of the people in the room don't know what these acronyms in the middle mean.

There are organizations that have been working on this for a very, very long time, but now we're talking about opening this door very wide to policymakers, the public, professionals, opinion leaders, legislators, whoever, who are saying is there something I should know at a very high level? Is there a way I can go through a common gateway?

It was mentioned yesterday a search engine. Sure. This includes a search engine or engines. It involves a variety of tools that need to be necessary in paper form that responds to the certain groups' needs, that responds to the different methods that anybody can come to get the information that we're envisioning being contained in this central box, and also to tell us where the gaps are, because the principal process that we learned from defining this access process on the right is what don't we have? What haven't we thought about?

So as we're talking about the kinds of questions that need to be asked by providers, and the kind of questions to be asked by the public and by consumers and by opinion leaders, as they tell us what they're looking for, and the us being us, then we have to look over here on the left side of the equation and say are we getting that data? Is it being translated into information that makes sense?

There was a discussion yesterday about Muin couldn't find some

information on the template report that Dr. Gutman put up. That's a minor consideration when you think about all the different ways people are going to be misinterpreting all the kinds of information that need to be made available.

The worst thing we can all do is duplicate our efforts. So our challenge, as was noted in the beginning, is to try to coordinate this effort from the beginning, try to anticipate what the Data Committee work is, bring together the organizations who are information organizations, who attempted to make available information, and to try to articulate what the various kinds of access are by different audiences and try to define that, identify the gaps and facilitate that.

Now, where we are in the process is we've had a conference call. This is very early in the process of trying to articulate much beyond this vision. So I don't have a time line. We don't have the software bought yet. We haven't designed the system. This is very, very early in considering what the challenges are. That's why they've been articulated as two different challenges, and acknowledging Challenge 1 really is going to grow larger from the Data Committee here in defining that.

Our challenge is to complement that with what kind of access, what kind of questions the different audiences are going to be important in helping to shape the work that you're doing in the Data Committee. We intend to be fully coordinated with the stakeholders meeting that Wylie Burke is handling.

We are going to put together whatever panels and whatever groups are necessary and appropriate along with the HHS agencies and other collaborating organizations, to decide what we need to do to create a coordinated system.

Let me reiterate. We don't see CDC as being the one doing this. We're going to help in this process. We're going to contribute to this process. You see that what Muin was talking about was basically the CDC circle in the middle. That's our contribution to this process.

Epidemiological and clinical information and some test information. Clearly, FDA has got a ton of the lab information and some of the clinical information.

HRSA's got information. GeneTests may be the repository where we put this information, and that's the best solution or it could be that we end up saying anything about services goes to NORD or any question about a particular disease goes to OMIM, and we have to improve that to make sure that's responsive as a group.

So this is not about who's going to be the one doing it. This is about defining the options, what kind of content, what's the best solution, investing resources there to make it work, but don't think that this is anything that CDC is doing a grandstand and saying, well, we're going to build the big empire down in Atlanta and buy all the Cray computers in the world and start crunching all this data for everybody.

The final tone that we're going to leave this discussion on are these questions that Muin put up initially, were the two kinds of challenges. The kind of data that would need to be collected, the plan for that data. We provide input as a group to the SACGT on data formats and work with all the other non-HHS organizations, and then strategies and options for improving efficiency of collection.

Keep in mind the extent to which we can make this data collection efficient, to reduce duplication of costs and effort, and there's enough to do without duplication, and then, finally, how do we improve access to that available information, and this is going to be very much an envisioning process.

I don't know if Alan Guttmacher is still here, but Alan's been leading a group called Genetic Resources on the Web, which is to look at the various technology-based tools for organizing available information.

Now, one of the challenges that you have to meet with the technology side is the content side. Technology is a tool. It assists you in doing the work, but getting that information defined, determining how you want that search engine to go fetch the information for providers separate from the public, when a search engine doesn't work for certain communities.

Some general comments about how do you extract something into a printed template and make it widely available. These are all technologies we use every

day, but the technology solution is only a tool, only a way to get it done, a very important tool for this data, but only a tool, and we have to help sharpen what the information is and then sharpen our options for doing that and then put some resources behind it, and clearly there's a whole lot of money already being invested in this.

The question is from a business point of view, is there a more efficient way of focusing those resources to reduce that duplication and supplement those resources with sufficient amount to really make this an achievable goal?

The balance between data collection and dissemination is really the issue, and then we're going to have to prototype some pilot projects, such as the ones that we're hearing described here and others all around. We don't have any specific time line. We're going to wait for your guidance as a group here. We're listening to the Data Committee's input, the agency's conference call that we initially had.

We basically decided to postpone any further action, pending feedback of this group as well as the work of the Data Committee.

So we're prepared and ready to assist in this process and look forward to working with you on it.

DR. McCABE: Thank you, Tim.

Before we get into a general discussion, are there any specific points of clarification for Dr. Khoury or Mr. Baker?

DR. KOENIG: Ed?

DR. McCABE: Yes?

DR. KOENIG: I just had a quick question about some of the presentation by Muin. Is this similar to the idea of the Cochrane Report in terms of -- and could you just clarify for me what the differences are, especially the HuGE --

DR. KHOURY: Yes, the Cochrane Group is a virtual collaboration of people from around the world that have been looking at evidence-based medicine, and genetics hasn't been on the radar screen yet, and what they do is they have annual meetings and collaborative work to do meta-analysis. For example, does aspirin prevent

heart disease? Is chiropractic good for low back pain? Things like that.

So they go review both published and unpublished literature and come up with Cochrane Collaboration-type briefs and statements, and this has been a fantastic movement that was driven by Archie Cochrane initially and then has continued as a legacy, and I think they are supported, if anything, primarily by AHRQ as a group from their evidence-based centers, and we had a representative from them at our HuGE workshop in January.

What we're talking about here is the whole spectrum of data, and obviously they're focusing on clinical utility, and before you get there, I think the problem with much of the genetic information is it's just too early. I mean, we're not there yet, and I guess what Tim and I have presented is an anticipation that the volume of data, because of the thousands and thousands of genes and with what we see every week, is going to expand rapidly, that unless we have a proactive way to collect and coordinate that data, that it may -- you know, 10 years from now, it's going to be completely chaotic to try to do this work.

DR. McCABE: David, do you want to comment on the Cochrane Report?

DR. LANIER: No. I think Muin explained it pretty well, that the focus of the Cochrane is much more on clinical utility and analyzing that data and coming up with recommendations for practice.

DR. McCABE: Any other specific points of clarification?

(No response.)

DR. McCABE: If not, why don't the two of you join us at the table here for the discussion or wherever you would like to sit comfortably, Muin.

So what about then some general discussion about these kinds of efforts of data collection and dissemination?

DR. BURKE: I actually think the comment about the Cochrane Collaboration is important and it fits with the point that I heard Tim and Muin both

saying, and that is there's already a lot going on, it's going on in a lot of different places, and one of the early tasks, in addition to figuring out what information is most important for the use of genetic testing, is finding out where that information is and basically creating links to it.

So I think there's a piece that's probably a pretty tough piece that will happen slow, which is creating those data systems that don't exist, but much earlier than that, it's finding out what's out there.

The Cochrane Collaboration is focused on clinical utility. We don't have much data on clinical utility in genetics, but we will, and when we do, Cochrane's going to be very interested in that, and we don't need to reinvent that wheel. We just need to have the connections in place, so that we know what they're doing and connect people who need to know about genetic tests/clinical utility information to that.

I mean, that's an example of a piece that might feel like housekeeping but is a central function of this kind of process.

DR. KHOURY: Can I add to that? Can I just respond quickly? You can even be more proactive than that. You can push them in that direction.

Actually one of the meetings of Cochrane that I attended in Baltimore a couple of years ago, they were thinking of creating a genetics interest group, what they called "fields." I mean, they have this weird terminology that is called "fields."

I mean, they have working groups around different diseases, but "fields" are cross-cutting across different disease entities, and it's going to take some time, but if they become interested, they begin to see some of the questions that need to be answered. You know, does BRCA1 testing reduce the risk of breast cancer? I mean, things like that, then follow with tamoxifen, whatever. I mean, they will become very quickly interested.

One of the non-clinical trial undertaking they did, which was pulling together the observation data around the relationship between HIV and chemokine receptor gene polymorphism. This is the only example of a non-clinical trial in genetics

that I know that they are doing right now.

But to work with them early on and be proactive and work with all these organizations, GeneTests, et cetera, and having some common ways or templates to look at data, then I think we will be great.

DR. McCABE: Yes, David?

DR. LANIER: Just one thing I would add is that in terms of the clinical utility data, the Cochrane Group really has a strong emphasis on randomized controlled trials, and that would be a challenge to shift the group over to looking at perhaps less rigorous forms of data for consideration.

The parallel to that within AHRQ is the evidence-based practice centers that we've established. We have 12 centers that are on a contract with us to specifically review all the published literature, and in some cases, they go to unpublished literature as well around one particular topic.

It's usually very disease-specific rather than test-specific, but I think there's a nice overlap between what we do and what the Cochrane Group does, and I think with the evidence-based practice centers, it may be possible as well to push them away from such a reliance on randomized controlled trials, which will be relatively infrequent, I think, in the near future.

DR. McCABE: Yes, Mary?

MS. DAVIDSON: Yes. I wanted to pick up on, Wylie, on your comment because I think it's really critical that we look at the flow of information and how people are getting information now, and one of the pieces that immediately struck me in looking at the diagram, and, of course, I think in terms of information delivery organizations, you're looking at more umbrella organizations, but in fact, when you're talking about rare diseases, people really end up going in particular to the voluntary health organizations or genetic support groups for that particular condition.

It's important to find the tie-in with this system because that is where the public ends up going, and there are lots of -- how shall I describe this? -- tensions or

challenges because a lot of, in particular the rare conditions, specific groups really feel that they have a sense of where the research is in their particular condition and very often have real problems with the kinds of information that's being disseminated on a central basis not only by public or government organizations but by some of the other umbrella organizations.

So I think it's important, and I'm sure there are other gaps. I mean, that's just one that we at the Genetic Alliance certainly have our eyes on right now.

DR. McCABE: Wylie?

DR. BURKE: Yes, I think you also brought out something that is a tremendous problem in coordination, and that is information is very uneven.

There are advocacy organizations for some conditions who take strong positions, that people informed by an evidence-based approach might disagree with, and then there are some inaccuracies in some sites, and I think that somehow there has to be some thinking about how you create the linkages, and at what level and when and where you do judgments about quality of information versus simply informing people about information being available.

I think it's a tough problem.

DR. McCABE: Judy?

DR. LEWIS: Just to follow up on that point, I think there are all different kinds of information, and for some decisions, it's the random clinical trial and the evidence-based that's important, and for other decisions, it may be some of that more qualitative data is important in terms of some quality of life issues that's so subjective, that it can't be put through a randomized clinical trial because you can't choose whether or not to have the disease and go back and do it over again.

But what you can do is you can look at the various kinds of information, know the level of the data, and all information is valuable when people are making decisions. They are looking at evidence-based information. They're looking at qualitative information. They're looking at information from the experience of

somebody who's been there and just having a sense of the level of the information. You know, not necessarily removing it but just giving people the sense of what is the level of information, and that'll help people figure out how to use it.

DR. McCABE: Yes, please, Joann?

DR. BOUGHMAN: It seems to me that at least in Part 2, the questions raised by the SACGT and at the suggestion of the Secretary and others that CDC has in fact taken some very good initial steps, I wonder if I might ask what your next steps or plans would really be? Where do we go from here?

We've heard about a couple of areas of gaps, but how now do we make the next step and start kicking it up a notch to a level of the complexity and include some of the other organization and touch points that we've mentioned?

DR. KHOURY: Let me answer part of this, and Tim, you feel free to kick in.

There is two parts to this. One, we are going full speed with our HuGE information system. I mean, sort of the CDC small box there that you see in the midst of that. A lot of these activities, although they are collaborative in basis, I think we have a good handle on them.

Now, I think the next steps towards the coordination of all that information depends to a large extent on the discussions that are going to go on in this committee at the August meeting, our Interagency Working Group, and frankly, I think this committee has really paved the way for that kind of discussion to go on because now, I think people can see a little bit the light at the end of the tunnel, because I think we're all together creating the framework or the empty boxes that need to be filled.

The FDA premarket process will fill some of these boxes. The postmarket processes will fill some other boxes. Services delivery and the evidence-based center will fill some other boxes. So I think we're on the right track. It's just a question of that ultimate coordination, and we intend fully to engage with the discussions with the other agencies and see what the best way to address these two

challenges. But I think the meeting in August is going to be extremely important along those lines.

Tim, do you want to comment?

MR. BAKER: And that's primarily for Challenge 1, but also certainly the Challenge 2 as well.

The members of the Interagency Working Group who have been working forward on this coordinated system are also members of the Data Committee, almost to a person perhaps, I think, and therefore we are waiting for the guidance from the Data Committee around the data models and so forth, and we have not yet scheduled an additional meeting.

We have not planned any sort of a project proposal at this point. Certainly CDC has worked on this part of it, and you see all the work that FDA is doing, and we have a lot that's moving ahead, that's going to guide that process.

We do expect to report to the Department soon on our progress along this line because we feel an obligation to do that. So some time in the next couple of months, we're going to have to provide a summary report that will include this committee's input and Wylie's particularly, their committee's input, and capture that plan and setting a time line for what we think we could do as agencies, and when and how we go beyond the stakeholder meeting in August to include others.

DR. McCABE: Wylie, did you have a comment on this?

DR. BURKE: Well, yes, just to directly comment, and I'd appreciate comments from other members of the Data Team, but it seems to me, in light of the things that you've just shown to us, that the best preparation for the August meeting in terms of this element is two-fold.

One is identifying all the stakeholder positions that should be around the table discussing these issues, and I think we need help from the committee in making sure that we do that right, and the other probably would be for the collaborative group to come to the August meeting with a proposal for a template, and I think we can

be very concrete.

Does the set of information that one wants to have access to in postmarket data collection comprise exactly the same data as in the premarket or are there additional boxes?

I think it's really as simple as that, and that's not assuming who's going to fill what box because I think what you're making very clear to us is that it might be that certain boxes go to certain Websites, and other boxes to other Websites, but it's what are the boxes?

I think to the extent that the collaborative group, the interagency collaborative group could come with proposals about that, I think that would help the August meeting.

DR. McCABE: Ann, and then Barbara.

MS. BOLDT: This is really a follow-up to Mary's comments, too, and I think this is a wonderful start to the coordinated system.

I guess another link that I would want to make sure is having the resource link to health professionals with expertise in genetics, and I know that since you're using the GROW Consortium, too, that will be a great way to get that information, too.

DR. McCABE: Barbara?

DR. KOENIG: I have two sort of conceptual issues with how these data sources are going to be set up and understood, and the first has to do with the issue of what is or are the diseases that are going to be the focus, because it seems to me -- or that as we move increasingly into things that are more complex, involve behavioral genetics issues, et cetera, that a lot of this is based on the notion, it seems to me, that all of these associations are with something, with X, and it's not clear to me, and it may just be because of the lack of knowledge on my part, how the difficulty of making those assignments of what is a disease -- hemochromatosis is a good example, but it's in psychiatric illnesses, it's even more complicated. It seems to me that it just seems all

too neat to me the way you set it up, but I'm wondering what happens when you have very complex -- how does that get into this?

Then I have a second question about ancestry. I can wait a second turn if there's other discussion.

DR. KHOURY: It's not that neat, Barbara. It's complicated. You know, our initial foray into this was driven by the database, the GeneTests analysis, and the initial classification attempts by SACGT and our own public health-driven considerations of the magnitude and burden of disease.

So this may be different for different organizations. The focus of CDC has been primarily on the integration of genetics and genomics into the complex diseases. I mean, we're not abandoning the world of single-gene disorders, but we want to at the outset define and go more into depth into that complex world of diseases like you've seen with this lumbar -- you know, the lower back disease example, and cancer and other things.

So we have a set of those priorities. Of the 750 tests, there's probably 50 that we can start on. Probably half of them have to do with newborn screening because they affect virtually every newborn. There's a lot of discussion about tandem mass spec and some of these fatty acid oxidation problems, although rare, but the genetic testing affects everyone.

Cystic fibrosis, et cetera, and as you move into the adult world, we go into sort of the public health-driven burden of disease, cancer and heart disease and diabetes and these things.

Now, the approach that has been adopted by different groups is essentially genetic. It might have to be tweaked, and I think there may be some major distinctions between low penetrance versus high penetrance genes, but other than that, the prevalence is the same thing. You define analytic validity and clinical validity the same way, and as FDA experiments more with the premarket template -- and I mean I appreciate Wylie's challenge to us.

We can get together here, and I think we have a lot of stuff that has been brought to the last two days. We can get the agencies together and look at the continuum of data from the premarket to the postmarket that has been collected and also involve the other organizations because I know HRSA is involved with a lot of data collection specifically around newborn screening conditions and AHRQ and NIH, of course.

So I mean we can try to do some homework between now and August, if the committee wants to see something more concrete. I don't know how much of a concrete proposal we'll be able to make, but at least we'll put the data side-by-side and see how we can begin to digest them.

DR. McCABE: Barbara, did you want to follow up with your other question?

DR. KOENIG: Yes. The second question is in terms of how the data will be stratified in terms of genetic variation across the human population, and we've had some discussions about how we might best do that in the most scientifically-appropriate way without creating additional burdens and social harms.

It seems to me that that might be something where we could make a contribution in terms of making some suggestions and recommendations about how to collect those data in terms of whether to think about using words like "continental ancestry" rather than race or figuring out what the meaningful categories would be to look at.

DR. KHOURY: I agree, Barbara. I think that there are two parts to this. One is what's the ideal data, and then second is what's the data that exists out there?

As you know, our public health system still collects antiquated data by race and ethnicity and things like that. So this is what exists, and this is what vital records and hospital records and medical records deal with.

So we're going to deal with those because that's what we have, but as

we think of more creative ways, I think that input would be very useful for the future.

DR. KOENIG: Right. Can I just follow up? But in particular, since it's fairly clear the ways in which those traditional categories are inappropriate in genetics, that this would be a leadership role that we could take.

DR. KHOURY: I agree.

DR. McCABE: I have a couple of questions, comments. One is that this is an incredibly intense effort, the way you've described it, in going from title to abstract.

I'm wondering if you're beginning to think about using any of the new informatic tools that are really involved in data mining, automated data mining, because if one tries to mount this disease by disease, it'll take forever, and we'll never have adequate databases.

MR. BAKER: Clearly, when we're talking about tools, we're talking about all sorts of intelligent engines that are going to have to be accessing distributed data.

One of the challenges in accessing data is the extent to which it's compatible and is more reliable. So if it's in three locations, but it could be aggregated in such a way useful, and then if it knows you're a clinician when you come in, you're profiled that way, that engine is responsive.

So those tools are inherently a part of the access tools we're talking about. However --

DR. McCABE: I was thinking more, though, in terms of your building the databases, and there's some things happening now where just search tools that are constant -- there's one that was developed by the Cal Tech spinoff that's now been purchased by Celera, the company has been.

They now have moved into genomics which was always the area they wanted to be in, but up until the last year or so, when they were purchased by Celera, their biggest client was the U.S. Government, and they wouldn't say how their machines

were being used, but it seemed to be State Department and security-type things. So they just were scanning all of the world's literature every day looking for appropriate groups of words that would then identify topics of interest to the various agencies.

So there are these ways that just go out and are constantly surveying whatever is being produced anywhere and are actually pretty intelligent.

DR. KHOURY: I mean, obviously we'll explore all available tools and means. Having said that, however, part of the problem here is the value added, and sort of when you look at a report, you want to go beyond gene name or exposure on a disease outcome. You want to be able to go in there and provide the value added as to whether the study is good design or not good design and score it somehow and distill the conclusions in a way that sometimes the report itself doesn't tell you what the data looks like, and that's more of an intensive effort.

It was a large part of our discussion during the January meeting we had about that, and that would involve essentially really a fairly intensive look, and that's why in a way, I am eager to begin this differentiation by disease and let the agencies and groups to begin to own this.

For example, NCI, we have lots of discussions with NCI about the Cancer HuGE Working Group because I know NCI is doing a lot of these collaborative efforts, and we'd like to do the same with all the institutes at NIH and then with the other agencies because eventually, the concentration of resources and expertise is by disease, not by gene. But we'll use all available means for data mining that will come to the market.

MR. BAKER: We would hope that that kind of observation that you're talking about would be what our colleagues on this committee as well as the multiagency will bring forward. That's the best solution. That's where we'd see investing in that solution, finding what's already being done that could be capitalized on and then strengthening that.

Let me add to what Mary Davidson was saying earlier. None of this

we're talking about can replace the information intermediaries, we call them, that are people that have to come obtain the data and translate it and validate it, so that what information comes from the various sources that we're all talking about.

If it comes out of my mouth, it means less than if it comes out of somebody of that community's mouth. So enabling that community, whoever that community is, to own it and be channeled into their resource in a way that's meaningful, we see that as a natural part of this access system.

Helping them get to the information is a challenge. Helping them to put it in a form that's useful to them is another challenge. It's a part of the whole access continuum that again I learned from dealing with HIV in the early days, of making sure consumers and professionals had the same information at the same time in their own way, or else you'd pay for it.

DR. McCABE: One other comment before the other people on the list here, and that has to do with the genotype-phenotype or genotype environment of phenotype.

There's a lot of evidence coming out now that many of us have gotten into molecular genetics, thinking it would help, that we could define phenotype by genotype, and it would help us with diagnosis and prognosis, and we're learning that that's not the case.

As one of our M.D./Ph.D. students pointed out, why did we ever think that humans would be different than fruit flies where they've known this forever? So that there are going to be modifier genes and modifying influences of the environment.

I think it's going to be very important because as we make that recognition, then we also have to recognize that we're going to continue to be in a probablistic world, and if you have a specific mutation, you may have a 95 percent probability of having one genotype but a 3 percent probability of having a slightly different phenotype and 2 percent of having even a different phenotype.

I think it's very, very important that some group, where there's going

to be access from non-genetics professionals to these data, will begin to catalog this type of information, so that if a patient walks into any health professional's office, they're going to be able to have knowledgeable information and not rely on that professional being able to quickly go back and synthesize the literature in this area.

I have Pat, Steve, and Joann.

DR. CHARACHE: I have a question that gets back to one of Barbara's and Mary's comments, and that's where the data's going to come from in the postmarket period, if we want to know more about the prevalence in different populations and penetrance, particularly for rare diseases.

How is that data going to be forthcoming? With the rare diseases, there may be very few labs testing for it, and the lab that's doing the testing will have no contact with the patient. We know that if we rely on the clinicians to report diseases, like communicable diseases, this has not been successful in getting a high percent return, and if it's the requirement for flagging these individuals are put on the laboratory, we've got all kinds of issues of security, confidentiality, laboratories doing a lot of work for which they're not reimbursed.

So I'm wondering how we're going to find out what penetrance is and all these postmarket things because NIH tends to lose interest on postmarkets.

DR. KHOURY: I agree, Pat. I mean, this is a big challenge. There are several approaches that come to mind. One is sort of some of these population-based registries or surveillance systems, like the birth defect surveillance systems that exist around the country.

Many states have them, and they register birth defects and many but not all single-gene disorders, and a lot of useful applied research and prevalence and case-control studies have been done over the years through these.

The other approach is driven by the consumers themselves. There is a lot of activities around disease-specific consortia that are driven by the consumers around specific diseases where they assemble registries and do genotype-phenotype

correlation, look at prevalence, look at modifiers, and one example comes to mind, is the PXE Consortium that Sharon Perry and the Alliance has been involved with.

The Cystic Fibrosis Foundation is, of course, a major player in that because they sponsor the CF Treatment Centers where there is a lot of data that's driven by the consumers and then the health care providers, sickle cell centers, hemophilia centers, et cetera.

So the world of single-gene disorders is a little bit difficult because it's rare, and I think coming at that from various approaches, some of them are HHS-based and some of them are driven by the consumers, and I think the collaboration will continue.

Of course, there is a lot of data collected around newborn screening efforts, and some of these things will be collected that day but not all rare diseases end up in a newborn screening panel. So there is no single answer to this but perhaps a variety of approaches to single-gene disorders.

DR. CHARACHE: Yes. I would think this might be very important to work on early because I suspect it's going to be a problem because you won't have the denominators through the Cluster Analysis Groups and so on.

DR. McCABE: Steve?

DR. GUTMAN: Yes. I think that the idea of linking, obviously of linking the premarket and the postmarket piece is really important and doing it in a user-friendly way is important, and that was one of the reasons why I think it would be valuable in the context of the August meeting to discuss both pieces.

Having said that, I have to point out that while I would agree that one would certainly hope that the questions and the template are the same or at least are very similar for premarket and postmarket or for our use and CDC use, I can't underestimate the difference in scope because for us in our premarket review, we're looking for thresholds in the history of the program to show that a product is safe and effective, but we're not necessarily -- in fact, I can't imagine a label that would go on a product that

would be quite as extensive as the notion that is underlying this data collection accumulation.

Nobody would ever read it, and it would cost manufacturer or the lab, you know, $10 more for the monograph than for the device. So there are different intents here, and they're appropriately different.

The objective of CDC is to gather a much broader range of data that approaches technology assessment or evidence-based medicine or meta-analysis or guidelines, and it reinforces what I've always thought, which is that as hard as our job might be in this, the job that they have is actually much harder, and I can only emphasize that by pointing out that one of the things that happens everybody knows is, of course, the literature never stops, and the information, you're always a day late and a dollar short.

I mean, you can take the oldest tests, strep or glucose or PSA, none of which are very novel now, and you can go into Medline on a weekly basis, and it will drive you insane, and that information about the nuances of the disease change, but in fact information about the underlying device themselves will change. You know, people will study glucose meters and find out things about them, find out the combinations of environmental factors nobody predicted would affect them in fact affect them, or human factors elements that nobody predicted affected them will affect them.

So the CDC or whoever, the consortium will always be an article behind.

DR. McCABE: Joann?

DR. KHOURY: Yes, I agree.

DR. BOUGHMAN: I would make a plea to both the Data Group, the Interagency Group, in fact all of us working on some of these issues, while exploring these ever-so-complex and sublime mechanisms and intelligence search engines, please remember that the folks back home, if you will, and maybe keeping alive certain key

phrases or key words used appropriately, so that those of us who are not yet working in the world of a downloadable system into a Palm that fits into every pocket, if I go to a machine, how might I utilize extant search engines to get to sites that you all know and live every day, but I can't remember the name of directly, and I think one of the coordinating things that we can do is make sure that some of those terms are out there and used appropriately, so as we develop our own Websites or talk with Internet experts or whatever, that we in fact can utilize pointers and links appropriately.

DR. KHOURY: Joann, we won't forget you.

DR. BOUGHMAN: Thank you.

DR. McCABE: Other comments about these issues? Discussion about how this should influence the plans for August?

MR. HILLBACK: Do we have a week?

DR. McCABE: No, we don't have a week. Any thoughts on bringing the premarket and postmarket -- I do think that we can't divide these, that while there may be issues having to do with the various agencies and their evaluation of the data, that in point of fact, from both a consumer and professional perspective, these are continuum and not discreet in any way.

Yes, Pat?

DR. CHARACHE: Just one thought, and that is that it might be very nice to review the template again that's been developed for the premarket and the template for the postmarket, and it may be there can be a single template with a designation of what has to be populated and what need not be populated premarket.

DR. McCABE: Is that something that the Data Committee had begun to look at, Wylie?

DR. BURKE: Well, what Pat said is conceptually entirely in keeping with our thinking. So I think it's just been a sort of sequential process, where we just got to at the last SACGT meeting to the concept of the premarket data template, and since then have been concerned with not so much making sure we had all the boxes,

because I think that happened reasonably quickly, but that we were defining the terms and knew what was in the boxes, and so now what we're saying, I think much more clearly, or realizing much more clearly, is postmarket is just a continuation of that process, and I think what Pat just said is the obvious thing to do.

DR. McCABE: Any other questions or comments? Yes?

DR. LLOYD-PURYEAR: Well, what's the process of identifying the other stakeholder groups? I think that's absolutely essential for this August meeting, to bring in, for example, GeneTests, GeneClinics. We certainly will bring in our state grantees and the pertinent newborn screening programs that need to be there, but that's not enough, and I think if we're going to get buy-off on this template, we need to bring in industry.

Going back to Jeff Kang's comments yesterday, bringing in the health care industry, and anyway because we need to let people know quickly when the meeting is, and what's going on, why we want them there.

DR. McCABE: Wylie, you want to comment on that?

DR. BURKE: I really appreciate Michele's comment, and it's very pertinent. If you look at the draft proposal that we put together for what we wanted to do in the August meeting, we talked about the objectives yesterday. Nothing has changed there.

We also talked about the who, and the list as it exists is SACGT Data Team, representatives of HHS agencies, representatives of professional organizations, and we noted particularly a concern for genetics and primary care, identifying that as a major clinician user, consumer representatives and private sector representatives, and we identified those as insurance, pharma and biotech.

There are two comments. The first is we all have to fit around one table. We won't get work done if we don't, and so we have to be mindful of that.

The second is that although we know who we want at the table, we don't have a clearly-specified process for getting the right people to the table, and I

would appreciate, I'm sure Sarah would appreciate, any help or any advice the committee could provide about what is the best way to identify the right group.

DR. McCABE: Elliott, did you want to comment?

MR. HILLBACK: No. I was actually going to just say what Wylie did. I think we agree with Michele totally, that we need that broad base and just need to get started inviting people and really twisting some arms to make sure we get a good selection of people there.

DR. McCABE: So one name that's come up a couple of times during this meeting is GeneTests, which is certainly an important resource for everyone these days and should probably be represented here.

Other thoughts? Again, Wylie and Sarah are asking for our help.

DR. LLOYD-PURYEAR: Do you want the committee just to send you within a week by e-mail the names of organizations and individuals, contact information, and then whittle it down from there?

DR. BURKE: I mean, it seems to me what would be helpful would be both perspectives that should be represented. So I mean, that's sort of one part of the process, making sure that we've got a complete concept of what perspectives should be represented, and then indeed, it would seem to me suggestions about people who might represent those perspectives is great.

Do you have anything to add, Sarah?

MS. CARR: The more specificity the better.

DR. LLOYD-PURYEAR: And then what do you think should be the limit on the number of organizations, total, for a good working --

DR. McCABE: Judy?

DR. LEWIS: I don't know that we have to have every organization at the table. I think we need to have a representative group of people. For example, when we talk about primary care, and we talk about clinicians, to make sure that we have clinicians who represent physicians, advanced practice nurses, genetic counselors,

perhaps social workers, so that we may not have to have every medical group or every nursing group represented, but I think we have to have people at the table who bring that perspective, and I think there's a difference between what groups are at the table and what perspectives are at the table, and I think that's a key point.

DR. BURKE: Yes, I agree.

DR. McCABE: Other comments? Questions?

(No response.)

DR. McCABE: Okay. Let's take a 15-minute break. So we will get back together at 10:20. Thank you.

(Recess.)

DR. McCABE: Let's get started again. We're going to be working on the letter, the draft letter, to Secretary Tommy Thompson, HHS. So any of you who are here from the public, I'm not sure whether this is available yet because it's in draft, but it's very similar to the letter that we had written before to former Secretary Donna Shalala.

All of the members of the committee ought to have the draft in front of you. There were a couple of comments that have been made, one having to do with the definition of genetic information, and we have reviewed the definition that is present in the first bullet within the letter in the context of the definition of genetic information, the federal definition or the one that came out of the task force, and it seems to be consistent with that, and that's the source and the reasoning behind that.

The other recommendation or point of discussion had to do with the next to the last bullet, and where it had previously read under -- there was one of the clauses that read, "Genetic information should not be requested, required, collected or purchased, unless," and if you go down to I think it is the third clause there, "unless the employee is informed of the individual monitoring results," it has been suggested that that be reworded to "individual monitoring results are made available to the employee." So it would read, "Genetic information should not be requested, required, collected or

purchased, unless" a series of other comments, and then "unless individual monitoring results are made available to the employee."

Yes?

MR. HILLBACK: Ed, on that same point, it seems to me in that first line, after "purchase," it ought to say "by an employer." There's no specificity in this letter who can't request, require, collect or purchase information. It's not defined as a company or a doctor or anybody. So it could be by an employer or their employer's agent or it could be something, but --

DR. McCABE: Yes. If you go up to the paragraph that leads into this at the bottom of the previous page, it said, "Comprehensive federal legislation should apply to individual and group health insurance providers as well as employers, employment agencies, labor organizations, and labor-management committees."

MR. HILLBACK: Right. The first five or six bullets, we say, "Health insurance providers should be prohibited," et cetera, et cetera, et cetera, but then when we get to this next to last one, we don't say who we're talking about.

DR. BURKE: I agree. I think it needs "employer."

DR. McCABE: Or would it be employer or their agents?

MR. HILLBACK: If you want to be complete, that's probably safer, given what happened in other cases.

DR. McCABE: So the recommendation is that that would say, "Genetic information should not be requested, required, collected or purchased" -- I'm sorry. So it's down here under the --

MR. HILLBACK: Next to the last dot.

DR. McCABE: The next to last, "by the employer or their agents." Okay.

MR. HILLBACK: Right. Thank you.

DR. McCABE: Reed?

DR. TUCKSON: I also want to make sure that the intent of the letter

is clear, and I want to make sure that I'm clear. Let me remind folks that I am in the employ of a health insurance company. So I want to be real clear as I ask my question.

The notion is that the latest IOM report is real clear -- it's called "Crossing the Chasm" -- on the need to overcome the fragmentation in health care delivery, and how we've got to get coordination of issues across traditional organizational lines, so that the needs of the patient are kept center place, and that care is provided 24 hours a day, seven days a week, in ways that are not subject to the narrow confines of just the traditional way in which we provided health care in the past.

We've got to decrease this fragmentation, and information is key to that, and what I'm just concerned about is that health care organizations in the modern world use information to coordinate care and to help patients coordinate care, and to the extent that genetic information is part of medical information, and medical information needs to be coordinated, you can get the sense from reading this that perhaps what we're saying is that there are no legitimate good uses of information by health care organizations, and that there will be a lot of prohibitions from doing things like care coordination, and so I'm just a little bit worried whether or not this will be read by people as to deny those legitimate uses of information for the purposes of helping patients across complex systems of delivery, and so I just wanted to ask that question and make sure that we're not restricting everything here.

DR. McCABE: Let's take points related to Reed's comment.

Michele?

DR. LLOYD-PURYEAR: Mine is. I was concerned, too, Reed, and there's only one bullet that I thought is relevant to that, and that is "Health insurance providers should be prohibited from requesting, requiring, collecting, purchasing or disclosing genetic information without the prior knowing, voluntary and written authorization of the individual."

It doesn't prohibit it. It asks your permission, and I had marked it also, and I thought, well, I was trying to remember -- I mean, you get asked that when you go

to a doctor. I mean, you have to sign off on that. Every time you go, you have to give permission for this to happen, I think.

So I mean, since I'm from the access agency, and what you spoke about is one of our mantras, but I don't think this is prohibited, because I was also concerned. But it's just that one bullet, I think.

DR. TUCKSON: That was the one I was concerned about.

DR. McCABE: Kathy?

DR. HUDSON: Historically, that provision was included in all sorts of recommendations from all sorts of groups prior to the development of any kinds of medical records confidentiality or privacy regulations, and it was always anticipated, I think, that at the point in which privacy and confidentiality rules were put in place, that our intention was that genetic information should be treated the same as all other medical information, and that they should all be afforded the same high level of confidentiality protections.

So this in some ways reflects the history of the evolution of this set of recommendations. So now I think the consensus is that genetic information should be afforded the same privacy protections that are included in the Secretary's regulations.

So maybe this could be made more general to be "Genetic information should be afforded high levels of confidentiality and privacy protections" without making a specific prohibition here that might mislead people to say, ah, genetic information should be treated differently and should not be shared within the health care provider community.

DR. McCABE: Wylie?

DR. BURKE: That makes a lot of sense, and it seems to me you're suggesting the rewording of this bullet, and I would support that.

DR. McCABE: So what is the change that you would recommend?

DR. BURKE: It's the fourth bullet down.

DR. McCABE: "Health insurance providers shall be prohibited from

requesting, requiring, collecting, purchasing or disclosing genetic information without the prior knowing, voluntary and written authorization of the individual."

How would you change that?

DR. BURKE: It seems to me what Kathy was saying is something like this. "Genetic information should be accorded the same strict privacy and confidentiality protections applied to other medical information."

DR. McCABE: So completely strike the bullet and reword it that way. Does anybody feel that we lose anything?

DR. CHARACHE: I do.

DR. McCABE: Pat?

DR. CHARACHE: I think that a lot of medical information is handled extremely loosely, particularly on electronic records, and I think that the present wording is appropriately strict because the data is more sensitive than your glucose level.

DR. McCABE: Kathy?

DR. HUDSON: The dilemma there is that the proposals and the position of the Department has been that all health information should be treated, that you don't want to have to go through a medical record and say, ah, this is genetic information, and then this is not, and so if you have different privacy protections recommended for different kinds of information, you're going to create a nightmare for organizations, such as Reed's.

But I understand the point that you're making, is that currently, we haven't yet implemented stringent privacy protections for medical records. So by linking the two, we may in fact be losing something in terms of our recommendations for privacy protection for genetic information. So how about this?

DR. LEWIS: I've been working on some wording.

DR. HUDSON: Let me just throw out a sentence. "Genetic information should be afforded high levels of confidentiality protection or privacy

protection," and just leave it at that. Don't compare it to medical records or other medical records.

DR. McCABE: Judy?

DR. LEWIS: But what I was going to say was I believe that the wording that's here is strong and specific, and I support, as Pat does, the wording, but how about if we prefaced it with something like "as is required by law for all medical information," and then make the thing about genetic information, because that reinforces both points?

DR. HUDSON: But there is no medical records privacy law.

DR. TUCKSON: What about HIPAA? What's the context of HIPAA for all of this?

DR. HUDSON: HIPAA required that medical information that was transmitted electronically, that either Congress couldn't place a law to govern the privacy of that information or the Secretary was allowed to issue regulations, and the Secretary issued regulations. They were put in final. Tommy Thompson revisited them, and now they have been adopted, although they may be tweaked. So there is regulation as opposed to laws.

DR. CHARACHE: But in fact, that regulation as we read it essentially prohibits you from putting such information on electronically in many forms that would cause problems. So I'm sure that this regulation will be tweaked quite a bit.

DR. McCABE: Barbara?

DR. KOENIG: I just want to return, I think, to what was Reed's original point, and Reed can correct me if I'm wrong, which is it's something that I've also been concerned with. It's the issue too much protection of privacy obviates the usefulness of all kinds of information.

I mean, if no one knows about it, and you might be in a situation where there isn't appropriate follow-up, you can't do research about what's going on in your own population you serve, et cetera. So maybe what we need -- and I don't have a

sentence -- is some way of getting in more the positive aspects of being able to use information, but then what protections are necessary as you're doing that in the same way that the very beginning of the letter talks about how the whole point of this is to allow people to take advantage of genetic tests, you know.

So you want just not individuals take advantage of genetic tests, then hopefully want services from their health care provider and follow-up. So you know, maybe there needs to be some other clause about in order to have the utility of genetic information manifest or something. I don't know.

DR. TUCKSON: And that, by the way, that was my point. You just want to be very careful that by trying to do a good thing -- which everybody supports the good thing. I mean, there's no argument about the need for the high level. I think the language that we heard, that is important. Just don't lose, as you just heard, the -- please be careful that you don't stifle the progress of the health care delivery system of the future which is information-based in a desire to tailor care to help individuals get the care they need, and you just want to be careful that you don't cut that off because you'll have information that doesn't get used.

DR. McCABE: Do you want more added to the first paragraph then or are you talking about down in the bullets?

DR. KOENIG: I don't feel like I've been adequately briefed yet about what's happening with HIPAA and the new privacy regulations in terms of how to integrate that. So I defer to Kathy's judgment about that because she seems knowledgeable about that. It may be a moving target, too. So it's hard to --

DR. HUDSON: Yes. I think that the bullet maybe we should just change to it should -- "Genetic information should be afforded high levels of privacy protections," but I think that Reed's point is to say something here about the importance of genetic information and enhancing health care and of benefit to individuals' health, and that it needs to be available to health care providers and in the health care system in order to provide that care.

So that's a first paragraph kind of positive statement, right?

DR. LLOYD-PURYEAR: Yes. Maybe if we had those two statements as sort of overarching first statements in the first paragraph, that we recognize the positive genetic information and what it can be used for, but at the same time recognizing the need for --

PARTICIPANT: High level.

DR. LLOYD-PURYEAR: -- privacy protection. Yes, but not as a point but as a --

DR. CHARACHE: Perhaps we could also simplify this by removing two of the five things listed. It now says, "Health care insurance providers should be prohibited from requesting, requiring, collecting, purchasing or disclosing," and I don't see any reason to prohibit them from requesting it. I think maybe requiring, purchasing or disclosing might be what would be of greater concern.

DR. McCABE: Well, some of the critiques of many of the state laws as well as the Executive Order are that if you do not prohibit the request of, that you've said that there is an initial bar, and people can elect not to work for that employer, if they wish not to honor the request, and so some people feel very strongly that the request is an important part of the whole equation.

Yes? I had Michele, Judy and Joann.

DR. LLOYD-PURYEAR: I already spoke.

DR. McCABE: Judy?

DR. LEWIS: Ed, one of the things that I think would help me a little bit is to be real clear on why we were sending this letter, and maybe I missed that piece in the introduction.

Is this because we're briefing the new Secretary?

DR. McCABE: Well, we had talked about this at the last time, that our reporting line is through the Assistant Secretary of Health. At this point, there is an interim individual in that position.

We felt that one of our highest priorities had been and continues to be the concern about genetic discrimination, and clearly the American public stated that as one of their high concerns, and, so that while we were awaiting the appointment of the Assistant Secretary of Health, we would move forward and not brief the Secretary per se but at least communicate with the Secretary one of the principle concerns, and we had discussed that last time.

This letter is what we had developed in the interim, and we would like to finalize it today, so that we can get it off to the Secretary.

DR. LEWIS: In that case, I wouldn't necessarily worry as much about the availability of information because I think that's a separate issue than the discrimination piece, and I think while Reed's point is well taken, I think that what we're focusing on in this letter is inappropriate use, and so if we're focusing on inappropriate use, we don't need to spend a lot of time talking about the appropriate use because that's a given.

What we need to focus on are our concerns related to inappropriate use, and I was just trying to be real clear on what the purpose of the letter was, and from that perspective, I don't think we need to deal as much with the other because that's going to be a piece that's going to be there. Patients can give consent.

DR. McCABE: Joann and then Elliott.

DR. BOUGHMAN: It seems to me that in reading this, this bullet actually was attempting to tie together the authorization or approval or consent of the individual with the action, not the general principle.

However, it could be restated, I believe, this one bullet, so that it would say, "Health insurance providers may request, require, collect, purchase or disclose genetic information only after obtaining prior knowing, voluntary and written authorization of the individual."

So we turn it to a positive rather than a prohibitionary station. I mean, I think that still ties the two pieces together, that you need the authorization first and

then the insurer.

DR. McCABE: Kathy, are you comfortable with that? You had recrafted this.

DR. BOUGHMAN: I think there's something to be gained with the specificity, is basically what I'm saying, rather than we should be careful with genetic information.

MS. DAVIDSON: Joann, could you restate that?

MR. HILLBACK: Just make it positive.

DR. BOUGHMAN: Yes. Rather than prohibiting, it would say, "Health insurance providers may request, require, collect, purchase or disclose genetic information only after obtaining prior knowing, voluntary and written authorization of the individual."

PARTICIPANT: I like that.

DR. McCABE: I have Elliott, and then Barbara.

MR. HILLBACK: I was going back to the other piece that we talked about for a moment, and I didn't want to leave that. I think, as Michele said, putting the two sentences up in the beginning about the overall value and yet the need for sort of high -- I hate to use high scrutiny. So high levels of confidentiality, whatever, is useful to set a tone that we're trying to get across, and I still like going back to where Kathy was, I think, on this. I'm not sure putting the positive spin is going to do it for everybody versus the more careful version, but with a clear focus.

DR. McCABE: Barbara?

DR. KOENIG: Yes, thanks. I'm going to agree with Elliott and disagree with Judy and Joann on this.

I think that the reason I'm disagreeing with Judy about the tone and how we could just focus on discrimination as opposed -- because of the purpose of this letter, but the real issue is the balance of protection that you need to have, and so I think it's always going to be a balance.

So I think that tone is important in this letter, and I think, Joann, my problem with your turning that one bullet into a positive is that it's putting way too much weight on informed consent. It's just making informed consent do too much work in this area because, you know, there's some protections that we want people to have regardless of whether they have to do some act.

At any rate, it just didn't seem to me right. It's not something that we just want to have happen after some kind of an informed consent process. So that doesn't help to me at least.

DR. McCABE: We had 45 minutes to complete this, and I definitely want to be sure we complete it and don't let it hang. If I look at the bullet we originally talked about, which is two below that one, it looks also to be fairly specific and in essence to be an expansion upon the one that we've been discussing, the fourth bullet from the top of that page.

But I wanted others to take a look at it and see because I see that the tension here is between those who like the specificity and those who want a more general statement. The more general statement was that "Genetic information should be afforded high levels of confidentiality."

I don't see that elsewhere in here, and the question is if we completely struck the fourth bullet from the top of this page and were -- do we really lose anything if we look at the sixth bullet?

Wylie?

DR. BURKE: I actually would be comfortable with striking it. I think that I like the specificity in the other bullets and particularly the one you mentioned, the second from the last, which is really directed toward discrimination by employers in the workplace, which I think is an appropriate place to be very specific, and I think the bullet we've been talking about is almost in a different category of information. I mean, in a different category of action.

It's about handling a certain category of health care information in the

routine course of health care, and that really isn't the point of this letter. So I think the solution would be to strike it.

DR. McCABE: What about if we then took the bullet that Kathy had recommended? "Genetic information should be afforded high levels of confidentiality" and make that the first bullet. I mean, we say, "Genetic information should be afforded high levels of confidentiality." That's sort of the overarching statement.

We then define genetic information and then move down into increasing specificity. Is that comfortable to everyone?

Elliott?

MR. HILLBACK: Yes. I have one concern, though. I think one of the things that we learned several years ago when we were quite active at BIO and working this issue was the separation of concepts of confidentiality and discrimination.

One is how the data is stored. The other thing is what you do with data you have, and where industry, and it's more PhRMA than it is others, but gets very concerned is when you start changing the confidentiality side. You get into clinical trials. You get into all those other problems, and that's why it was relatively straightforward and easy, nothing's easy, to get a consensus, but to get a consensus within BIO and PhRMA and everyone else on the discrimination side, and we have taken publicly very strong positions asking for antidiscrimination legislation.

We wrote to the previous Administration from BIO, and I believe PhRMA did, I'm not certain of that, but I know BIO did, taking very strong stands there but trying to keep people from going crazy on the confidentiality side because there were great harms to the way we need to do things.

So I don't want to lose that separation of the church and state bit here as we go forward. I don't mind saying that people should be careful with this data. I think it's similar to all other medical data, to be honest. I don't want people knowing lots of other things about me besides my genetics. So I'd rather make sure we don't fuzzy this up too much and say our real strong message is do something to try to prevent

and punish people pretty badly if they discriminate and keep a pretty laserbeam sort of approach here rather than start getting this diversified too far.

DR. McCABE: So are you concerned with the general bullet at the outset?

MR. HILLBACK: No. Again, I'd like to keep it. You know, I think it's still similar to other medical information because I'm not sure it's all that different when you come right down to it.

DR. McCABE: Well, if we say, "Genetic information should be afforded high levels of confidentiality," does that --

DR. LLOYD-PURYEAR: Well, how about other medical records?

DR. McCABE: Okay.

MR. HILLBACK: If you do that, and you lump them all together, we would feel much more comfortable. I remember that from many battles we had. But then I think most of the focus of this ought to be on we really want a new law or more laws around what people do with this information and making that a really bad thing, and that you'll have very strong support from lots of players on that one.

DR. McCABE: Kathy?

DR. HUDSON: I agree that that needs to be the general gist of this letter, but I disagree with the clear separation between privacy and fair use of information. If you cannot control where information goes, it's very, very hard to be able to overcome the burden of proof that it has been misused.

How would you know? I mean, in the Burlington Northern case, the only reason why people were able to even find out that that information had been obtained and potentially was about to be misused was because of the real activism on the part of a few persistent individuals, and so where there's no need to have information, you need to prevent the information from ever going, and that's a good preventive for it ever being misused.

So I think that that privacy and fair use are two important interlocking

pieces here that both have to be in place.

MR. HILLBACK: But again, I don't think when you say you can't collect data without the patient's knowledge, that's not about confidentiality to me. Confidentiality gets back to medical records storage things, et cetera, but, you know, maybe I'm trying to split hairs now in a way.

I don't totally disagree with you, but again I think the strength of this ought to be antidiscrimination, not try to start relegislating all the storage issues, et cetera.

DR. HUDSON: Right, and medical records privacy and research privacy are very complicated issues, and to the extent that we get very specific here, we run the risk of later being asked to defend why we took this very narrow point of view when other people are taking this one or this one or this one or this one. So I think the general statement is more safe.

DR. McCABE: So the first bullet then, with the additional discussion, "Genetic information, as with other medical information, should be afforded high levels of privacy and confidentiality." Do you want the privacy in there, too? They are slightly --

PARTICIPANT: They are different.

DR. McCABE: Okay. Yes, Pat? And, I'm sorry, with that, we strike the fourth bullet from the top of the second page, the fifth bullet overall, and substitute this as the first bullet.

Pat?

DR. CHARACHE: There's a very broad band of opinion as to how private medical information needs to be. I'm a little concerned about saying that it's just like all other medical information. It should be, but it's just not.

Perhaps you could add the one word "sensitive." So it would be like "all sensitive medical information."

DR. BURKE: Actually, I'd like to comment on that. I think what we're saying is that "Genetic information, like other medical information, should be accorded a high protection," but we're not saying that there are different levels of sensitivity, and I would argue that we should avoid doing that because we're making a

very simple statement, and a simple statement of principle, and to introduce into that differing levels of sensitivity, even though I think we would all agree that there are differing levels of sensitivity to various medical information, would be to propose that that's an important principle.

My problem with that is that what one person considers sensitive, another person might not, and the other way around. I think we need strong privacy and confidentiality rules for all medical information because it's private personal information.

MR. HILLBACK: My male pattern baldness problem, I don't want everybody to know about.

DR. CHARACHE: Could we say that all personal and private medical information -- I understand what you're saying, and I give up.

MR. HILLBACK: But I think Wylie's right. We're not trying to develop policy here. We're trying to set a tone. The tone we want to set is like all medical information, genetic information, should be kept confidential, should be afforded high protection, and then we go from there on our discrimination point, where we are making more specific suggestions.

DR. BURKE: And it might well be in the real world, I think policy implementation or implementation of systems under a policy guidance might well put a higher wall around some information than others, but that's not the sort of overarching principle we're expressing.

DR. McCABE: Michele?

DR. LLOYD-PURYEAR: I agree with all of that, but I want to go back to do we want a positive sentence in the first paragraph, also? That we say something like we --

DR. McCABE: I wanted to get this one cleared before we went back to that one.

DR. LLOYD-PURYEAR: Oh, okay. I just wanted to make sure you didn't forget.

DR. McCABE: No, we haven't forgotten.

DR. LLOYD-PURYEAR: Okay.

DR. McCABE: And I also had Judy and Ann on the list, but that was before we got started on this. So we probably need to finish off that sentence at the end of the first paragraph.

Does anybody have a suggestion? Did you have any notes, Sarah?

MS. CARR: I'm sorry?

DR. McCABE: The sentence in the first paragraph?

MS. CARR: That's the one Michele has.

DR. McCABE: Do you have that, Michele?

DR. LLOYD-PURYEAR: Well, I had thought it should go right as the second sentence, and I just had "We recognize the value of the utilization" -- this is just what Reed said or Elliott. I can't remember -- "We recognize the value of the utilization of genetic information in the provision of health care."

PARTICIPANT: Use?

DR. LLOYD-PURYEAR: Use? Okay. Use.

DR. McCABE: Can you read it again for us?

DR. LLOYD-PURYEAR: "We recognize the value of the use of genetic information in the provision of health care services."

DR. McCABE: Is everybody comfortable? So that fits in between "I'm writing to express our support" and "We urge the Administration to support much-needed federal legislation." Everybody comfortable with that? So it's a strong sentence about the need for communication.

Yes, Elliott?

MR. HILLBACK: I'm happy with that, but I want to go back to your point about taking out the fourth bullet.

DR. McCABE: Okay.

MR. HILLBACK: Because the one important point that that one makes that I don't think we make other places is about the authorization of the individual.

DR. McCABE: It's actually in that sixth bullet.

MR. HILLBACK: We rewrote the sixth bullet to focus on employers, and this is focused on health insurance providers. We sort of have two groups of bullet

points, one focused on health insurance providers and one focused on employers, and I think we want to make the same point both places. So you could take it up to a more generic comment that says, "The collection of this information should not be done without authorization of the individual knowing," you know, voluntary, et cetera, and cover them both.

By the way we changed the sixth one, we've not made it a good substitute for the fourth one.

DR. McCABE: See, that's why I had, before we changed the sixth one, that we were really covering everyone who was in the lead-in paragraph --

MR. HILLBACK: But all the things after the colon in the sixth one talk about employer-related things.

MS. CARR: Yes.

MR. HILLBACK: In the workplace, toxic substances, and it uses the word "employee." It's all about employers and employment and employees. So it doesn't get to the issues around health insurance providers at all, I don't think.

DR. McCABE: Wylie?

DR. BURKE: But don't you think that the general statement -- I mean, the general statement that we're putting up front is intended to replace that bullet, and I can't remember how it reads, but it's something like "Genetic information, like other medical information, should be afforded high levels of privacy and confidentiality protection."

DR. McCABE: And should not be collected without the written authorization of the individual.

DR. BURKE: You know, that's actually difficult because, yes, of course, that's true, and yet I think any health care provider can imagine a circumstance where, you know, one provider's talking to another, and the idea of going back and getting a written consent -- so I think high privacy and confidentiality protections without defining it is a better way to go.

MR. HILLBACK: You guys think about this a lot more than I do. So if Kathy's nodding --

DR. McCABE: Sarah?

MS. CARR: I just have a question, though, Wylie. This bullet was talking about health insurance providers, not health providers, and I recognize that sometimes the information has to cross the two, but what you just described, it seemed to me, was sharing of information between providers, and I just wanted to --

DR. BURKE: Yes, I agree, but I think I read into Dr. Tuckson's initial comments a concern not to create a statement that then might be extrapolated and broadened.

In terms of limits on health insurance providers' use of genetic information, I would think that the three preceding bullets have addressed our concerns. I mean, what we're really concerned about with health insurers getting information is what Elliott said.

We're concerned about their not taking it and doing something with it. So to then add something about not collecting it without people's written consent is very redundant.

DR. TUCKSON: I'm trying hard not to make advocacy points but to raise the issue, and I'm trying to be very careful, and I would just want to underscore that this is a critical issue here in the sense that it's tough to think about health care insurers as being just a small group of people who send bills in and out.

I mean, they are interacting and will be doing more so with each passing day with varieties of advance practice nurses, the continuum -- there's a lot of people that are all involved in this game. So don't think about it in the static way, and that's the reason why I'm saying it. That's all.

DR. McCABE: Can we move on? Do we have enough of a consensus on this?

So Judy, this was from way back when.

DR. LEWIS: I've already said what I needed to say.

DR. McCABE: Ann?

MS. BOLDT: Mine is now Bullet Point 2, about the definition of genetic information, and I would just like to add at the very end of it, where it says, "and information about the occurrence of disease or disorder and family members," and add "in the form of a pedigree or other written documentation."

I just want to be very explicit because I know a lot of the state laws, they do state pedigree versus written, and I think that is important.

DR. McCABE: So you're again getting more specifics than what we have here?

PARTICIPANT: Why? I don't understand.

DR. McCABE: Yes. I'm not sure I understand what the implication is.

MS. BOLDT: Okay. Well, just in terms of someone looking at a pedigree versus -- if someone is savvy enough to understand how a disease is inherited, it's easier, it's more visible, if you see it through a pedigree versus if they're just stating that this father or this aunt had a certain condition. You'd have to then know if it's X-linked or dominant or whatever, but a pedigree more clearly defines how things are inherited.

DR. McCABE: But the way it is here, wouldn't it cover both?

MS. BOLDT: I think it does. I mean, I think it does, but I want to be -- well, I guess I'd prefer to be more explicit in saying a pedigree would be included in that.

DR. LLOYD-PURYEAR: But then you would exclude other forms of transferring that information.

MS. BOLDT: Or other written documentation. I still would want to have written.

DR. LEWIS: I think a pedigree is a form of written information, and so I think that saying it the way it does covers it because if we specify one piece, there might be another piece we don't specify that then is also important.

DR. McCABE: Yes. This doesn't say written. This just says information.

DR. KOENIG: I think your comment is extremely helpful, but I think it's more appropriate at the regulatory level perhaps than at the sort of broad policy level. So it would be something you'd want taken on when regulations are actually written in detail.

DR. McCABE: Kathy?

DR. HUDSON: Ann, I want to respond to your comment, too. But the purpose here is to outline what kind of information insurers and employers can't in some cases get and can't use, and the way in which that information is normally collected by those entities is not in the form of the pedigree but is simply asking a question.

Diabetes. Any diabetes in your family? So that's the way that information is collected and has the potential to be misused in the context that we're worried about here. So by saying in the form of a written pedigree, you're actually saying, but if you collect that information in another way, by saying does your Aunt Mary have cancer, that would be permissible to be used because this defines the scope of what's protected. So you want to be as broad as possible in defining the scope of what's protected.

MS. BOLDT: Right. I mean, I want to include an and/or kind of thing, not just the pedigree but or other written documentation. I understand what you're saying, but I guess it's my experience to testify in terms of Indiana State. This is something that they asked me very specifically, and yet that was more of about health insurance, but it's a concern I have.

So as long as it's explicitly stated -- I mean, if you think that that's going to cover everything, then I will defer to that.

DR. McCABE: Other discussion on this point? Do we want to get more specific or do we want to leave it information? Judy, do you --

MS. YOST: Not on that point.

DR. McCABE: What's the consensus here?

DR. CHARACHE: I think this is a very broad swipe anyway, and it's very helpful to keep it broad.

DR. McCABE: Judy, you had another comment? Different comment?

MS. YOST: I agree with the broad on that. The suggestion I had from the first iteration of the letter, and that's just maybe an efficiency-type thing, is I see that four times we talk about legislation prohibiting discrimination on the basis of genetic information for health insurance and employment reasons.

I just thought it might be more effective to kind of say it fewer times and instead make the statements at the introduction and at the closing more strong. I think that gets the message across.

For example, in the first paragraph, that "effective federal legislation is critical in preventing genetic discrimination" dah, dah, dah, and then at the end, to say, "We believe that the enactment of legislation based on these key principles will prevent the misuse," dah, dah, dah, and then, "We strongly urge the Administration to." You know, words like that to kind of really reinforce the point as opposed to saying it four times in the letter. It kind of just goes on and on.

DR. McCABE: So what would you delete then?

MS. YOST: So the letter has changed. In the second paragraph, it's listed. It's also in the first piece that I have, in the fourth paragraph. It's also in the first, second, third and final paragraphs. So I'm just suggesting take two of those out some place, and I think, Number 1, it gets the point across a little bit more effectively than just reiterating the same -- it's the same exact words over four times.

MS. CARR: So what you're saying, Judy, is that you would maybe leave it in the first paragraph --

MS. YOST: And the final.

MS. CARR: -- and keep it in the second but take it out of the beginning of the third paragraph, and so that would start "Comprehensive should apply to." We don't need to reiterate.

MS. YOST: No.

MS. CARR: Okay.

MS. YOST: The 3 and 4 are in the bullets. So I mean, that's six more times. So I think we got it.

MS. CARR: But I only see one place to take it out. So help me again. We would take it --

MS. YOST: I have an earlier --

MS. CARR: Do you have the one that was e-mailed maybe?

MS. YOST: Yes. This was the e-mailed one.

MS. CARR: Oh, I know what happened. Yes. A big red pen came after that.

DR. McCABE: So on this version, we'll take it out of the third paragraph.

DR. LLOYD-PURYEAR: So the SACGT you'd take out?

MS. CARR: Yes, so that paragraph would start "Comprehensive federal."

DR. BURKE: Actually following on that comment, just from an editing point of view, we say, "On behalf of SACGT, I am writing to express our support for federal legislation prohibiting discrimination on the basis of genetic information. We urge the Administration to support much-needed federal legislation." I think that's your point, and what we could do is go "On behalf of the Secretary's Advisory Committee on Genetic Testing," and then just go to the second phrase.

PARTICIPANT: We urge.

DR. BURKE: We urge.

PARTICIPANT: We still have to do something with that other sentence.

PARTICIPANT: No. Oh, the positive sentence.

DR. McCABE: Well, that can still go as the last sentence of the paragraph.

MS. CARR: Except that if I could just say, I was going to suggest that that second sentence, the positive sentence, start, "While we recognize the value of the use of genetic information in the provision of health care services, we urge the Administration." It seems to just sort of hang out. If it's just a stand-alone sentence, it sort of hangs there.

But if you're concerned about the other is greater than --

DR. BURKE: No. From my point of view, it's an editing issue. It's just however it reads best is fine.

DR. McCABE: So we'll work on the details and not say genetic discrimination more than three or four times. Is that your point? That's your point, right, Judy?

MS. YOST: I'm a person who has too much to read. I always look for duplication and get rid of it instantly.

DR. McCABE: Okay. So with that guidance, do we have the assent of the committee that we'll go ahead and get this letter out to Secretary Thompson?

I think this is very important, that we communicate with the Secretary on this position that we have taken very strongly in the past with the previous Administration.

I take the nods of the heads as agreement that we will move forward. We'll get this out within the next week or two.

DR. TUCKSON: Dr. McCabe, at some point, moving on on this, given that the issue has been raised about our relationship with the new Secretary, I don't know whether we can or should know whether if there's any further information about whether he is aware of us or just any context of where we stand with this. Are we just sort of out there in limbo or --

DR. McCABE: Yes. I think that there has definitely been discussion with the Secretary's office at high levels, and we're determining what the appropriate protocol is, and the protocol is that we do report through the Assistant Secretary of Health for the transmitting of recommendations and those sorts of things.

We have the option, when we feel very strongly about an issue, as we do with the genetic discrimination prevention, that we can then communicate directly with the Secretary, and we have been given the go-ahead to do that on this case.

DR. TUCKSON: And is the Surgeon General still as of today the Assistant Secretary?

DR. McCABE: No. The Surgeon General stepped down as Assistant Secretary of Health with the new Administration. So there is an acting interim individual right now in that position, but we have been urged for our more routine activities to await the appointment of a permanent Assistant Secretary of Health.

Is that accurate?

MS. CARR: Right. I will say, though, that Dr. Art Lawrence is the Acting Principal Deputy Assistant Secretary for Health, and he receives weekly press

clips from our office. We update him on the activities of the committee after every meeting. He gets a briefing book.

We briefed him on all the issues that all the working groups that we have going, and the oversight report, the recommendations the committees' made on patents, and he's sort of in handling the patent letter now, and Dr. Satcher's the one who sort of forwarded the letter to Dr. Koski on third parties or secondary subjects. So that was done before the change in Administration.

But Dr. Lawrence is very interested in the committee, very concerned that, as he is the interim ASH, that he make sure he doesn't let any ball fall, and that he briefs the Secretary as needed, and so what we'll do with this letter is forward it through Dr. Lawrence, and he'll transmit it for us to the Secretary.

DR. TUCKSON: That's a very great answer, and it sounds like Dr. Lawrence is doing well.

MS. CARR: He wants to do the right thing by the committee, and he wants to --

DR. TUCKSON: Good for him.

The next question, and I don't know whether it's appropriate, but have we at any point had any concern come back the other way on any issue that we are dealing with in any way?

MS. CARR: No.

DR. McCABE: No, that is not the case. You may recall that Dr. Raub has been at our meetings in the past, and he is still in the Secretary's office as well. So I don't think we need be concerned about whether or not we are communicating.

There are some other priorities. There are agency heads to be appointed and other activities with getting a new Administration going, and we have to recognize that there are additional priorities.

DR. TUCKSON: We're not the only thing?

DR. McCABE: We'll communicate that, Dr. Tuckson, that you were concerned about -- no. I think it's just, you know, a lot of business getting a new Administration going.

DR. TUCKSON: In some ways, it's better to be quiet.

MR. HILLBACK: Be glad.

DR. TUCKSON: Yes. That's what I was getting at, actually.

DR. McCABE: Any other questions or concerns?

(No response.)

DR. McCABE: The next is the progress report from the Education Work Group.

At our February meeting, Dr. Boughman reported that the Education Work Group would be presenting a background report on "The status of current efforts and the existence of gaps, if any, to enhance genetic education of health professionals in the public and private sectors." Dr. Boughman suggested that the group would endeavor to complete its work in time for presentation to the full committee at the May meeting.

I will now turn to Dr. Boughman for an update on the group's efforts, which include a slight shift in plans. Before doing that, though, I'd like to congratulate, for anyone who hasn't heard, Dr. Boughman will be changing positions and will be the First Executive Vice President of the American Society of Human Genetics, a position which she will take up on July 1st of this year.

So congratulations on your new position, Joann.

DR. BOUGHMAN: Thank you very much.

Yes, there are gaps in education out there, and our slight shift in plans has been shifted again in the last day or so, I might add, for appropriate reasons.

We had said in February that we would in fact endeavor to put together the information that would be most useful to this group, and I would like to once again compliment staff on their very hard work. In fact, there is a white paper in

progress that has many, many addenda to it with a gathering of quite a bit of information about genetic efforts.

However, when looking at those pieces of information and in trying to synthesize the information, it has become obvious to those of us looking at these volumes of information that a discussion and open conversation not just among ourselves but that would include other key stakeholders would be of great use to this committee.

Building on the style of meeting we had last year at the point that we were getting public comment, and given that we were able to gather and synthesize a great deal of information in even one day, the Education Work Group is proposing that the Secretary's Committee actually make a sort of "all call," if you will, to groups that are developing and providing educational efforts across the spectrum of genetics issues.

We had been discussing several possibilities, and in Tab 7 was an original kind of proposal that we had put together for this group to discuss today on an education summit, and I'll go through a real broad overview and then open it up for discussion.

Our first thought was that we might be able to pull the summit together in August. However, given that we have just given ourselves and the Data Work Group both premarket and postmarket full-blown discussions with, for example, Elliott saying did we have a week for that meeting, it may in fact be as we had discussed earlier this morning and last evening, that it may be appropriate for this group to consider moving the Education Summit to a different date rather than right around the August meeting. So we'll want to discuss that in a moment.

Our objectives are very broadly laid out here, and some of the basic areas in curricula development, training, continuing education, some new and innovative kinds of approaches to education, and we started on a list of key stakeholders.

Rather than trying to make either an exhaustive list or even a relatively complete list, we put some ideas down on paper and are seeking some input from members of the committee. For example -- and last night, Elliott and I spoke about this for a few minutes -- we need some ideas about how to include industry, to

pick or choose for presentation and/or discussion specific companies versus organizations that might present is something I think the entire group may want to talk about a little bit, and I think its bottom line is the great value of the Secretary's Committee actually putting forward this idea that via the Federal Register, we can in fact have a very open meeting, where many people would come, gather, and not only discuss best practices with some ideas presented, but we could hear concerns from a variety of groups on where they believe the gaps really are, because that's one of the difficult pieces of information to actually garner in any other way rather than to pointblank ask the question and have people come tell us what they believe the answer is.

So with that, unless other people on the committee have additional comments, I'd like to throw it open and write down notes from our colleagues on the full committee.

DR. McCABE: Any other comments from members of the Education Committee? Yes, Judy?

DR. LEWIS: I'd just go beyond the Federal Register, as we did with the meeting last February, and be real proactive in developing a list, and in one area, several of the federal agencies, the Office of Women's Health, Bureau of Health Professions, Division of Nursing, several other groups, got together several years ago and looked at women's health content in curricula, and there was a survey that was designed that started out with medical schools, then went to dental schools, then went to undergraduate nursing schools, and I was on the expert panel that looked at women's health in undergraduate nursing schools, and by the time the thing got to us, the behaviors had been modeled on undergraduate medical education, which is a very different animal than basic undergraduate nursing schools.

So I wouldn't want to see us go to developing a survey instrument that we put out to the world. I think having people come and share with us rather than having us define the data elements and then asking people if they're present is definitely the way to go, and we may move to that, but if we do move to something where we're looking at data elements, they really need to be broadly gathered.

So I would support having a "ya'll come" meeting and looking at it, though, in terms of a real proactive invitation list and making sure we include people and schools where diverse populations -- you know, so that we target some schools that are some of the non-traditional schools.

DR. McCABE: Michele, and then Kathy.

DR. LLOYD-PURYEAR: I agree with the change in dates, and I'm representing HRSA because the HRSA person isn't here for the education.

But I also think we need to include the health care industry as a very important stakeholder, and in fact, some health care financing organizations actually train, I don't know about nurses, but medical students and residents. So I think it's very important to have that.

DR. McCABE: Kathy?

DR. HUDSON: I'm wondering whether or not this meeting can go beyond the sharing of current activities, and if in fact some of that collection of current activities couldn't happen in advance, and I note that many of the members here that are listed are members of the National Coalition for Health Professional Education in Genetics, and Joe was willing to offer the assistance of NCHPEG in collecting this information in a survey form in advance of the meeting, so that the meeting could sort of go to the next level. So now what?

My other comment was to sort of support those comments made by others to broaden the inclusion here, particularly to minority-focused health professional organizations, Hispanic Nursing Association and others like that.

DR. McCABE: I think it would be very important for people to look at this list and make additions. I'd suggest that we add the NMA to the list as well.

Elliott?

MR. HILLBACK: I was going to say somewhat what Kathy did, but let me say it in my own weird way. I'd hate to spend a whole day ID'ing the problem and not get anywhere in terms of what to do about it, and there's a lot of people, I think, I know Kathy's been instrumental in a number of things, other people have, in trying to ID the problem.

We've listened before to people coming in here, and I think the prep for the meeting should be to do as good a job of ID'ing the problem and limit the number of speakers talking about what's the problem to one or two people who can summarize history, summarize what we know, and see if anyone violently objects to their picture of where we are, and then spend most of the time saying okay, if that's more or less what the planning field looks like now, what do we do?

I think that's of a much higher value than us sitting there being told what every different one of these organizations does for education, and we haven't gotten anywhere. We're just maybe smarter or maybe asleep, and we ought to be doing the opposite, which is assuming that work can be condensed for us in a Reader's Digest sort of thing, and then we can use that to work from. I think that's what you were saying, too, and I totally agree.

DR. BOUGHMAN: I think that's one of the advantages to moving the date for the actual summit out further, because we have gathered quite a bit of information already in the form of lists and curricula and Websites, and for example, some of the NCHPEG information.

We have not yet synthesized that in a good enough way that we can figure out the best few people that might be able to crystalize that and give us a picture of the landscape and get a useful reaction, and I think that's the piece that can come together between now and August in preparation for really having a much more useful and positive meeting.

MR. HILLBACK: I'd just like to come back on that, if I can. I think we ought to think about how do we get some hospital representation, not just the physicians or the nurses or the counselors. They have to live with this, the same with an HMO representation, in that they're trying to manage the process of delivery of health care, and they have to think about this problem, and how they keep the education moving, and they may be one of our best allies in moving this forward.

I start to wonder whether one day would even be enough, if you start to really think about action, and if you think about the size of group we're talking about, that you may need to be able to break it down into some working sessions and then come back together.

So I think we ought to be open in terms of design as well as very inclusive on attendees, and you have some clear deliverables at the end and not just feel like we had a nice conversation.

DR. McCABE: Barbara, and then Michele.

DR. KOENIG: I pass.

DR. McCABE: Michele?

DR. LLOYD-PURYEAR: I'm going back and looking at the list again. As everybody I think knows, we were about ready to begin a workforce analysis, and I think we'd need to look at the workforce or the education of the workforce very broadly, and what I don't see here, besides not health care industry or industry, but public health, and in fact anybody -- public health, allied health, they are missing, and I think you need to view a genetic test in a broad context.

DR. McCABE: Do people agree, though, that -- first of all, we have August. We're going to have the Data Work Group. That's going to be a busy meeting. There is some overlap in the membership of these work groups.

In addition, I think it would be asking an awful lot of staff to put together two major satellite meetings at the time of the August meeting, and I think there is, as we've discussed, benefit of preparation, additional preparation. I think we may find November is even a bit ambitious, but that's what we're going to be targeting right now.

The other thing that I'll mention that we're considering, but I don't know if it will be possible for financial reasons, and that is, that if at all possible, we're going to try and hold the Education Summit on the West Coast and see if we could do that, and we've had two universities volunteer their sites. So we'll be having a battle within the PAC 10 for a position. But we'll be looking at both Stanford and UCLA as possible venues for this.

Other thoughts about the educational program? Yes, Judy?

DR. LEWIS: I'd love to go to the West Coast, but just to speak to that, if you're looking at leaders in education, and you look at the fact that a lot of these organizations have their office on the East Coast, if we're looking a little more central, because people, when they travel to the West Coast -- I mean, I know when people

come here, you lose two days in coming, but if we're looking at getting attendees to come, it may be that somewhere central is preferable to the West Coast because you may lose some people who just can't take three days out of their schedule to do it. So I think that's a piece to explore.

DR. McCABE: We may end up in Washington again for financial reasons. So we have to recognize that, but we're at least going to explore it.

DR. BOUGHMAN: A point I would like to make, because I feel somewhat apologetic about postponing and not having what seems to be a product on the table for this committee, but I think that the education issue is very different than some of the other issues that we have been talking about because there is a great deal of useful activity and progress being made out there, and a lot of organizations are working together, and I think via this committee and some of the people on this list, there is a spirit of coordination and collaboration out there that is building in this area.

I think we are not in quite the same position that we are with data formats or whatever, where this group around this table needs to make some decisions or help formulate something, so the organizations and the agencies can make more rapid progress.

I think we are kind of on a different time scale, and I think that the foregoing of the August date will not in any way deter these organizations from continuing development of their programs and teaching a lot more people a lot about genetics between now and then.

DR. McCABE: Yes. I think it also should be clear for the record that this was not Dr. Boughman who suggested the delay, but rather it was Sarah and I who felt that we really needed to consider postponing this until November for staffing as well as other reasons.

I think the point is also very well taken that we've discussed what the problem is, and it will be very important to try and begin to address solutions or how one would begin to approach developing solutions from this.

The white paper. When will the white paper be completed? By August, do we think? The white paper won't be completed until after --

MS. CARR: That's my understanding. Is that not so, Joann?

DR. BOUGHMAN: In part, it depends on whether, at the end of the white paper, we really want to take the approach of having crystallized recommendations as we have in our other documents, and if that is the case, our thinking was that in fact the recommendations could come as a result of the discussion and proposed solutions.

However, if a white paper just on where we are and our first step of proposing the summit itself is the goal, then we could go ahead and have that document ready.

DR. McCABE: Elliott?

MR. HILLBACK: I would suggest that if this group is going to talk some about education at the August meeting, which I think we should, that we ought to do that second version of the white paper; i.e., not try and make it the conclusions but use it as a knowledge base-builder for the full committee, that we can get, even if we got it in a few days or whatever, a week before our August meeting, then this committee could have a little more involvement in helping the subcommittee think through how that summit should work and what some of the points would be. So I would push pretty hard, if we can, to try and get that version of the white paper out.

DR. BOUGHMAN: Would the committee feel comfortable with the work group putting forward a draft version to be looked at and discussed by the larger committee, and then that the actual conclusion of that could either be this is okay with a few minor kinds of things or we would rather wait until after the summit to finalize it?

MR. HILLBACK: I think we want to wait till after the summit to finalize it because that's when we're going to have the impact. This thing will get impact once, and I'd rather only put it out to the public or whatever once, and I'd rather do that when we have something to really say. So I think that's after the summit personally.

DR. McCABE: For the draft?

MR. HILLBACK: But a draft for the August meeting as a learning exercise for all of us here, so that maybe we get some more feedback from the full committee to the subcommittee in the August meeting about what we ought to try and not try to do at the summit, then we have the summit, and after the summit, we then add

to the white paper what we've learned and come out with one punchy, focused, let's get it done paper.

DR. McCABE: Sarah, then Judy.

MS. CARR: I just want to clarify. Staff have put a lot of effort into the development of the white paper, a draft of it now, but I think you had a good idea, in that the outline that's here and the questions that we were thinking would be posed at the summit would really be information gathering ahead of time. Is that what you're -- that sort of thing.

And then, so I'd ask Kathy Hudson if Joe McInerny -- it sounds like you've been in touch with him about doing this. Can he get information back to us in time for us to incorporate into the version that we have now? I mean, what's doable?

DR. HUDSON: I don't know if I can comment. I know he's willing to utilize the NCHPEG information system to collect this information. What time frame, I don't know, and maybe Joann could talk to him directly about how that could be utilized.

DR. McCABE: Judy?

DR. LEWIS: What I'd suggest we have ready in August or whenever -- you know, as soon as we could get it available -- would be something that looked like the state of the science that gave us a current status, and that could then be the basis for ID'ing the problem, as Elliott called it, and could be the basis of the document we gave people to start the summit, which is a current status of where we're at.

So I don't know if that would be a white paper or state of the science, an integrative-type of literature review, which I know Susanne has been working on, but a piece that didn't include the policy recommendations but included sort of the first half of the white paper, the where we're at piece, and that would probably be helpful for everyone around the table, but I think it would also be a helpful document to give to participants who are coming to the meeting whenever it is and wherever it is that we hold it.

DR. McCABE: Is that doable, do you think, for August?

MS. CARR: One of the things that we were worried about in terms of sharing a draft of what's been done so far is that we were worried that we hadn't

captured everything, and that part of the idea of doing an open meeting and a hearing and gathering is to make sure we haven't missed anything, and so I think it will be very important for -- and whatever Joe can do in terms of reaching out to anybody we might have missed, because we've done a lot of reading and trying to scan and survey through contacts and Websites and so forth.

But I'm sure there's a lot going on that we haven't taken account of, and that was I think just one concern we had.

MR. HILLBACK: But if you just portray this as what we know and what we don't know, and I think if we just portray it for what it is, which is our current level of knowledge going into the process, then we don't have to apologize for that.

DR. McCABE: And it can be done as a draft, so that it can be embellished basically --

MR. HILLBACK: Yes, right.

DR. LEWIS: And that's why putting the draft on it, I think, is so important because that way, if we're missing something, the quickest way -- you know, everyone presumes -- I mean, I presume everybody knows what I know, but if I see something that has something in it that's missing, then I'm going to provide the information and put it forth. So it could be used as a data-gathering tool.

DR. McCABE: Joann, are you comfortable with this?

DR. BOUGHMAN: We'll do our best.

DR. McCABE: And Sarah, do you have any idea when we would be able to determine the time and place of the meeting?

MS. CARR: I guess our original thought was that we would use the dates of the November SACGT meeting, but if that's not the case, then we'll have to --

DR. McCABE: You'll begin working on whether or not -- what the fiscal impacts are and --

MS. CARR: Yes.

DR. McCABE: Other issues about the Education Work Group?

(No response.)

DR. McCABE: Joann, any additional?

(No response.)

DR. McCABE: Lunch is at 12:30. Pat, would you be in a position to talk about your report from the CLIAC?

DR. CHARACHE: Yes.

DR. McCABE: Do you need any audiovisuals?

DR. CHARACHE: No.

DR. McCABE: Okay. So Dr. Charache is our liaison between the SACGT and the Clinical Laboratory Improvement Advisory Committee. Dr. Charache will now update us on the progress with the development of a proposed rule to augment the CLIA regulations addressing laboratory quality control and assurance issues in genetic testing.

DR. CHARACHE: I'm going to begin by just taking a moment to summarize the five steps that have been completed in terms of strengthening CLIA for addressing the issues that have concerned this committee, and then I'll comment on next steps and where we are.

First, as you know, in 1997, there was a Genetics Working Group established for CLIAC. CLIAC advises on all aspects of CLIA and, like this committee, it's a Secretary's committee, and I think the issues of whether Mr. Thompson knows about us or not I was listening to very carefully, because I think that's also relevant to that body.

In 1998, the Genetics Working Group reported to CLIAC, and at that time there was work begun on a Notice of Intent to publish the directions in which CLIA was to be strengthened by regulatory change. That Notice of Intent got caught in the interstices of CDC and other bodies, from which it was released by a letter from this committee, which asked that its priorities be raised by the three groups involved, and that was the FDA, CDC and HCFA.

The Notice of Intent went out in 2000, received some very perceptive comments and some which showed some misunderstanding of the regulations being proposed, and a second Genetics Working Group was established to review the comments and make final recommendations on what the regulatory features were that were to be addressed. So they had the input from the Notice of Intent, and then the

Genetics Working Group made recommendations to CLIAC of what the recommendations for change ought to be.

These are substantive because, as Michele pointed out yesterday, the CLIA and its surveillance approaches through HCFA and its authorized surveying groups has emphasized the analytical phase of testing, which is what goes on in the laboratory and how the test is done.

These changes in CLIA add to it an emphasis of the pre- and post-analytical phases which are very complex and very comprehensive and address a great deal of the aspects of oversight of genetic tests that has interested this group, things like not running the test if you lack the clinical information that lets you interpret the results, how the results go back, what the content has to be, what type of counseling should be available, and how should this be handled.

So they're very comprehensive extensions of the oversight of what goes on in a laboratory that then complements the other two steps that were recommended to the Secretary and which former Secretary Shalala addressed. Specifically, the review of the test before it ever gets out into the marketplace, which the FDA has been advancing on, as we heard yesterday, and then the aspect that we heard about today, the collection of data and ongoing ability to provide increasing amounts of information. This will impact on availability of information because of the new requirements, and so these are very comprehensive, very extensive.

At the February meeting of CLIAC, which was one week prior to the February meeting of this body, the Genetics Working Group's results were presented to CLIAC as a whole and were finalized in terms of what the recommendations are for new regulations and what the new regulations will say.

That was three months ago, and again things get stuck. Now, that's not the fault of the two groups that are going to be involved with putting these regulations on paper, but once these regulations are drafted, there will be a great deal of discussion held both within CDC and within HCFA to come up with enforceable regulations that meet the goals of what is being proposed, and that has to get out there before anything can happen, for everyone to have an opportunity to know what these substantive changes are and respond to them.

So my concern at this point is that we not get stuck again with excellent but extremely busy groups, in this case CDC and HCFA, and go for another three months without action.

So I would want to raise the question whether now, or perhaps in August, because we have another meeting of CLIAC the end of this month, a letter that parallels the one that freed up the Notice of Intent might be very useful from this committee, and I wanted to raise that on the screen for the group.

DR. McCABE: Any discussion of this? Whether we should move forward with a letter at this time? Michele?

DR. LLOYD-PURYEAR: Well, can CDC speak to --

DR. McCABE: We have CDC and HCFA here.

DR. CHARACHE: I obviously spoke to CDC and HCFA before making this recommendation.

DR. KHOURY: Joe Boone is here, and he can make some comments directly relevant to Pat's comments.

DR. McCABE: Joe, you want to join us here?

DR. CHARACHE: It is Joe's group and Bob Martin that will be involved in early drafts, and they do have a very full plate.

DR. BOONE: We do, and so does HCFA.

DR. CHARACHE: And so does HCFA.

DR. BOONE: So we've got a lot of work to be done. We actually have crafted a rule, at least the preliminary parts of the rule, right now, and this process does take time. So it's not as if it gets stuck because of lack of effort. There's a lot of pieces that have to be put together, but once it does reach the point where it can start moving through the Department -- let me kind of outline what some of the steps are very quickly for you.

Once we have something that we feel comfortable with sharing with HCFA, then we have to share that with them and make sure that they're comfortable with what we're proposing, and then we get a joint effort, and then it starts moving through the clearance steps in the Department.

It's at the point of clearance through the Department that I think the letter needs to address because that's where we want to make sure that it does have attention of the Department. There are going to be so many issues that are going to be going through this new Administration, we don't know exactly how they're going to react to this, but having it on their radar screen is very important, and I think that's what Pat is talking about. We would support that.

DR. McCABE: So you and Judy, you would agree that this letter might be helpful to you within HCFA?

MS. YOST: Again, it's the clearance process that gets this. We have often discharged our responsibility in drafting regulations, but it's once it leaves our hands, we often do not have a lot of control over who sees it and what they do to it.

So that's clearly where the difficulty is. We have met with CDC actually as of late last year to set up priorities for the program, particularly as far as regulations are concerned, because it's basically the same people in both of our agencies who do all the regulations for CLIA, and this isn't the only one we need to do.

We've got one right now that is in progress that actually should be on its way fairly shortly. That has a deadline of something that's going to expire. So that clearly takes precedence, and that again is going to be on its way in a very short time because it's already been written, and once that begins, then we can begin the joint process of working together.

CDC in this case is developing, based on the recommendations of the CLIAC, this draft. What we will look at it for is obviously whether it's implementable because that's clearly our job. Not only are we responsible for helping to write, but we also have to be able to implement whatever it says within the sense of reality and with the constraints of our budget.

So that's where it is. I mean, we have no intention, because we know that that's the next priority on our list. So we will do it as quickly as we possibly can, but again it's the system that is something that is much less within our control, and again our new administrator, for example, in HCFA, has not yet even been approved, and actually I was reading newsletters, waiting for this meeting to start this morning, and saw that there was a stack of regulations waiting for his arrival. Apparently the acting

person, there are some things that she doesn't care to deal with, and so there's a backlog already of eight to nine months of regulations sitting in HCFA because we obviously are a very highly-regulatory agency.

So just so that you get the whole picture of what is being dealt with.

DR. McCABE: What would be the time --

MS. YOST: We would be happy to -- whatever.

DR. McCABE: Thank you.

What would be the timing of a letter that would be helpful to you? It sounds like it might be premature at this time.

DR. BOONE: I think it probably is at this point in time. Maybe at your next meeting, there might be --

DR. McCABE: So maybe we could bring a draft of a letter that you could work with Pat on, on a letter, and we could bring that to the August meeting, but we would rely on CDC and HCFA to give us the green light to move ahead with.

MS. YOST: Once the regulation is drafted and goes through the clearance, it actually becomes a HCFA publication because we're the agency that is responsible.

DR. McCABE: Michele?

DR. LLOYD-PURYEAR: I think if we're going to write a letter of support, I think the Secretary's Advisory Committee needs to see what it is that you're putting forward, don't we?

DR. McCABE: What I hear is that it's not necessarily a letter supporting the rule. It's more a letter encouraging the consideration of the process.

MS. CARR: And it's a proposed rule for public comment.

DR. LLOYD-PURYEAR: Except that it gets interpreted as a supporting -- I think we need to be able to see it.

DR. CHARACHE: There are two things on that. Last meeting, in February, I did provide copies of slides which summarized most of what they did. No, no. What I presented then were the conclusions that were agreed to by CLIAC.

I did distribute today a draft of the minutes of the February meeting of CLIAC, and it doesn't have the details in it, but you can see the topics that were

covered, and I'd be happy to redistribute a list. We can do that in February of all of the recommendations.

But I think the point that Ed made is key. We want to get this out there for people to be able to address, and we want to be sure that what goes out there is implementable, which is the point that Judy made.

DR. McCABE: Sarah?

MS. CARR: I think the first letter we did in late 1999 was simply an expression of this committee's interest in seeing the Notice of Intent move forward, and this committee has not taken a position on the details of the CLIA proposed changes.

So I think it's a good idea to be briefed about them, and perhaps Joe and Judy could do that at the August meeting, of the details of what's going to be in the proposal, but I think this committee would need to think carefully about actually making recommendations about the details because I think those are CLIAC's purview, and I think we wouldn't want to see something really horrible, I suppose, if that would be in there, if this committee felt something really damaging was there. But, nonetheless, I do think we need to keep the two purviews separate.

Does that --

DR. McCABE: Yes. I really saw this letter more as a nudge than as a position, and I think it was clear before that that's what it was, but I think it would be valuable if you felt that you would be in a position in August to brief us on the status at that time and any draft that might be available that you could make public at that time.

MS. YOST: Well, obviously the Administrative Procedures Act precludes us from providing specific regulatory language before it's published in the Federal Register, but we can certainly talk in concepts.

DR. McCABE: Yes. Principles and concepts.

MS. YOST: Absolutely.

DR. McCABE: Whatever you were able to provide us with in August would be helpful, but again not so much to inform us what to write in the letter but more just in keeping us apprised of what's happening.

MS. YOST: Sure. Not a problem.

DR. McCABE: We can work on the letter before then, more in the spirit of the last letter.

DR. CHARACHE: I would point out that this group has been apprised throughout this process of what the content was, and I've shown slides three times, and thus far, the group has been very positive in terms of the proposals being made. So that can be reassuring.

At the same time, I think the same types of scrutiny and contributions that this group has provided the FDA would be very welcome at this point, as you look at the individual recommendations being made and why they're being made.

MS. YOST: But again, we're looking at the intent of CLIA, which is to ensure the quality of the laboratory testing. We're really not the scope of what this entire committee deals with, all the other issues. It's a fairly narrow piece of the overall things you're dealing with, so just remember that when you see the standards that we will not be addressing of those other types of things, specifically laboratory testing.

DR. McCABE: Right. The other thing that might be helpful to us in educating the SACGT would be perhaps to discuss the boundaries between CLIA and the FDA, because that's an area that I still find a little bit -- you know, that I'm not sure of where that bright line is, but that was my guess, that it may not be a bright line.

But I think it's helpful for us to continue to try and understand that, those of us who are not in the regulatory arena the same way. So perhaps as part of that could also look at when interstate commerce takes over from CLIA versus things done within states and that sort of thing, in addition to the update on whatever you can provide us on the rule.

DR. CHARACHE: In a way, this leads to the second thing that I wanted to comment on here.

The FDA, as we've seen it, really has an independent role of CLIA in terms of evaluating and approving of new tests, and now they've moved into the home-brew kind of test, which has always been a problem.

They also now have a direct role within CLIA, which is that of classifying tests into the three categories that determine the oversight that is received

from the rest of the CLIA program. The categorization is dividing all tests into high complexity, moderate complexity and waived tests.

One of the current areas of concern, which is being looked at with the FDA by CLIAC, is the issue of waived tests. Now, this will be the third meeting in which I've called this to the attention of this group because I think it will have long-range implications on all tests, including genetic tests.

The model for determining that a test is waived has changed, largely as a result of the 1997 FDA Modernization Act. To determine that a test is waived required in the past two factors. One is that the test be so simple to do that it's very hard to get the wrong answer, and the second is that if you get the wrong answer, it's not going to seriously harm the patient.

Those two were linked in the FDAMA, the FDA Modernization Act. So it now reads in that paragraph that a test must be waived if either it's easy to perform or it does not cause serious harm. So that that makes the easy-to-perform part as an independent feature.

In other words, you can drop Solution A on to a card and Solution B on to a card, and you're unlikely to guess that it's pink as opposed to white.

There is difficulty with this obviously as you apply it to something like a genetic test, because we foresee that this type of test would be very easy to perform, and it has raised some concern therefore on how tests are determined to be ready to be waived.

The CLIAC again established another working group to work with the FDA and to think through what the criteria should be and how guidelines should be applied to make the ability to get a waived test through as permissive as is reasonable but not more permissive than is reasonable, and that working group has met a few weeks ago and will be reporting recommendations back to the parent committee.

One of the recommendations under consideration is that any genetic test should not be waived, and I don't know where that's going to go, but that is one consideration, and I think that with the pressures of FDAMA and the pressures on the FDA, this may become an issue that will interest this group further.

DR. McCABE: Thank you. Perhaps that could also be discussed, the status of that, for that to move forward, at the August meeting.

Any further discussion with Pat?

(No response.)

DR. McCABE: If not, we're going to break for lunch a little bit early, but we will also return early. So we're going to be starting sharply at 1:00. I know that people have travel plans, and so we will be trying to start early and be able to leave certainly on time, preferably a little bit earlier than planned. We will definitely be done by 3:00, if not before.

Thank you.

(Whereupon, at 12:05 p.m., the meeting was recessed for lunch, to reconvene at 1:00 p.m.)

AFTERNOON SESSION (1:07 p.m.)

DR. McCABE: This is the time set aside for public comments, and I have two speakers. One of our speakers, Dr. Michael Watson from the American

College of Medical Genetics, has said that he really made his comments as part of his presentation yesterday. So we have two public comments. If there are additional individuals, please register at the desk.

First is Paula Rieger, who is President of the Oncology Nursing Society. Ms. Rieger, if you would go to the podium, please.

MS. RIEGER: Thank you, Dr. McCabe, and I thank the committee for allowing me to be here today to provide commentary.

ONS, or the Oncology Nursing Society, is a national organization that represents more than 28,000 oncology nurses and other health care professionals that are dedicated to excellence in patient care, teaching, research, administration and education in the field of oncology. It is within the scope of oncology nursing practice that oncology nurses with specialized training and skills provide cancer genetic counseling and contribute to the evolving body of knowledge within cancer genetics. We thank the Secretary's Advisory Committee on Genetic Testing for the opportunity to testify today and to provide input to the development of a Food and Drug Administration premarket review process for genetic tests. The committee has gathered important information regarding premarket review and the FDA's labeling authorities as they pertain to genetic testing. We commend you for your thoughtful and timely consideration of this issue and the progress you've achieved thus far.

In general, we consider the proposed template to be very comprehensive. It addresses many of the areas of concern that have been expressed in previous testimony and research conducted by the SACGT. We commend you on this work. As the template is further refined, we have several suggestions for improvement.

Number 1. The template should address who will be able to order the test. For example, will it be physicians only or other providers of genetic counseling services? Patients will be better served and providers more informed if specific information on the providers involved in the process of ordering, receiving and relaying results is included.

Number 2. Along with indications for the use of the test, consideration should be given to addressing the consent process for obtaining the test. For example, is an informed consent required? Is genetic counseling a prerequisite to

having the test conducted? As tests are granted regulatory approval, the clarification would help to ensure that adequate education and counseling for patients is regarded to be an integral part of the process.

Number 3. Under Section 5, Methodology, is the methodology described better than others, if others are available? In essence, the chosen methodology should be placed in context. Also, if published reviews are available that support the use of the chosen methodology, they should be cited. The completeness of this section will be helpful to providers in understanding how a test was conducted and in learning more about the different types of genetic testing available.

Number 4. Under the reporting of results, there should be discussion of the chain of confidentiality. For example, how will results be handled in the laboratory's computers? Who has access to those results? This knowledge will help providers to give assurances to patients who have major concerns about these issues. It is possible that precautions already in place for HIV testing may serve as a useful model for maintaining confidentiality of genetic testing results.

Under Section 8, Quality Control Procedures, we suggest that answers be provided to the following questions. Is there correlation with clinical findings? Are there additional tests using a different approach that would substantiate the results?

Number 6. Under Section 10, Clinical Interpretation, it should be defined who is responsible for the reports. For example, is it a pathologist, an M.D., or a Ph.D. signing off on the results?

Number 7. Information regarding the clinical utility of the test is especially important with respect to cancer predisposition genetic testing. In many cases, there exists no standard of care to determine the best strategy for managing risk. As research progresses, we will begin to have evidence-based strategies for addressing such risks. At this time, consensus guidelines for the management of risk could serve as an example of how information on interventions to manage risks could be incorporated.

With respect to cancer genetic counseling, it is often equally important to address strategies for managing risk for those with a negative test result as well as for those with positive test results. A negative test result in many situations may

represent no news for the family, and the family would continue to be considered a high-risk family.

For example, in a family with a strong history of early onset colorectal cancer, if an effective program tested negative for alterations in genes known to be associated with hereditary nonpolyposis rectal cancer, at-risk relatives would still be considered at risk for colorectal and other cancers. The at-risk relatives as well as the proband would still need to be counseled appropriately in terms of diet, exercises and recommended screening.

Consideration must be given to how these criteria will be enforced and reviewed. The field of cancer genetics is rapidly changing and likely would require frequent updating of the information included in the template to keep it as timely and educational as possible. Further, there must be assurance that cancer predisposition genetic testing would always be held to the highest standards and levels of scrutiny and would fall under CLIA regulations.

ONS wishes very much to continue this dialogue with the committee as it develops its recommendations for the Secretary. We look forward to further work that will assure that cancer predisposition genetic testing is accessible to those who need it, and that those individuals are supported with the highest quality of counseling and professionalism.

ONS has established that advanced practice nurses -- in other words, those with master's preparation -- and those with specialized training in cancer genetics are best suited for practice in counseling and education regarding cancer predisposition genetic testing. ONS has a significant number of nurses who currently provide these services, and many are recognized nationally for their knowledge and expertise.

ONS stands ready to work with the committee, the Secretary and other stakeholders to ensure that genetic testing is accessible, safe, responsible and meaningful for those individuals seeking cancer predisposition genetic testing.

We thank you very much for the opportunity to testify today and to provide ongoing input to address the issues related to genetic testing in this country.

Thank you.

DR. McCABE: Thank you very much. Why don't you wait up there? We'll see if there are any questions or comments to you.

Wylie?

DR. BURKE: Thank you very much for your comments. I just wanted to comment that I think amongst the many very important issues that you address in your comments, some, per our conversation of yesterday, may be more pertinent to the issue of development of clinical practice guidelines than to premarket review, and I just wanted to register I think they're all tremendously useful, and I think we should try and incorporate them in whichever part of the process they're most relevant.

MS. RIEGER: Absolutely. Thank you.

DR. McCABE: Other questions or comments?

(No response.)

DR. McCABE: Thank you very much.

Our next speaker is Wendy Uhlmann. Ms. Uhlmann is from the Division of Medical Genetics, University of Michigan, and is presenting as an individual genetic counselor.

You'll recall that Wendy is the former President of NSGC and appeared before us in that role but is now presenting as an individual member of the public.

Thank you.

MS. UHLMANN: Thank you.

The proposed elements in the FDA template are appropriate for genetic test submission and essentially capture the critical elements that were previously identified by the SACGT.

My main concerns are how will clinical utility information be incorporated, and how will the FDA's template be applied to labeling the more complex genetic tests and panels of genetic tests?

It is critical that the FDA's template be applied to more complex genetic tests. For the most part, the FDA's template examples have included relatively straightforward genetic tests that have few mutations, and where there's general

uniformity in how these genetic tests are performed in different laboratories across the country.

However, for many genetic tests, there is not uniformity in how the test is performed. Different testing methodologies and mutation panels may be utilized, depending on the laboratory. Therefore, selection of a laboratory can make a critical difference in test outcome and can have significant implications for patient care, and in my written testimony, I've included some examples of such differences.

An example of a very commonly-ordered genetic test that poses several labeling challenges is cystic fibrosis. Over 900 CF mutations have been identified, which obviously cannot all be cited in test labeling. However, there are different rates of mutation detection, depending on ethnicity and genotype-phenotype correlations, that should be noted.

In addition, laboratories across the country differ in the number of mutations that are included in their genetic tests for cystic fibrosis. The ACMG recently recommended a standard cystic fibrosis screening panel of 25 CF mutations, and I strongly support further efforts of genetics professional societies to help establish test standards for specific genetic conditions.

However, given the fact that a cystic fibrosis genetic test can differ, depending on which laboratory does the test, will the FDA have to review dozens of cystic fibrosis genetic tests submissions from different laboratories for labeling purposes? Think of the work this would generate for test labeling for just a single genetic condition.

Just as laboratories can include different mutations for a single test, laboratories may also choose to bundle different genetic tests together. For example, there are several laboratories that offer test panels for individuals of Ashkenazi Jewish descent. However, laboratories differ in which genetic tests are included in their Ashkenazi Jewish genetic disease test panels.

How will labeling be done for these bundles of multiple genetic tests? Depending on the number of genetic tests included in a test panel, this could result in very lengthy labeling information.

The FDA's example of labeling for Fragile X syndrome, which tests for a single mutation, was three pages of text. As it is unlikely that this will be read or understood in its entirety by the clinician ordering the test, I think it is critical that a simple readily-recognized test classification system, much like the one that exists to classify teratogenicity of medications be developed and appear at the beginning of test labeling.

For example, Test Category A would be for a test that is routinely ordered, and Test Category B would be for tests that should be ordered by, in consultation with a specialist or genetics professional.

Similarly, a test classification system could be developed to stipulate that documentation of informed consent that needs to be obtained. For example, Test Category 1 would be for a test that requires only verbal consent, up to Test Category 4, which requires written informed consent.

There needs to be the basic assumption that most genetic tests will have multiple applications, and this needs to be included up front in the test labeling. Such is the case in fact with many genetic tests that exist today. The same genetic test can be used for diagnostic, predictive, carrier and prenatal testing applications.

I think that off-label use should be addressed proactively by having labeling that will be inclusive and address the multiple applications.

I recommend that the test template include entries for diagnostic, carrier, predictive, prenatal testing, and that the FDA have a standing genetics expert panel, including clinical geneticists and genetic counselors, to work with the FDA in making these labeling determinations.

It is important to keep in mind that even as the labeling is being done, the information is rapidly changing. For example, labeling for the BRCA1 and BRCA2 tests for hereditary breast cancer 1995 would have cited the penetrance figure of approximately 85 percent. Less than two years later, this penetrance figure would have changed to 56 to 85 percent. Labeling of genetic testing needs to be regularly reviewed, and there needs to be a way to rapidly update labeling information.

There are two elements I would add under the heading of additional influences. One, genetic heterogeneity. Two, genotype-phenotype correlations. Both

of these elements can be significant in determining test usage and interpreting test results. Overall, it is critical that sufficient clinical utility information be included as a test can be clinically valid but of limited clinical use.

In closing, the proposed FDA template needs to be applied to commonly-ordered complex genetic tests, particularly those tests that involve multiple genes, many mutations, genotype-phenotype correlations and penetrance issues, and to genetic tests that differ significantly, depending on the laboratory doing the testing.

The SACGT is to be commended for its thoughtful, comprehensive deliberations. Thank you for making the effort to have transcripts of your discussions available and for giving the public the opportunity to provide input on these critical issues.

DR. McCABE: Thank you. Any questions or comments for Ms. Uhlmann? Yes, Barbara?

DR. KOENIG: I just want to thank you for the very thoughtful presentation and also thank you for raising the issue of the multipanel test, which I think is a true challenge.

DR. McCABE: Other comments?

(No response.)

DR. McCABE: Has CLIA addressed the multitest bundling?

MS. YOST: A test is a test. It still has to meet all the requirements, which are many.

DR. McCABE: Okay. So this is getting more into the labeling issues as you put them together.

Thank you very much.

And we have a third speaker who has been added to the list. Finley Austin from Roche has asked to address us.

Ms. Austin?

MS. AUSTIN: I just want to encourage you to think about a third group and your inclusion of the stakeholders meeting in August, and listening to the discussion, you mentioned in representation from industry, pharmaceuticals and biotechnology. That will not cover actual in vitro diagnostic manufacturers. They are a

very separate entity, and even though we all have very common interests, and even though some companies actually have activities in all these areas, I really think you need to consider having somebody from the manufacturer's side as a stakeholder and would suggest that you discuss this with AdvaMed, who is their trade organization, or Dr. Kelly and I from Roche would be happy to put together some names of suggested experts because they do have a very unique perspective and a great deal of history that I think everyone would benefit from hearing from.

DR. McCABE: Thank you very much. Perhaps you could give us the contact information for AdvaMed. Thank you.

Any questions or comments for Ms. Austin? Pat?

DR. CHARACHE: I'd also like to thank you for raising this issue. I hadn't thought about it in that context, but I think you're right. I think it would be a major added depth to the discussion.

MS. AUSTIN: Well, we had a meeting with FDA recently, and we had people from all sides at the table, and I think everyone very much benefitted from it because the pharmaceutical side is coming at this with a different perspective, and they're the only ones who can also answer the question that I heard raised of why aren't some things being turned into kits, and I can get into some of those issues with you.

DR. McCABE: Thank you very much. It's helpful to have your input. We appreciate your attendance and providing input to us.

Any other comments or questions before we move on?

(No response.)

DR. McCABE: Okay. We will now have the progress reports from the other work roups. We've heard from the Data Work Group and the Education Work Group. The chairs of the other work groups will now provide us with updates on their progress.

You can refer to Tab 8, and then there was information in the blue folder updating the information in Tab 8 that summarizes the progress of all five work groups. So I'd refer you to the updated information that was in the folder.

We're going to have Mike Watson speak to us on Rare Diseases. He's co-chairing the Rare Diseases Work Group with Mary Davidson. Mary was unable to stay this afternoon. So Dr. Watson has agreed to update us.

DR. WATSON: This will put you ahead of your schedule at least.

Mary and I haven't even really had time to talk yet. I've briefly gone over a few of the things that we spoke of at the last meeting.

I do know the people at the American College of Medical Genetics, and I can tell you that they have an agreement with the American Society of Human Genetics to very actively pursue issues of CLIA compliance in research laboratories, to go out to our membership of researchers, clinical lab directors and investigators, to try to learn issues of compliance with CLIA, if there are impediments in it, what they perceive as their impediments to compliance, so that we can develop tools and resources to encourage them to either license or associate with licensed laboratories.

So we're going to be developing that survey outside of this organization as an interest of our own because we're very much interested in trying to help the laboratories, both research and clinical, in dealing with some of these issues.

MS. YOST: And again, since you're on that topic --

DR. McCABE: Can you speak into the microphone, please, Judy?

MS. YOST: Anyway, I think it's important to this that we work with you, and we have the facilities at hand. There are many times that we can help individual entities identify existing practices that will facilitate their meeting requirements without having to do additional work, and so please include us in that process.

DR. McCABE: I would also suggest that, in addition to looking at the federal CLIA, you should look at those states where they supersede the federal CLIA requirements, and therefore you need to meet the state requirements.

I know in California, the requirements are much more stringent for those of us that live in the state of California than for CLIA, the federal CLIA, having to do with the qualifications of individuals doing the testing.

So please, also, as you're considering this, look at those issues as well.

DR. WATSON: Yes. It cuts both ways. I mean, we intend to look at the exempt and the deemed CLIA organizations, but I mean while some have comprehensive programs that are beyond CLIA, not all are as comprehensive in the genetics area as they might be. So we'll be looking at all those aspects.

The other things that we're paying -- actually, apropos to the last public comment on the Rare Diseases Committee, I've already talked to Judith, that there's a huge overlap here with access issues. I mean, that is the fundamental issue in rare diseases, is protecting access, and among the things that we want to do is revisit a few of the issues that the Task Force on Genetic Testing had developed, where we actually put together data that told us there was a problem.

We know as of 1996, for instance, what proportion of the NIH budget was focused on rare diseases. We know what was going on within NORD and other organizations as to developing information to facilitate access to that information for the public and for the physician community.

So we have some baselines, and we can look at how the recommendations that the task force made to deal with some of those problems, whether they've actually made any difference or not, or whether they've been addressed to get a sense of whether or not any of these activities we all spend our time doing actually amount to anything at the end of the day, and if not, look at how we might improve the way we've approached making recommendations.

We clearly want to look very carefully at issues of development and delivery of rare disease tests, and this is not just the laboratory side but also the manufacturing side, because there's issues that face the service providers in the laboratories as to how they go about R&D, what they have to devote to R&D, and whether or not all the genes how common and being identified related to common disease are going to shift people's focus away from the rare diseases and really make them much more difficult to bring online.

Up until 1996, there were tax incentives, for instance, for companies to help them with the R&D side of orphan device manufacture, and we have AdvaMed already on our list of people to talk to about the issues that both the manufacturers face in being encouraged to develop the products for rare disease testing, not only for rare

disease testing, but also because I think the manufacturing community does have probably a better base of resources on which to comply with regulation than do the laboratories themselves, and to the extent that we can shift some of the responsibility back to the manufacturing sector for test development and trials and such, I think we'll be in a better position.

We also want to look at some of the issues of where cost impacts manufacturers. Clearly, the greatest impact is in the area of clinical trials. With rare diseases, there obviously needs to be a very different perspective at many levels about how we approach these things.

HCFA has to recognize that these things come in, will come in very quickly. They have to be able to adjust to pay for rare diseases without an N of 2000, so that these labs are not hung out to dry. So there's a wide range of things of that type that we want to begin to look at, revisit the concepts of provisional or directed 510(k)s as mechanisms of getting things into FDA with some latitude for humanitarian device exemptions and other ways to ensure that they are at least registered, listed, and to some degree overseen by recognizing that rare diseases inherently cannot be overseen to the same level as statistical satisfaction that other types of tests might benefit by.

Then unifying the definitions obviously, and I think that's very much tied to the process you've gone through in defining what a test is. As we begin to get more and more focused on defining the test around its intended use, as we begin to look at the humanitarian device exemptions, they're really only going to apply to the diagnostic application of these tests, at least in those early days when one needs to be incentive to develop the kits.

I don't think anybody's jumping in with a rare disease screening test for the population as a first test. So if we look at the way these things really are translating out, I think we can really hone down and tighten up a little bit and facilitate some translation of investigation into service by really looking at how these things flow out of laboratories and into the service sector.

DR. McCABE: Any questions or comments for the Rare Disease Work Group?

(No response.)

DR. McCABE: So you're going to move ahead with that, Mike, and you'll be working with Mary Davidson to try and move forward on this.

MS. YOST: You can download our application off our Website.

DR. LEWIS: And Ed, we'll be working together where the intersection between access and rare disease. Mike and I haven't had a chance to talk, but we'll be doing that.

DR. McCABE: And with that, why don't we move on to your presentation, Dr. Lewis, on updating us on the Access Work Group?

DR. LEWIS: There's not much to update. We've had some activities since the last meeting but not much.

In terms of where we're at, we had some responses that we received that were looked at in response to the presentations and in response to a follow-up from our meeting, our working group meeting at the last meeting.

At this point, we're going to go ahead and continue to work on looking at agency efforts to address disparities as they relate to genetic testing and hope to be able to present to you -- am I still correct that we're going to try to do this in August? Yes?

MS. CARR: Yes.

DR. LEWIS: Well, I just want to make sure we're still okay with that time line with everything else you all have to do.

To look at what's going on across the agencies and to get a sense of where the agencies are at in terms of looking at issues relating to health care disparities, because that's clearly, as Dr. Stith-Coleman told us at our last meeting, that's clearly high priority in the agencies.

So to be able to really have a good handle on what all of the agencies are doing, and then to go ahead and move forward, looking at developing a white paper on billing and reimbursement, so that we have a sense of what's going on in terms of how people are able to bill for and be reimbursed for teaching and counseling components of genetic services.

And then the other thing we're talking about, at one point, we had talked about trying to develop a model package of genetic services, and we had a draft

of that, and we looked at the draft of the model. You know, what would an ideal genetic services coverage plan look at, and as we looked at that, we realized that we really couldn't set up that because that was really more in the realm of practicing health care rather than making policy.

So we're going to try to work on that from more of a broad brush perspective, to get a sense of what are some of the basic principles that we believe should be incorporated by those who are developing genetic services plans, but to be much more broad brush than be specific because we really didn't want to get to the level of what tests should be covered, what tests shouldn't be covered, because that's really getting into practice as opposed to policy, and we didn't want to go there because we feel there are people who have a lot more specific information, and that that was the kind of list that would not have very long life because it's too much of a moving target.

So that's where we're at. We hope to be back to you in August, and we'll be moving forward, and as we heard yesterday, I think that a lot of the issues are really pushing into the area of access, and that it's time for us to move into higher gear.

We've been a little bit slow because it seemed that the work we were doing was dependent on a lot of the other work, and I think it's time for this group to become more active, and I welcome all of your comments and participation.

DR. McCABE: Regarding the health disparities, I'd just like to point out that an area that has received a lot of press, and the term "health disparities" is used consistently in this press, has to do with newborn screening, and the fact that some states screen for three diseases and others screen for more than 30.

This is an area that really has gotten public interest in it, to the extent that it was even a subject of one of the segments on "ER" about a year ago, to heighten public awareness when it makes it to prime-time TV.

So I would suggest that you perhaps talk with HRSA. Michele has stepped out, but her shop funds the National Newborn Screening and Genetics Resource Center, based in Austin and San Antonio, Texas.

In addition, you might check with Mike Watson because the American College of Medical Genetics recently received a contract or is in the process of negotiating a contract with HRSA regarding developing a national agenda for

newborn screening, but as a very concrete focus, it's a well-identified health disparity. Here is one, and it would be a good place to start.

DR. LEWIS: Absolutely, and Michele's on our working group, and as we continue to work and collaborate, I think that yes, I think you're absolutely right because it's not a baby's fault that it's born in Massachusetts and has a much better chance of having things identified.

DR. McCABE: Right.

DR. LEWIS: No one should be systematically disadvantaged for not being born in Massachusetts. Some of us were.

DR. McCABE: And it's four million babies, with multiple tests per baby. So it's a significant segment of the U.S. population. The entry to the population by birth at least --

DR. LEWIS: Well, we will certainly make sure that Michele keeps us on target with that. Yes, Michele, you just volunteered.

DR. LLOYD-PURYEAR: I'm sorry. My stomach was upset.

DR. LEWIS: That's okay. We're going to use newborn screening as a concrete example when we start to look at health care disparities.

DR. LLOYD-PURYEAR: That's a very concrete example.

DR. McCABE: And there are data, and Brad Thurow, who's head of the National Newborn Screening and Genetics Resource Center, presented 2001 data a couple of days ago in Baltimore, at the Pediatric Academic Society meetings.

DR. LEWIS: Thank you.

DR. McCABE: Other questions or comments regarding the Access Work Group?

DR. LEWIS: And again, having Reed be involved with us certainly helps us look at some of the reimbursement issues and some of the case management issues that -- you know, in addition to our ad hocs, who are all coming from the insurance industries, and also, the other thing that we added last time, and we may even want to focus on, is people who are purchasers of health care insurance. So we've tried to make sure that we do have the major stakeholders, and that was one we identified later rather than earlier, but certainly people who purchase health care insurance. The

Small Business Administration is where we're going, but we're going to continue to look at that area.

DR. McCABE: Well, certainly small businesses are one of the areas where we heard from the public a number of anecdotes because for the small employer, they are also the insurer, and that means that decisions about employment are being made by the individual who has the medical information as the insurer.

Yes, Sarah?

MS. CARR: I think Michele Puryear wants to be added to the Education Work Group. Is that right, Michele?

DR. LLOYD-PURYEAR: Yes.

MS. CARR: And there's someone representing HRSA on it, but if Joann doesn't have any problems with that, and I'd like to ask Judy Yost about Rare Diseases.

Ginny Wannamaker's a member of that work group, but I know that you've lost her for a moment, and so I was wondering whether we should add you for the time being. Would that be appropriate?

DR. LEWIS: Sure.

DR. McCABE: Anything else for Access?

(No response.)

DR. McCABE: Any other comments, Judy?

DR. LEWIS: No, except that we're getting anxious, and we'll be back to you soon.

DR. McCABE: Thank you very much.

Our next work group is Dr. Barbara Koenig, Informed Consent.

DR. KOENIG: Thank you. Since I have these lovely overheads prepared by Sarah, maybe it'll help people stay awake over lunch or right after lunch.

The Informed Consent Work Group has been engaged in our task, and the first thing I'd like to report is that we've added Ben Wilfond from NIH as a co-chair of this committee for a number of reasons.

I think in many cases, the work of the subcommittee chairs parallels their usual activities, but in my case, I'm actually not an expert on informed consent

within bioethics. So I wanted to get some help, and you'll hear throughout the presentation how we've also engaged other help for this task. Specifically, we've added three consultants who have done empirical research in this area, and I'll mention their names later.

So since our goals have moved around a little, I'll go over the goals quickly. To enhance the informed consent process for genetic testing by creating a seamless system from the research phase through the marketing of tests for clinical and public health uses.

But there are 400 tests already in clinical use. So the priority is to address consent issues in clinical practice and in public health as opposed to in the research phase, although we will be considering this, the intersection between research and practice.

The other problem that we're having, which I guess is no different than the other working groups, is given -- you don't need to read this one, I think. There's so many activities going on nationally in terms of informed consent and human subjects, sort of recrafting the human subjects protection enterprise in the United States as well we -- there are a lot of things we have to keep abreast of. So it makes our task more complicated.

So our charge has been to first develop a genetic testing brochure for consumers that provides basic information and outlines essential questions that should be asked about a genetic test in order to enhance informed decisionmaking. To develop criteria defining which types of tests warrant what kinds of consent and the locus of responsibility for obtaining consent. To consider the work of other groups, such as NBAC and PRIM+R, and develop further guidance for investigators on when experimental genetic test results may appropriately be returned to research participants, taking account of the need for basic oversight elements, such as those by CLIA. With the fact that the privacy rules have moved forward, we will hopefully now eventually be able to act on this task, too.

Prepare a white paper exploring the evolution of informed consent from the research phase to clinical setting. Look at the social risks of genetic testing and how such risks should be considered during the review process, and, last,

challenges to informed consent posed by directed consumer marketing, and direct access, such as over the Internet, to genetic tests, and explore issues and challenges associated with informed consent and institutional review of multisite protocols involving genetic testing.

We've had a number of conference calls. We had a meeting surrounding the last SACGT meeting, and we're actually having an all-day meeting tomorrow with two of our three consultants, and the goals of that meeting are going to be, first, to review this revised consumer brochure which we talked about in February, and to come to closure on its presentation and dissemination, and, second, to begin the development of our report on defining levels of consent appropriate for different categories of genetic tests used in clinical and public health practice.

In terms of the information brochure, we're going to review the revised version of the brochure which we're very, very fortunate to have had a lot of input from Wendy Uhlmann, who basically has rewritten this, taking into account her experiences as a genetic counselor and ability to communicate this very complicated information. So we now have a completely updated draft which you haven't seen yet, and we hope to be finalizing that tomorrow.

And then most of our meeting tomorrow is actually going to be devoted to the issue of addressing questions on what we're actually going to do with this brochure once it's developed, and how to coordinate it with the other templates and information brochures we have. The final version will be sent to you for approval in August, hopefully for approval.

In terms of what we're going to talk about, what we talked about in February, I think we've brought up already in the meeting that we came to the conclusion that we didn't want to talk about informed consent as optional in genetic testing, but that we would begin with the position that it was necessary for all genetic tests in clinical settings, and what we were talking about in terms of suggestions about implementation was more having to do with how it would be implemented or what level of documentation would be included.

We also talked about the fact that there must be good sources of information about tests for patients and consumers. This overlaps with our other

activities. Defining criteria for tests, for types of tests that warrant documentation of consent, and when it should just be a check box, say, who should do it, and when it should be an actual signed document.

In terms of progress on our report, we actually contracted with Kathi Hanna to serve as the science writer for this effort, and she has created the beginnings of this report, and everyone on the Informed Consent Committee has read it, and we're going to be reviewing it tomorrow.

We've also involved the academic experts I mentioned at the beginning, all people who have worked on informed consent, and for those of you who don't work in bioethics, what's happened I would say over the last five years, there's been an increasing amount of empirical research documenting what are the limitations of informed consent? What are its strengths? What are its limitations? What work can you ask it to do, and what is inappropriate work to ask the informed consent process to do, as opposed to other means of accomplishing the same goals?

So Pam Sankar is particularly useful on that topic because she's done work on that. It includes Gail Geller from Johns Hopkins, Nancy Press, who you know from OHS, Oregon Health Sciences, and Pamela Sankar from the University of Pennsylvania. I was just informed she doesn't like to be Pam.

In the report, we're going to review the literature and codes of practice and state laws, and then the preliminary draft will help our discussion tomorrow. So tomorrow, when we will spend the whole day, we're going to specifically look at the last -- in terms of the first two, I don't think we need to talk about. The locus of responsibility for obtaining consent. We're going to continue discussing the issue of what should be the lab's role, if any, as opposed to different providers, and specifically focus on trying to develop a categorization of genetic tests that possibly will spin off of our original classification but to find a way, and Wendy Uhlmann presented another one just in her testimony now that we'll consider, about how to put together the issue of what kind of consent do you need with what categories of tests.

We're going to talk these through and then work out some potential methodologies with some case studies, and our goal is to have a draft of the report to the

full committee in August, and we're also hoping that some of the background papers and our work might be published, and that's that.

So I'm happy to take any questions.

DR. McCABE: Yes, Judy?

DR. LEWIS: I think the idea of doing a brochure is wonderful. I'm hoping that your brochure can be something that can also be webified, because I think a lot of people, if they don't have the -- it's really a word. We webify everything these days.

But a lot of times, patients and humans really at this point in time don't necessarily know where brochures are available, but people turn to the Web and to search engines, and so having it accessible that way, I think, is going to really increase the distribution of people before they even get to the point of getting to a provider who's going to hand them a brochure.

DR. KOENIG: We can consider that, but we also are always thinking about the populations who don't have even a computer. So hopefully in California, since we don't even have electricity, it's going to be --

(Laughter.)

DR. KOENIG: -- a particular challenge.

DR. McCABE: Michele?

DR. LLOYD-PURYEAR: I'm sorry if there's already been a great deal of discussion on this, but why are you doing a brochure?

MS. CARR: I can speak to that.

DR. KOENIG: Thank you, Sarah.

DR. McCABE: Sarah?

MS. CARR: The committee charged the work group with doing it.

DR. LLOYD-PURYEAR: We did?

MS. CARR: Yes. It was to be a corollary of the provider summary Q and A, which has evolved into a Q and A.

DR. KOENIG: There are Q and As, and they're actually nicely in parallel.

MS. CARR: Exactly. But may I add that some of the members of the work group have actually -- part of why you don't have it in front of you at this meeting for review, and that was our goal in February, was because some members of the work group had sort of second thoughts about the -- I won't call it propriety, but the appropriateness of our committee doing a brochure because there have been many, many done. Many other organizations have done them. Consumer organizations are preparing them, and so I think part of the discussion tomorrow will be to sort through some of these issues.

Not only have we got a much better version of the document, thanks to Wendy Uhlmann, to look through, but we also need to look again at the questions of the appropriateness of our doing this, and who we're really trying to reach, and with what scope of information, and then how we will do it, how we will disseminate it and so forth.

DR. KOENIG: Also, the issue of how useful is something that's a generic presentation of this as opposed to things that are focused on either specific settings, like newborn screening or specific conditions.

DR. LLOYD-PURYEAR: Because what I was thinking, that it may be more appropriate or more beneficial to do points to consider in this process, which sounds like what you will come up with, with a lot of the background paper, and then that would be actually very valuable and generalizable.

MS. CARR: Well, the brochure provides information about genetic tests. It's not a consent document per se, although it has questions that it tries to provide the kinds -- empower, I think, as Reed Tuckson has said in the past, empower consumers and patients and the public with the kind of information they need to ask.

But your idea I think is an interesting one, and it could be a solution to the problem that some people may have about why we're doing it and whether it's useful, but that is to perhaps lay out some principles for others who do put such brochures together, not unlike the guideline for the guideline development process. So that's certainly something that Barbara and Ben can perhaps discuss with the group tomorrow.

DR. KOENIG: Please remind us. Thank you.

DR. McCABE: Wylie?

DR. BURKE: Yes. I actually also want to sort of point out, and it's very much in keeping with Sarah's comments, that I'm not sure those are mutually exclusive goals.

One of the reasons we're ending up in a Q and A format for the physician information is just because that's coming across to us as a very user-friendly format, and it might be that even if -- I mean, there's points to consider that go out to people that are making documents, but there also might be here's the things you should be looking for when you're thinking about a genetic test, and the Q and A document may be helpful to people.

DR. McCABE: Other questions or comments?

(No response.)

DR. McCABE: Thank you very much.

Any other wrap-up that anybody wishes to bring on the work groups in general or any specific follow-up on any of the individual work groups? Yes, Barbara?

DR. KOENIG: Well, I actually had a general comment for the final discussion that bears on the work groups. So is this a good time to bring up something like that?

DR. McCABE: This is a very appropriate time.

DR. KOENIG: Okay. One of the things we had discussed in a previous meeting was how to deal with the complicated issue of thinking about while we've talked about it in terms of our reports, how to use concepts like race and ethnicity, and we came to some conclusions about those things.

Then in a fairly recent meeting -- and Sarah, you're going to have to help me with this. Was it the February meeting where we made the decision about the Ancestry Group?

MS. CARR: It was November.

DR. KOENIG: November. In the November meeting, we actually had a discussion about whether we needed to address this more systematically, and we

created an -- we called it an Ancestry Work Group, which was to be co-chaired by me and by Reed Tuckson.

We did have a number of phone calls and some consultation about how to carry this out, and in the end, it's become somewhat apparent that it's perhaps not a good idea at this point to take this issue and have it be highlighted in such a way, but I wanted to make another proposal about how we might keep these issues on the table because I personally think they're extremely important, and I brought it up a bit this morning, which is the issue of one way that we can keep seriously thinking about the issues of in genetics, how to keep looking at real genetic variation as opposed to confusing it with social categories of difference, is to perhaps add that focus to two of the existing working groups, which is the Health Disparities Group, because that group is also going to be considering issues of health disparities among different populations -- or Access. Pardon me. Wrong word. You're calling it Access.

So it could be part of the Access Group, where it's coming up naturally, as well as part of the Data Group, because I think the issue of how we now begin, as we're creating all of these big data collection strategies for how genetics data should be set forth on the Internet and elsewhere, it's going to be very important to rethink the kind of categories we're using when we talk about genetic variation across the human population.

So I think perhaps we should dissolve the Ancestry Working Group and instead insert this domain into the two existing groups.

DR. McCABE: And I think it came up this morning with CDC as well in terms of the discussion of the access discussions that are going on there.

Yes, Wylie?

DR. BURKE: I think that's a good suggestion. If I could just follow up briefly on Muin's comment this morning when you raised a question about race, ethnicity, and the conflating of social groupings with pseudobiologic concepts.

First of all, I think I'd like to mention that in the most recent issue of the New England Journal, there are some data that are of precisely the kind that come under this discussion. That is, data that look at a differential response to a particular medication by race, and two very interesting accompanying editorials, one of which

makes very forceful points about the importance of separating what are wrongly interpreted as biologic concepts from the true social realities of racial classification.

I think the committee might find those editorials very useful to look at. The two editorials take different viewpoints on this issue.

The problem that I think we will have in the Data Committee that Muin mentioned is that we're stuck with how data comes to us. In other words, the best we can do is organize and present for greater understanding or disseminate in some way data, but the data often comes already categorized in a way that we can step back and say maybe isn't the most useful way, and I think that's really the point the editorial makes.

So I think really what your suggestion gets to is that this should be in all our minds, in every committee, where the issue comes up, and it may ultimately, I think probably down the line, after we've completed some more tasks, become an issue we make a position statement about.

DR. McCABE: Yes, Barbara?

DR. KOENIG: I just want to follow up briefly on this issue. I agree with you that we have some complex issues in terms of the past collection of data, but I think it's also important to remember that a lot of those practices are purely ritual practices, and that they don't necessarily need to be continued, and you don't need to continue them for all data collection.

I know you agree with that, and you can say more about it, but I think, for example, in genetics, you don't need to move to social categories of difference before you collect the genetic data directly, and often that's done, I think, without a lot of reflection.

So I think there actually might be other ways to think about this. You ultimately need to merge the two, especially in certain kinds of health disparities research, but I think it's conceptually very challenging. I mean, I clearly take one side of this, and I recognize that there's another side.

DR. BURKE: I agree very much from the point from which you're coming, the perspective. The reality that Muin referred to this morning that I'm referring to now is this is not a past practice or a ritualistic practice. This is actually a

requirement for people that receive federal funding. There's a tremendous concern that people have included in their research of data on the racial identification of the subjects from whom they generate data, and that that data is categorized or analyzed accordingly in many circumstances.

DR. KOENIG: Right, but there's no requirement that that is the only way that one classifies one's data, and that's why that rule is usually misinterpreted, and I think also that NIH is already reconsidering what the problems are with that.

So I think we need to go on record as supporting these efforts, of tailoring the way you talk about difference to your scientific and clinical problem rather than using something that's not relevant to the question you're studying.

DR. BURKE: And I think really you've gotten to the most important point. We have to work with and not counter to other ways that this issue is being addressed federally.

DR. KOENIG: It can't be changed in terms of the way people submit grants. It's going to take legal and regulatory changes because this is now in statute, but the irony is that it was meant to promote inclusion, and it may in many ways be harmful in terms of the way in which research then gets set up. So it's an ironic thing.

DR. McCABE: Judy, did you have a comment?

DR. LEWIS: I was just going to say, we can add categories that are much more inclusive, like when Barbara was talking before about continent of origin rather than ethnicity, so that we're looking at those, and the other thing we can do is I think we cannot reinforce bad practices. Just because you have data doesn't mean you have to include it in your report.

So that if there are categories of data that we feel aren't helpful, you know, if we don't report on them and report on broader categories, you can choose which variables you include as you report. You don't have to report on everything all at once.

I mean, if there are categories that we think are non-helpful because they're reinforcing some of the potentials for discrimination, then maybe the documents we put out don't include those as necessary fields.

DR. BURKE: Yes. Obviously, I'm very sympathetic to the viewpoints that are being expressed here.

One of the points that was made in one of the editorials I just referred to is that social groupings that have previously been viewed as biologic and which we now view as indicating perhaps more cultural and social issues are still very real groupings in our society, and particularly when you're wishing to get at the issue of health disparities, it actually may be important to retain some of those data.

So I think that's an important point, and I think another important point is that we can identify data fields that we think data should be analyzed on, but those data fields may simply not be available yet.

So I'm only trying to capture how complex this issue is and I think the most we can hope to do is try and think very carefully about this and add some positive direction and guidance as people try and struggle with this issue.

DR. LEWIS: Wylie, is it this week's New England Journal?

DR. BURKE: Yes, yes.

DR. McCABE: Michele, and then Joann.

DR. LLOYD-PURYEAR: You know, I think with the conversation here, I think there may be a need for a discussion with some outside consultation, because I think there is a great deal of misunderstanding. I think there may be some disagreement, because I don't think people necessarily know how to articulate this and necessarily understand it scientifically, and I think there may be disagreement on the science and where things play out.

I mean, the New England Journal of Medicine article, the editorials are a good example. Both of those arguments were based on their perceptions of science, and science would have backed up each of them.

So I would really look to NIH to bring some science to this discussion, so that it can go forward. I mean, I do think the Secretary's Advisory Committee can serve as a very positive force in this area and especially as we go forward with data collection.

How to categorize it? One, how to make sure that you have a broad population that's included in the development of tests, but also at the same time, when

you're reporting that data, what does that really look like? I mean, how are we going to do it differently, and I think we need to understand as a group what the implications of all of that are.

DR. McCABE: And I would just remind everyone of the discussion we've had before, and that is that the social classifications frequently differ from the scientific classifications. Our own perception of ourselves is very different than our own DNA frequently.

There was just a report in one of the genetics journals looking at the islands off of Scotland that have changed genetic hands at various times, and there, if you look, the mitochondrial DNA gives a very different heritage for the people on those islands than the Y chromosomal DNA, which just recognized where people came from as they were invading and bringing other individuals with them or stealing them away from other places and taking them there.

So it's going to be very complex. We as a society have tended to look at this issue incredibly simplistically, and as we get into disease pharmacogenomics and have to rely on the science, it will challenge that social simplification that we've had.

I have Joann, Reed, and then Judy.

DR. BOUGHMAN: I'd like to thank Barbara Koenig for bringing this back up this late in a two-day meeting. I don't often have an aha moment, but in fact, I think you have brought into focus an opportunity that we have as a Secretary's Advisory Committee in the area of genetics.

I might remind folks that when some of these categorizations and the NIH obligation to categorize and make sure on gender issues, that women needed to be included in more studies, it was the geneticists that stepped forward and said every time we take family histories, there are mothers as well as fathers involved in the data sets, and that turned out to be an aha kind of moment.

At least in the study sections that I was on, Geneticists led the way in that perspective, and I'm feeling one of the same kinds of things here, given the fact that we may have new, different, creative, appropriate, sometimes more appropriate ways to look at heterogeneity variability and diversity than has been done in the past.

I think that the message I'm taking away today is think about these classifications every time you create your classification schemes and collect your data and make sure that you are doing them as logically and as carefully as possibly can be done, when necessary, to collect it all a priori.

DR. McCABE: Reed?

DR. TUCKSON: Me, too, aha. I think that Barbara really has done a good job here in bringing this this way. I just will very briefly say that I think that as I was thinking about this originally as we started to think about these issues a couple of meetings ago, we sort of have been kicking this stuff around, I began to really understand now that this is the best way to approach it.

I think that I was impressed by the Census report. You know, people checked off four or five different categories of things.

What we report to the Secretary for Health and Human Services about what he can do better and how his agencies -- they report data. They collect data in all kinds of ways. It's essential to the function of a government, and now with the new information that we have in this new era, to bring some opportunity to bring clarity to light, to some ideas that sort of make the collection of data around these issues make sense, and to be able to make the divisions or whatever they are, the distinctions between political, socioeconomic classifications, versus the new scientific information, and what is the relationship, if any, between the two, and what does that mean ultimately for the systems of information collection and dissemination, I think is an enormously important service and being able to use our opportunity to bring that discussion to bear I think is essential. I think it's much more important perhaps than where we started out on this a couple of meetings back.

DR. McCABE: Judy?

DR. LEWIS: And I was just going to comment and to build further on what Reed and Joann just said, is I think that there are two issues. The science issue, which is based on one set of variables, and the access issue, which is based on the social construction piece, because even though we could redefine and say that some of these genetic conditions aren't necessarily based on social construction, but access to care and access to services may well -- you know, that's going to be the hard one to move.

We can deal with the science, I think, through experiments, but in terms of moving the access issues, we still have to pay attention to the fact that the disparities are still there, based on the social construction of reality, not necessarily on the scientific construction.

DR. McCABE: Barbara?

DR. KOENIG: I was just going to say that Sarah and I had an interesting exchange recently about a new FDA-approved drug for glaucoma, which is being targeted specifically to African Americans, and that was one of the things that led me to think about this more specifically because, again, the whole issue of how we're going to label things in terms of what populations they should be -- you know, how it's appropriate is a very important kind of concept, and it's going to be much more important in genetics.

DR. McCABE: Other comments? Questions?

DR. TUCKSON: I guess a question, though, I have then is how do we operationalize this, and what is the thinking about where this goes, and how does it go?

DR. McCABE: Well, I think the discussion is that, rather than having a separate work group and compartmentalizing the issue, that we really need to think about it broadly within each of the work groups, and every time there's an opportunity to consider it.

Wylie?

DR. BURKE: Yes, and I would just add to that. I think we've identified a very important opportunity for the committee, but I would echo Michele's suggestion that we need to have consult help, that we need to make sure that as we try and put our arms around the complexity of this issue, that we've got help from people that are already thinking deeply about it.

DR. TUCKSON: And I would also wonder whether we could get a presentation some time soon from the Feds -- go ahead. Actually, what I'm wondering is, is whether we can get a presentation from, you know, is it the National Center for Health -- whoever the data statistics genius is for the government.

DR. KOENIG: OMB.

DR. TUCKSON: And then have them tell us how they collect it, and what uses and purposes it is done, maybe have somebody from the Census come and give us a sense of what that stuff is looking like because they've had this whole debate about this stuff forever, and then, finally, some other experts. But I'd like to just get at least somebody from HHS and somebody from Census to give us the lay of the land on this, on how this stuff is used, much more how it's collected.

DR. McCABE: I would be curious, also, the process that led to the change in the Census last time, whether that was a political process. My guess is it was political, but that was a huge change in our perception of ourselves in this country, just to acknowledge that we may be more than one classification within ourselves.

DR. TUCKSON: And clearly, their discussion really did teach a lot about how different people in this country view the nature of those distinctions, and it was all over the board. So to distill that would be essential.

DR. McCABE: Go ahead.

DR. KOENIG: No, I was just going to comment to Michele that we did, in our initial efforts, we did also consult with a number of people who are population geneticists who are particularly informed about this topic. So we have actually already begun the process of identifying some contacts and people who can do that. The whole group hasn't heard it yet.

DR. LLOYD-PURYEAR: Yes, that's what I thought.

DR. KOENIG: Yes, because that's what we're now trying to do, is figure out another strategy. So I think you're absolutely right. It would be good for us to hear from those people, but we've at least started that.

DR. McCABE: We could also ask Kathy if there's anyone within NHGRI and the ELSI group or the ELSI-funded folks.

DR. HUDSON: Right. I was going to make the same recommendation. When NHGRI was creating our sample resource for SNPs discovery, we went through a process of informing ourselves and thinking about how would we identify these samples. So they are 750 ethnically- and individually-anonymous samples.

But we wanted as much diversity in that set as possible, and so we had individuals identified from their region of geographic origin, and in creating that system, we had lengthy, lengthy meetings with population biologists principally, but we also heard from the folks who are the big data collectors for the government, and that really informed that process, and I'd be happy to share their report from that sort of decisionmaking process as well as the names of people who have worked with us.

We also have a set of grants through the ELSI program looking at various issues and genetic variation, and I'd be happy to share that with Sarah, and if there's a particular person or group of people who would be useful to make recommendations.

DR. KOENIG: And then there is also this NIH-wide issue that I think is centered in the Office of Social and Behavioral Research now or whatever the exact name of it is --

DR. HUDSON: Right.

DR. KOENIG: -- which is to think again about all of the foundational categories in research, like race, ethnicity, culture, and to try and further refine those, especially in light of the health disparities initiatives.

I can give you the names of -- I mean, I was part of the initial meeting that started that process, and the person from CDC actually who was most involved in the specific race part of that is Robert Hahn, who's headed a couple federal initiatives to rethink issues of race and ethnicity in health statistics and is extremely knowledgeable and actually would be a good person, another good person, to talk to us about those issues.

DR. McCABE: Anything else that we want to discuss here?

(No response.)

DR. McCABE: Okay. I will now take the opportunity to wrap up and provide an update on one issue.

We had submitted our recommendations, the final report, a summary of that, had been submitted to JAMA. We received a notice of rejection from JAMA with some very, as we always say after the initial reading of the letter, some very

helpful comments that will help us refocus our attention, largely having to do with organizational recommendations and the like.

I'm going to contact Jeanette Smith -- Dr. Smith is the editor who was responsible for this -- and see if this is an irretrievable decision or not. If it is, we'll move on. We'll work on reorganizing it in response to their comments because I think they can be helpful to us. Just so you know where that is, we're going to continue doing this.

JAMA seems to have taken a different perspective on these kinds of policy pieces lately because we're not the only one that I've heard of that's been rejected of late.

Any questions or comments about that issue?

(No response.)

DR. McCABE: Any further questions?

(No response.)

DR. McCABE: If not, we'll see you in August. I've been requested by certain members of the committee to announce that there will be a much more informal dress code. In keeping with being in the Mid-Atlantic region in August, there will be --

PARTICIPANT: Shorts.

DR. McCABE: There's certain of us who you would not want to wear shorts to this meeting, but I think that those of us who might not be caught dead in shorts might not wear ties to the August meeting. So dress as you wish, but I can tell you that the chair will not be wearing a tie in August.

Have a safe trip home, everyone.

(Whereupon, at 2:20 p.m., the meeting was adjourned.)