SECRETARY'S ADVISORY COMMITTEE
ON
GENETIC TESTING

FIFTH MEETING

Monday, June 5, 2000
The Governor's House Hotel
1615 Rhode Island Avenue, N.W.
Washington, DC

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P R O C E E D I N G S

DR. McCABE: Good morning, everyone.

Today we are going to start with talking about enhancing genetics education of health care professionals. One of the goals of our very first meeting last June was to identify issues that we thought should be a primary focus of our work. Before deliberating as a group, we each took a turn outlining our own individual high priority issues.

As we went around the table, I remember being struck by how many of you highlighted the importance of genetics education and the need to ensure both a well-trained health care force and a literate public. Our work this past year on the oversight issues has, I think, only clarified and reinforced our view that education and training have a critical role in assuring the safe and appropriate use of genetic tests.

Today, we will begin to explore one part of education, the education and training of health care professions. Our presentations this morning will provide an introduction to the issue and to some of the initiatives planned and underway in the government, in the private sector and through public/private collaborative efforts.

I think it will become clear that there is much for us to learn about this issue and that today will only begin to touch the surface of this important topic. I will be introducing our guest speakers today with just a brief background sketch. Their bios are in your briefing books. We will forego formal introductions of the two presenters, Dr. Puryear and Dr. Burke, who are well-known to us.

Before we start, let me remind presenters to please keep within the time allotted for your presentation. These are ten minute presentations. We have a lot to get done this morning. We also want to have time for follow-up questions from the committee members for each of the presentations.

So, Michele, Dr. Michele Puryear, will begin with an overview of the issue and the current federal efforts.

DR. PURYEAR: Good morning, everybody.

This whole next session is actually to look at a variety of federal efforts and also some collaborative projects and it is not just about health care professionals, but health professionals. We are reminded often by our public health -- our CDC partners, public health agencies, the other public health agencies, that this more than just about health care professionals. It is also about public health practitioners.

The presentations that a variety of people will be giving are not meant to be exhaustive. It is just to highlight areas of need and what is being done at this time through either the federal government or some public/private partnerships. And we are focusing on health care and public health practitioners, not research training programs. I think that needs to be emphasized.

I would like to take just a moment to introduce -- Dr. Carol Bazell is not here but she will be here later, but Drs. Norman Kahn and Eugene Rich, who are the co-project directors for the Genetics in Primary Care project that is going to be presented this morning. And both Carol Bazell and Drs. Kahn and Rich will be available, along with Wylie and Dr. Ruth Kahn, to answer questions about that project. Besides talking about federal efforts, I was also asked to present a memorandum of understanding that has been established between some federal agencies here and also to talk a little bit about Healthy People 2010.

The issue that has been before us for awhile is to answer the question of do we have an adequate number of public health and health care professionals that are trained adequately to understand and use genetic information and technology. There are several studies that indicate we do not and certainly as we move towards common complex disorders, the consensus in the genetics community is that we do not.

The management of high prevalence disorders, such as diabetes, hypertension, heart disease, cancer, has been the purview of primary care practitioners. So, certainly, it has been well recognized that we need to include them in any training effort.

As a point for later discussion when we get to the roundtable, I would like to add that the evaluations have always or generally have been done within the context of how we currently practice medicine and nursing. And I think as we move towards the future, we need to think how medicine might change and how thinking genetically within that future direction may need to change also.

I think this was talked about a little bit yesterday. There are approximately 3,000 board certified genetic professionals. Not all of these are in clinical practice. This includes genetic counselors, physicians and nurses. Genetic professionals do not reflect the demographics of this country. Medical school courses in genetics are research intensive, rather than oriented to primary care.

There are few public health professionals with genetic training. We have established with CDC and five universities a genetics and public health collaboration. I think that is how it began, how it has been called. The first project had been to look at competencies that would be needed and to go back and design public health programs and genetics around those competencies.

There are a few states, a handful of states, with state genetics plans and this is important because states actually finance -- most states finance higher education. However, within those state genetics plans, training and education of health professionals is not always included. Almost every state does have a state genetics coordinator. However, those coordinators are not always trained in genetics, per se.

There are few nursing or primary care residencies with formal genetics curricula and most genetics professionals have training in the care and management of rare diseases, but are less knowledgeable or maybe less comfortable in the care and treatment of more common, complex diseases. So, I think we even need to look at the education of what perhaps genetics professionals may need.

Therefore, in the current model, I think the consensus is that we -- of health care and public health

practice and delivery, health professions training and capacity is inadequate.

On these next few slides, I am going to point out to you how many of the training programs are financed. I don't have state specific data because that varies by state. For the federal government, the federal programs, I think this comes to about $660 million from HRSA, the Bureau of Health Professions, the Department of Defense and VA.

However, the most substantive amount comes from Medicare and Medicaid and this is about $9 billion and it is significant. There is an additional $25 million that my bureau gives to target specific competencies for interdisciplinary training. This is across all the health professions, this $25 million.

For nursing, again, the Bureau of Health Professions and HRSA has $65 million. Our bureau has only about $2 million. The primary amount from other sources, other than state funds, comes from Medicare, which is about $200 million.

For allied health professionals and public health professionals, there is no, other than what the state may allocate, there is no outside funding, other than what comes from the federal government. From HRSA, combined between Maternal and Child Health Bureau, and Bureau of Health Professions, it is about $10 million. Public Health Professionals, that money that goes to the School of Public Health.

I make a distinction here. HRSA and CDC give about 40 million combined. They also individually have several programs that target training and education for individuals or programs within public health agencies. Tim Baker, I think, will talk more about what CDC is doing in that area.

So, in conclusion for this part of the talk, federal funding is not substantive at all, but we have been able to target specific programs with our funds. Drs. Kahn and Burke are going to be talking about the Genetics in Primary Care project. In your packets, there are several projects that are described that are funded by NIH or HRSA, that target health professionals. These projects range from curriculum for social workers to physicians.

Dr. Weiss is going to be talking about some projects that are ongoing in nursing education and also some plans that we have with NIH around this area.

There are few national efforts. I think this is where there is a great need that target either public health or allied health professions. There is a project that is financed by NIH and is a project in collaboration with allied health professions, the Genetic Alliance and the Genome Institute that is developing a model educational project for those professions. And again, Tim will be talking about some specific projects with public health professionals.

This last part is noteworthy to me. The Bureau of Health Professions in HRSA has supported many of the projects that are going to be talked about today. Except for the Maternal and Child Bureau and the Genome Institute, no federal agencies have specific mandates or specific allocations for either health professions education or training. The federal agency that is mandated for training is actually -- or the bureau is the Bureau of Health Professions. Although, they do not have a mandate to do that, they have supported both nursing and genetics projects with a great deal of funds and also expertise.

But of concern, is the 2001 President's budget, that there are no funds allocated towards primary care or nursing training programs. So, that effort and that support from the Bureau of Health Professions is significantly threatened.

So, the next thing I am going to talk about is the memorandum of understanding. This was established by several of the federal agencies that are here and out of that memorandum of understanding came, again, several of the projects that are going to be presented this morning, but also the establishment of an education interagency, interdisciplinary working group that I will be talking about.

The memorandum of understanding was finally signed off during the winter, this past year. It is between AHRQ, Centers for Disease Control, my agency, HRSA, and the National Institutes of Health. It was established to have a mechanism whereby we could share information regarding genetics research, service education and policy, to identify opportunities for collaboration and to reduce any duplication of efforts and actually combine some resources so our efforts could be more targeted.

Global goals were to ensure that research was appropriately conducted, to increase our knowledge of genetic variation and apply that knowledge, to facilitate the integration of genetic technologies into health care and public health activities, to ensure that protections are in place, to improve the genetic literacy of the public and, last, which is significant for this talk, is to facilitate the development of a well-prepared community of health professions.

Added to that and to look at this effort in a more focused manner, we established this working group with a long range goal of creating a five year plan for health professions, workforce development and to look specifically at capacities, competencies and training needs. We are beginning with a workforce analysis.

And Dr. Herb Traxler will be presenting those initial efforts around that.

Then, finally, Sarah asked me to talk about 2010 and the reason why is to outline a mechanism by which federal agencies or at least the public health agencies establish their funding priorities. Healthy People 2010 actually or Healthy People, the agenda, grew out of a 1979 surgeon-general's document. This was later expanded in 1980 to actually be a Healthy People agenda for the public health service agencies at that time.

Since then, it has been updated every ten years. There was a report in 1990 and there was a report this year. This agenda outlines national health promotion and disease prevention objectives. It is viewed as a national effort and the states often take these objectives on themselves.

The idea specifically for Healthy People 2010 is that it is a set of measurable targets to be achieved by the designated year. In Healthy People 2010, there are no specific genetics objectives. All the ones that were proposed by the genetics community eventually were taken out.

But, there are objectives that are relevant. Some specific ones that target public health and primary

care providers for what is termed appropriate education or training and other ones that talk about the incorporation of specific competencies into training. Unlike previous Healthy People agendas, this one gets looked at in another two years and can be changed and you can submit developmental objectives. However, they must be measurable and I think that has always been the problem with specific genetics objectives is having the ability to measure them.

So, in summary, although there are several federal efforts underway, there are certainly are only a small amount of federal dollars allocated to training. I think it is insignificant when we compare it to the research funds that have been allocated thus far. The establishment of a Healthy People 2010 genetics objective may be one mechanism to establish training as a public health priority for the PHS agencies.

DR. McCABE: Thank you, Michele.

Are there any questions for Michele?

DR. PURYEAR: We could wait until the end. Do you want to?
DR. McCABE: Okay.

DR. PURYEAR: Wait. Aren't you using the slides?

DR. McCABE: We will move on, then.

Thank you, Michele. I also want to thank Michele for the significant contributions, which I know you made planning for this session. It was helpful for you to bring your broad knowledge of the issue and current programmatic efforts underway in the Department to us.

Now we are going to turn to Dr. Herbert Traxler. Dr. Traxler is senior economist program officer for HRSA's Bureau of Health Professions. Dr. Traxler is responsible for providing technical assistance to states to advance health professions analysis, modeling and research in order to assist policy deliberations and decisions.

He also serves as a program officer for four cooperative centers for health workforce studies. Dr. Traxler was initially educated in Vienna, did graduate study as a Fullbright Scholar in Bologna, Italy and earned a doctorate in economics at Florida State University.

Dr. Traxler will provide us with an overview of the Bureau's efforts in assessing health care workforce needs and its current view and future plans regarding the challenged posed by advances in genetics.

DR. PURYEAR: I have to apologize for Herb. He has been out of the country, and this is the first time he has seen his presentation.

DR. McCABE: We could ask you to tell us about the Lippizaners.

DR. TRAXLER: It is not that I have seen them for the first time, but it is only a portion of what I was going to talk about. It is the later part of it. I do still want to say a little bit about the Bureau. You have

it in your package, which I sent. You have a lot more materials. So, I don't have to talk a lot about this anyway.

The Bureau of Health Professions, as Michele mentioned, is within HRSA and the HRSA mission just very briefly is to improve the nation's health by assuring equitable access to comprehensive quality health care for all. The Bureau more specifically, HRSA has four bureaus. Michele is in one of the bureaus, of course, the Maternal and Child Health Bureau. We are the Bureau of Health Professions. There is then also the Bureau of Primary Health Care and the HIV/AIDS Bureau.

In addition to that, it has Office of Rural Health Policy. The Bureau's mission specifically, our bureau, Bureau of Health Professions, which I am part of and Ruth Kahn, Dr. Ruth Kahn, of the Division of Medicine and Dentistry and then we have the Division of Nursing here. These are two of the main divisions and I am in the National Center for Health Workforce Information and Analysis. I am a senior economist there and a program officer for the four centers for health workforce studies.

I am also the editor for the Health Workforce News Link, one of our main -- one of our functions is dissemination and, so, that is a quarterly publication. And I have brought up a sufficient number of copies here of the latest issue, which have come out Winter 2000. The Spring issue is in preparation and will focus on medical error.
And I hope at some point we will have an issue, which will focus on workforce for genetics. That is what -- with a feature story, which always focuses around that, and this one was emphasis on primary health care and education and delivery. I happened to write the feature story for that, which is more general, but we certainly could focus on genetics.

I also brought, which is in Ruth Kahn's division, the very recent -- I didn't take those things to Austria. I have them at home -- a very nice booklet on COGME, the Council on Graduate Medical Education, which certainly would have a role, a very significant role in any training for genetics.

What you have in your handout, I am not going through this yet, but the Bureau, what we are doing, we are trying to -- basically diversity quality distribution, the areas, meaning to have the right people with the right skills in the right areas. So, the right people in diversity -- we don't have to go much into that, but it is basically that the health professions workforce more or less reflects the population it serves with the right skills and we have divisions, which focus on that; for instance, the Division of Quality Assurance is a strong component in that and distribution in the right places.

Our center's research effort is very much going to that third component, for instance, in the health workforce distribution.

The rest of what you have in your handout I will not go in detail in it except for mentioning that HRSA has a $4 million budget, 4 plus million dollar budget. The Bureau has 7 percent of that, which is 300,000, 300 plus thousand. You have that in that nice pie chart -- 301 million. I am thinking a thousand because this workforce analysis and for workforce analysis, our center has 700,000. So, if you think about a $4 billion agency, a $300 million bureau, specifically for workforce analysis, $700,000.

We beg, borrow and steal from other agencies, from other components of the Bureau. For workforce

analysis, for instance, our centers, they are funded at $250,000 each. So, $1 million for those centers for workforce analysis and research. That is what we are focusing on. That is a major component of the National Center for Health Workforce Information and Analysis is the cooperative agreements, which our center signed off on.

This was a very brief summary of the things you have in your handouts already and what you have in your folders. The title, as you know, has changed. It is not specifically workforce assessment, but talking about the National Center for Health Workforce Information and Analysis.

I do encourage you to afterwards, we will hand out the News Link and the COGME and the News Link has my e-mail on it, too, which is very simple, HTraxler@HRSA.Gov. They are very simple at HRSA. It is just the initial, the name and @HRSA.Gov. So, for instance, it is MPuryear@HRSA.Gov, RKahn@HRSA.Gov., if you have any questions.

The National Center was established -- has been around for a long time under various names. When I joined the Bureau a little more than ten years ago, it was the Office of Data Analysis and Management, with the elegant acronym of ODAM, which was changed later on to OPAR and then became the Workforce Analysis and Research Branch and then was established as the emphasis was seen that we need more workforce analysis into a National Center.

We have about ten staff, ten professional staff, which is not very much for a National Center, but it is very nice to have it called a division, you know, that we have become a National Center. We have the funding, as I said, about $700,000, which also is not in line with most funding for National Centers.

But we do have cooperative agreements, which help us extend our analytical capacity. Our focus very much is towards the states also because more and more analysis and policy making and decision-making is in the states. What you see in the first one, adequate data, some of the issues we are addressing is allied health and public health workforce. As you know, there were several reports, maybe, you know, the NIH report, the Institute of Medicine report on the public health a few years ago and there was Allied Health Commission and Allied Health Collaborative, looking at the data needs in allied health, which they have for a long, long time and it still is really, really in bad shape, especially in allied and public health.

There are insufficient data on certain aspects. Physician data are much, much better, of course; many of these collected by the American Medical Association with their rotating census. It is a three year census, where everybody is -- they have one-third of the physician workforce every year and very detailed data off of that is somewhat being cut back, which is of concern to us.

The dental and nursing work for us has also fairly good data; among other things, the National Nurse Sample Survey, which looks at that. Yet, there are still problems with those data sources, the sample survey, which is very detailed. It is only periodic. The physician is rotating. So, these are some of the data issues.

We have created a network of federal/state centers. They are actually Centers for Health Workforce Studies. We initially called them Health Workforce Distribution Studies, but they look at more than distribution. They look very much, for instance, the California center at diversity, the Proposition 209.

They looked at the impact, what does it have -- the influence that proposition had on the applicants, the metriculants, for instance, on medical schools.

So, they are looking at all aspects of that. There are four such centers. They are coming up for renewal next year and we hope to keep the four and maybe to expand two additional ones. They have both a regional focus and a national. So, they have two pillars really; one is a National Center for Excellence, where they are focusing on certain areas and the regional focus, where they are a resource for the state and the surrounding states. Right now with the four we have very good coverage of the West, between UC-SF and University of Washington, the Midwest, University of Illinois at Chicago and the New York Center, SUNY-Albany.

We hope to extend that with two centers so we have the Southeast and South maybe; North Carolina, a center focus and Texas a center, which cover those regions.

We are conducting in conjunction with the corroborative centers research to provide data for national, state and local health workforce policy analysis. As I mentioned, it is -- we are working very much with the states and with the regions on that.

Supply and requirements has sort of an additional function, which the analytical unit has done for 25 years at least, work for supply and requirements. They used to have biannual reports for Congress, which are not required anymore, but we are still issuing -- for instance, in the Health Workforce News Link you will find a lot of that.

The county level data sources for health professions, that is the area resource file, also known as ARF. Organizational charts for the center, it is a national center, the products are forecasts and data on the health workforce. We are working and assisting the Council on Graduate Medical Education, COGME. You will get that booklet on the various COGME reports, which are done mostly by COGME staff and also with contracts very often, involving some of our centers, very often, our Center for Personnel, like Gary Hart or Ed Salzberg and also us.

The federal and state centers, that is our cooperative centers, we are holding technical assistance workshops. We are working with the centers in terms of policy issues, which are of interest to the states and the regions and to the nation and what are the national implications of some of what is happening in some of these key states. I mentioned California Proposition 209, for instance, that was of key interest to the California State Legislature and, of course, has a lot of national interest, too.

Finally, I mentioned the area resource file. That is a comprehensive secondary data source, which is used widely in policy analysis and research. Dissemination research findings, part of it is through the News Link, part of it is through workshops and other things.

I mentioned already the cooperative agreements, which we started in 1997. They are to work with the state agencies, address health workforce issues and examine the distribution and other issues across the states and across disciplines. Initially, they were charged to look at the five I would say key health professional areas; that is, physicians, nursing, allied, public and dental health professionals. Dentists, public is missing from here -- okay, that is non-physician providers; allied,

dentists, nursing, physicians, okay, and public health professionals. There were five areas.

When we talk about physicians, that also includes -- it goes beyond just looking at physicians. There is a big issue of non-physician providers and there are substitution issues, complementarity and competition issues and the centers have looked at that and we are looking at that and we have various items written in the News Link on that.

This you have in the handout. This is very briefly, you can find a lot more information on these centers, what they are doing on the Web sites. They all have Web sites and I will go -- a little bit later, I will go into the detail at the University of Illinois at Chicago Web site. I will mention that again.

As mentioned, it is 250,000 per year for a three year project period, 1997, the first one started. That is UC-SF. The other one started one year later in terms of funding, fiscal 1998, which means UC-SF is in its last year and the other three have one more year to go. We are, hopefully -- were successful in extending UC-SF for one more year. So, they are on the same cycle and next year we have to have a new round of funding and, hopefully, get them for five years and, hopefully, have two more centers, if we can get the money. That would be another 500,000 for two additional centers, if we keep them at the same level of 250,000. It is not a lot of money for looking at all of that.

Some money was transferred from MCHB, from Michele to us, and asked that the centers look at the genetics workforce and, so, specifically we asked the University of Illinois at Chicago -- they expressed interest in that, that is Trudy Cooksey and the center directors to look at their genetics counselor workforce.

The University of Illinois at Chicago Center for Health Workforce Studies, you have the Web site and I have asked Trudy, Dr. Cooksey, before I went on a very much too brief vacation, to put the report on the Web site. So, you will find the report, which you will see here, the Genetics Counselor Workforce, you will find on the Web site by -- of the University of Illinois at Chicago.

If you look in your folder or if you don't have that, if you look at the last page of the News Link, which if you have the Winter issue, you will have the Web sites on that and if you are interested, you can find the full report. It is not a very thick report and it is a summary overview study.

It looked at the training, professional practice and supply and demand of that component of the genetics workforce. What it found and, again, this is secondary data analysis. This is a lot of interviews, which they did, and basically the first counselors completed training in 1971. There are 24 programs currently. They are based in academic medical centers. They have funded 20 to 130 graduates per year and about 1,800 master's trained genetics counselors are in the workforce now.

Most of these are working as clinicians within medical teams in urban academic medical centers and hospitals. There is, like in so many other areas, these is a distributional issues. You have to have a certain concentration to make it worthwhile for a genetics counselor or to make it worthwhile for a genetics counselor to be employed or to be paid.

Traditionally, they are working in prenatal and pediatric clinical areas. In recent years, they expanded the practice to other areas, adult medicine and specialty areas. Starting with pediatric,

prenatal, they extended the practice to other areas. As I mentioned, geographic distribution is uneven. They are mostly in urban areas, urban academic medical centers, which is obvious and makes sense, but several clinical studies show shortages and reduced access to genetic counselors.

Dr. Cooksey came -- made some recommendations in her report, which has maintained the current training programs that monitor the growth in genetics testing and demand for the services. So, she doesn't come out -- after looking at all this, doesn't come out and saying we need more or we need less. She does come out we need them better distributed, but she says you cannot -- the second one goes you cannot look at genetics counselor work for this one component, which is a specialized workforce genetics counselor in isolation. So, what you have to do is you have to assess both genetic specialists and practicing health professionals, who are working in genetics.

She is saying -- that is the second line down there -- it is very difficult to assess the single profession in isolation from other genetic specialists and other professions that provide genetic counseling services, notably physicians and nurses. You will hear more of that from Dr. Kahn and Dr. Weiss of the Division of Medicine and Dentistry and Division of Nursing, more specifically. So, I won't say more about it because they will talk about it and I don't know more about it, much more about it.

But anyway, the conclusion from this look at one slice of the workforce, one which is specialized genetic counselors says very strongly that you cannot look at this in isolation. What have we gone from there? We have got a monthly telephone conference call, the center directors and me, as program officer, and sometimes Paul sits in and we have had in the -- not the most recent, the next to most recent phone call, you were in there, Michele, and we talked in, we dialed in NIH and the Maternal and Child Health Bureau and talked a little bit what can the centers do in terms of a workforce assessment study.

They will come with the proposal to look at the more comprehensive approach, which Dr. Cooksey's study said basically don't look at just one component of the workforce in isolation. So, the proposal for the workforce study is basically to evaluate the workforce needs in the context of health care delivery modes and what came across is the three models, public health, primary care and genetics model were a point of view to look at it with the -- I would say -- it is not blinders, but under the premise of looking at it from the public health aspect, from the primary care aspect and from the genetics specialization, specialized aspect, like the genetics counselor.

There may be another model approach to that. We are awaiting a proposal from the centers. It may be there. As I said, I have not been back to the office. We are having -- at the Association of Health Services Research, they have got their annual meeting in Los Angeles on June 24th through 27th. On the 25th, we are having a, like we have had for the past few years, the same annual meeting of the center directors, who are all presenting there and have papers and so on. We are meeting for a few hours and this will be -- the proposal will be there and we will discuss that and, hopefully, have some input from this and from the NIH, so we can discuss what are we going to do with this, where are we going there. That will be on June 25th at the center directors meeting.

This is all the slides I was given out of the collection, which I had. If you have any questions, there is a lot more, but -- any questions to what we are doing with the centers, the cooperative agreements,

analytical program of the Bureau of Health Professions or anything else.

DR. McCABE: Okay. Thank you very much, Dr. Traxler.

I think what we are going to do is move ahead and pick up any questions in the roundtable.

DR. TRAXLER: Sure.

DR. McCABE: We are now going to turn to a joint presentation from Dr. Ruth Kahn and Dr. Wylie Burke on an important collaborative faculty development project in primary care medicine. The project is jointly funded by two bureaus within HRSA, NIH and Dr. Lanier's agency, AHRQ. Dr. Kahn is a health professions educator in HRSA's Bureau of Health Professions. She develops and implements interdisciplinary faculty development programs and special initiatives in primary care to encourage innovations in undergraduate and graduate medical education.

She also plays a role in developing medical education initiatives in genetics, substance abuse and women's health and has been actively involved in assisting the health professions education community to incorporate Healthy People 2010 goals into curricula for health professions.

Dr. Kahn received her bachelor's degree in nursing from the University of Minnesota and a master's and doctorate from the Catholic University. Dr. Kahn has a leading role in the design and implementation of the contract that supports this project and Dr. Burke is a member of the project's Executive Committee.

Dr. Kahn will describe the overall purpose of the project and Dr. Burke will talk about how genetics and primary care are interfacing in a curriculum designed to train primary care faculty to incorporate findings from the Human Genome Project into the education and training of medical students and residents.

DR. KAHN: Thank you.

First of all, I would like to straighten out a confusion that always happens at these meetings. I am not related to Norman Kahn. Norman Kahn is not related to me. He is not related to my husband. So, that is all done. Thank you.

I also wanted to introduce Dr. Carol Bazell, who is the director of the Division of Medicine and Dentistry. Dr. Bazell is the one that gave me the assignment to work on this project. So, we owe a lot to her..

What I am going to do is just sort of give you some idea of the structure of the project. The content of the project is really going to be talked about by Wylie, who is the genetics educator on the Executive Committee.

I am going to rather zip through these slides. So, if you have any questions about it -- really, we gave you a handout on this entire project for your bedtime reading or your reading on return on the airlines. I am not going to go into great detail, but don't hesitate to ask me if you have a question.

You know, the reason we do faculty development is really to develop champions. I think that genetics education will go nowhere unless we are able to develop champions in schools of medicine, who are not geneticists, but who are primary care educators. Otherwise it will just never get picked up. So, kind of if you think about it as you listen to this, what we are really talking about is the ultimate goal of developing a champion team at an academic setting that will set the tone for what is now, everyone agrees, I think, the information age.

Some people think we have an eight year hiatus between the industrial age and the information age, but I am not sure they are right. I kind of think we are almost there.

So, with that introduction, let me say that the Genetics in Primary Care project is a faculty development initiative that will cover a three year period of time. It is a $1.3 million contract -- a $1.6 million contract that was given to the Society of Teachers of Family Medicine to bring together the leaders in primary care, to look at what to do about faculty development in those disciplines.

It is funded, as you know, by HRSA, the two bureaus, by the National Human Genome Research Project and by AHRQ. I know that David Lanier is sitting at the table. So, David, we appreciate your money. We also appreciate your money, too, Dr. Guttmacher.

The goal of Genetics in Primary Care is to enhance the ability of faculty and to incorporate the clinical application of genetic information into undergraduate primary care medical education and also, incidently, into graduate medical education, such as residency programs.

Specifically, we hope that this project will increase the number of primary care physician faculty, who are trained to conduct faculty development and training activities in genetics in a culturally competent manner and that this group of people will represent the mix of primary care faculty, including those whose primary responsibility is as a clinical teacher, teacher-researcher, administrator or leader.

Currently, our contract has not taken up the issue of the highest level leader, but we know that is an unmet goal of the project and the Executive and Advisory Committee at some point will take a look at how that is going to be done.

And finally, we hope to be able to develop varying models. I am going to ask a little bit later for Norm Kahn to stand up and tell us about what has happened with our call for applications. But I will just wait a minute on that.

So, the goal is to develop faculty, who are adaptable to a variety of teaching settings in primary care. We have completed Phase 1 of the work, which went from September 1998 to June 2000, where we formed an Executive Committee, a very large Advisory Committee and a smaller Genetics Education Consultant Committee.

We selected the evaluation consultants and an external evaluator and developed a master plan. We are now currently in Phase 2 of that, which is the development, implementation of the education and training projects and that is mostly what this discussion will focus on.

And finally, although we identified Phase 3 as the evaluation phase, evaluation -- and it was done at the initiation of the project and we will go over the term of the project. We are looking at this process and saying this is a really relatively new area, not claimed by anybody. So, is this a way of doing this that is going to work?

As you know, Dr. Norman Kahn from the American Academy of Family Physicians is the project director, two project co-directors, Modena Wilson, representing pediatrics, and Eugene Rich, who is from Creighton University Medical Center, represents general internal medicine and Wylie Burke, you know well, represents the geneticist educator on the group.

The project administrator is from the contractor, the Society of Teachers of Family Medicine, Roger Sherwood and our evaluation consultants are Rebecca Henry, well known for her work in the Kellogg project, and Richard L. Holloway, who has done a lot of work over a number of projects.

We are waiting for a resident to be named. They keep having babies or keep getting changed or whatever. So, we lost our last resident due to a baby.

Then the representatives from the funding agency include Dr. Puryear, Dr. Mann, Dr. Bazell and myself. Dr. Lanier, Dr. Guttmacher and Elizabeth Thomson from the ELSI Research center or program director for ELSI Research is also a liaison to the project.

Not to give you the list of names, because you have them, and the reason we wanted you to have those names is you are going to pick up the phone and call somebody and give them your view of what that advisory person ought to tell to the committee. You have their name, address, e-mail and everything, but just to know that on the consultant committee there is a chairperson who is Wylie Burke, 11 genetics experts, two federal advisors and representatives of the contract manager.

Now, the big thing is the Advisory Committee they get lots of advise. The five key organizations of family practice are on that committee, six of internal medicine, six of pediatrics, four other medical specialty organizations, three osteopathic, four genetics and eight other medical organizations, plus the federal representatives.

I am sure you are asking how do you get anything done. It worked. We did get something done. They were very good about giving us excellent advice. So, I really -- even though this looked like it was unmanageable, it was a very significant contributing group or groups within the group, if you would. The outcome of the Advisory Committee meetings is going to be picked up now by Dr. Wylie Burke and I will turn it over to her.

But before I do that, I wanted to mention that in your package, we gave you the information on the RFP. It is too time consuming to go through what the requirements were, but essentially what this project did was make an announcement to schools of medicine requesting them to apply with a team representing the primary care disciplines and a genetics educator in their setting to produce a model for faculty development.

I am going to ask Norm Kahn to just talk for just a moment about the response to that because I think that will help you understand a little bit of what is happening out there in schools of medicine related

to this.

DR. McCABE: If you could come to the microphone, please, so we can record this. Thank you.

DR. NORMAN KAHN: My name is Norman Kahn. I am the project director of the Genetics in Primary Care project.

DR. McCABE: Excuse me, Dr. Kahn. Could everybody turn off their mikes here. We have had trouble with feedback from that one when these are on. Thank you.

DR. NORMAN KAHN: Alright, I'll stand back from it and give it another try. You have heard about how this project is described and I would point out to you that as I read your draft report, where this project really fits in is addressing the clinical utility of genetic testing. This is one of the answers to the questions of who is going to provide information. Who is going to provide information to the majority of patient encounters in the United States, which take place in primary care physicians' offices?

That is what this project is designed to do. We put out a request for proposals. They went out to the nation's medical schools and osteopathic schools or 124 medical schools or 19 osteopathic schools. But also the other groups that were eligible were primary care residency programs in community hospitals. There is not a lot of money in this project.

We are basically looking for folks that are willing to put together model faculty teams in an interdisciplinary manner. They have to have a mix of the primary care disciplines on the team and they have to have genetics expertise on the team. What that team is going to do, they are going to get training. Dr. Burke is coordinating the training. It is a train the trainer model. They are going to go back and multiply the faculty development effect in their locations.

We are providing all of the expenses, plus a $10,000 support. Just an anecdote, I will tell you that we had one or two department chairs in medical schools, who basically said it is not worth my time to put together anything for $10,000. And at this point I feel very good about the fact that 53 of that person's colleagues did feel that it was worth the time to put together a proposal because that is how many applications that we did receive.

We have enough money to fund ten train the trainer faculty development teams and we have 53 that are interested. Of those 53, there were just a handful that did not meet the eligibility requirements that I outlined to you. So, we are vastly oversubscribed. It will give our Advisory and Executive Committees a real job to pick those that will prove to be a good model in this demonstration project. I would be happy to address any other issues, but I think that specifically is to let you know that primary care medicine in the medical education community is working with you to address the area of clinical utility through this demonstration project.

DR. KAHN: Thank you, Norm, for that last up-to-date piece of information, which I didn't know because I was out to see two of my grandkids graduate from high school.

DR. McCABE: Dr. Burke.

DR. BURKE: Thanks.

Well, you have already heard the structure and general outline of this project and what I want to talk with you about is what we have learned and perhaps some of the implications of that generally for trying to accomplish this goal of educating health care professionals in genetics, who do not have genetics training themselves.

As Ruth Kahn mentioned, the structure of the project includes a large advisory committee with representatives from organizations involved in primary care, medical education and genetics. It turns out when we looked at the group of members of our Advisory Committee, and I should mention that one of them is at the table, Mary Davidson, we -- it broke down generally into about half of the group having considerable genetics expertise. That included the representatives from the genetics organizations and also a number of the primary care organizations chose to send as their representative someone from their membership, who had genetics expertise and then about half the group turned out to be predominantly people with expertise in primary care and medical education.

The result of that has been an incredibly dynamic dialogue. We have had two meetings, both of which included an all day session talking about what should genetics curriculum be and often getting to what I think is the key question, what is the buy-in. How do you get people from primary care interested in genetics?

And as that dialogue went forward, it became very clear that we are talking to some extent in a cross cultural mode. Genetics approaches the problem of genetics education for primary care in a certain way and primary care approaches it in a somewhat different way. And as those two groups talk, interesting ideas emerge and interesting concepts about buy-in.

I think we are still in the beginning of this process. One of the things we are going to be doing over the summer is developing a model curriculum based on the discussions to date. But I consider this just the first stage. This whole process is testing out ideas for how to create that bridge.

In terms of where we are now, we can start by saying that from the genetics perspective, there is the concept of the need to look at primary care through a genetics lens. So, this is the message that we get from primary care to -- from genetics, rather, to primary care. When you break down what the elements of those are, they seem to be predominantly the four points I am showing you here; very importantly, expanding the differential diagnosis to include genetic conditions.

So, geneticists are very concerned that primary care not miss the genetic explanations to disease that might be important to see. Clearly concerned with appropriate use of family history to identify genetic conditions, a lot of concern with getting that three generation family history that geneticists know is important often. Very great concern with the important tradition in genetics of non- directive counseling and with that, of course, a broader recognition of ethical, legal and social issues that are raised by a genetic diagnosis in a family.

When you talk about this from a primary care perspective, though, you begin to turn it around and say you can also look at genetics through a primary care lens and it is equally important to recognize that

perspective. When I have tried to piece from our conversation what are the elements of that view, first and foremost it is evaluating the utility of genetic information in terms of health outcomes. And this reflects primary care's concern. Our mission in primary care, I think it would be fair to say, primary care folks would describe, is to make people better, is to apply medical interventions and diagnoses that will result in a net health care outcome and avoid those potential interventions that aren't in a given situation going to improve health outcome.

And that focus is a very important element to recognize as genetics moves into primary care. It includes needing to think about what the health care outcomes are. Some of them are measurable improvements in health status, but some of the health care outcomes of the use of genetic information aren't easy, measurable health improvement outcomes.

So, this is a very important discussion. Interestingly, another issue that comes out loud and clear when primary care talks about how it practices medicine is a respect for patient preferences. That is different from non-directive counseling. It often gets expressed as promoting shared decision-making. There is a different nuance there. It includes acknowledging that there are perhaps most of the time in health care need for the professional to make health care recommendations, which is not formally a part of non-directive counseling.

Yet, the spirit behind that is very close to the spirit of non-directive counseling. We think there is a tremendous room for dialogue. There has actually been some heated discussion on what is non-directive counseling, what is respect for patient preferences. And I am sure that dialogue will go on.

Finally, what comes out loud and clear when primary care starts thinking about genetics is we need to protect patients from media hype, not just in genetics but generally. This is one of the roles that primary care takes on, but it is clearly extremely important in genetics. There is, as we know, a lot of media hype and a lot of folks bringing in something from a Web site or from a newspaper article that seems to imply magic bullets that we know aren't there yet in genetics.

So, primary care needs to be prepared to answer those questions. This is -- you can see, looking from these two different perspectives, you are looking at overlapping circles.

Now, out of those discussions, we have begun to develop an approach to develop an approach to curriculum. It starts with the notion that we must develop teaching cases that are based on presentations familiar to primary care physicians and connecting genetics to a more comprehensive primary care framework and just to make that clear, what we are talking about is the right opener, the right sort of lead-in for primary care is not here is Fragile X, let me tell you why that is important to you.

It is rather, one of the things you do a lot is look at kids with developmental delay. In your approach to kids with developmental delay, one of the things that it is reasonable to think about is Fragile X syndrome and here is why. And here are the implications of making a diagnosis of Fragile X. Clearly, Fragile X puts a label and allows some prognostic information that may actually get a kid services that the kid needs and all of those are the immediate benefits of making a Fragile X diagnosis. But as we know, it leads into a much more complex issue of inheritance of Fragile X in the family and

getting into terrain that really isn't familiar for a lot of primary care folks.

But the point is the lead-in is primary care docs deal with kids with developmental delay and if we approach it by you need to know about Fragile X, it doesn't really open doors, but if we approach it through problems that primary care folks are already dealing with, there is a much more obvious buy-in.

As we do this, we are identifying questions for consideration, as opposed to simple right or wrong answers. What I am really thinking about here is it is really important for geneticists not to talk to primary care providers and say you should do this, you should do that, but, rather, here are problems that we are dealing with. You have made a diagnosis of Fragile X. You have an issue of trying to sort out who else might be affected in the family. You need to sort out who is talking to who in the family and how you can begin that dialogue and what kind of choices the family might be interested in making in terms, for example, of prenatal diagnosis and so on and let's talk together about what are the strategies for accomplishing that.

Now, as we go through this and clearly one of the things that happens in this process is a sensitization on the part of primary care practice to, again, issues that they are perhaps not often thinking about, there is also a tremendous need to identify available resources. And I know we will be talking and hearing more later today about particularly Internet resources, but this project has already identified that as we develop a teaching case, one of the elements that needs to be there is what are the Internet resources.

Another piece and something that we expect to be helping our ten teams that are coming for train the trainer is what are the resources in your community. Who does genetics? It turns out when you talk to primary care providers, a lot of them don't even know what a genetic counselor is or what a genetic counselor is or what a genetic counselor does. Primary care providers are often not enthusiastic about referring to specialists whose services they don't understand.

But as we begin to accomplish this dialogue, one of the important parts is connecting people in given locations with the experts in their area so that they can have dialogue. The structure of our teams will, obviously, mandate this to some extent because one of the requirements for our teams for the train the trainer process is that both primary care and genetics expertise are represented on those teams.

Clearly, our curriculum will emphasize certain principles. One is rational use of family history and genetic tests to improve health, recognition of the potential risks of genetic knowledge, recognition of important debates, particularly that around duty to disclose. We have had some discussion about that and, obviously, as we all know, this is an ongoing issue for genetics. What is the duty to disclose if there is it and how can providers discharge that duty if they have a duty to disclose information about genetic risk to family members.

This is, I think, a perfect example of an entre between or an opening of a dialogue between genetics and primary care in which primary care is invited to enter into a problem-solving exercise and may actually bring some very interesting ideas to the table that haven't necessarily been part of a genetics specialty discussion yet. This is an unresolved issue and one that all specialties need to be

participating in.

Clearly another important issue and it relates to identifying resources for our case studies is the rapidly changing nature of genetic information. Primary care docs are used to rapidly changing information. This is a common part of practice. We need to underscore this and emphasize what kind of resources are there to help docs to update periodically on particularly diagnoses that they don't see very often.

We are going to have our first train the trainer session in which our ten faculty teams will attend in October and at that train the trainer session, we will have for their purview 10 to 12 topics developed as model curriculum material. Examples of the kind of topics that we are going to be addressing, breast, ovarian cancer, colorectal cancer, developmental delay, hemochromatosis, hypercholesterolemia, multiple congenital anomalies. In all cases, we are really emphasizing issues of prevalence, the kinds of conditions that connect to problems that primary care docs are seeing commonly.

The materials that we will include in our model curriculum, based on our discussions with our Advisory Committee, will include a syllabus that provides background information in kind of a blueprint to how genetics fits into this particular topic. Key references in those, obviously, include Internet resources. As we develop our curriculum materials, we are going to be asking both geneticists and primary care members of our Advisory Committee to review the materials, including the Internet resources that we are going to recommend for use with the materials. And we are going to be developing teaching cases.

These are cases that are going to be constructed for interactive teaching so that you can go through an if this, then that kind of discussion with different kinds of outcomes, starting with a particular patient presentation. They are going to be based on typical primary care presentations and the idea is that you develop teaching cases. The teaching cases are so much based on patients that are like those that walk through the door that the kind of teaching skills you are developing can also be used in clinic when attendings or supervising residents or medical students seeing patients because these are the kind of patients that walk through the door.

In the interim period after we have introduced this teaching material to our trainers, each team is going to be encouraged to adapt the curriculum that we have developed, in other words, take these model curriculum materials back. Do they work? Do they make sense? Do they help? How can they be modified to be better? Can you use the principles that we have used to develop these topics and expand them to other topics that seem to be coming up at your center?

We will also be conducting site visits at each of the teams' centers during that interim period and we will have a second train the trainer session in which we will have reports back from the teams, evaluations of successes and failures and from that a plan for final curriculum. Clearly, there will be discussion as we go with the Advisory Committee as well being included in this evaluation and reporting back process.

So, obviously, one of the outcomes of this is curriculum approaches, principles and materials that have been vetted a bit in these sites of our faculty teams. I want to just very briefly use some of the

principles with a particular topic of colorectal cancer, just to make a couple of the points that I have made with a specific example.

When we start thinking about colorectal cancer as a teaching example for genetics, we start with using family history. But I want to point out that when we think about the approach we are developing in GPC, we start with family history as a guide to the age of initiation of colorectal cancer screening and then only secondarily as a method to detect high risk families, which is a little bit different from the traditional genetics approach. It makes a lot of sense from a primary care perspective. You can show primary care docs this kind of epidemiologic data that says that if you have a family history of colorectal cancer, you have got a two-fold higher risk of developing colorectal cancer and your risk kicks in somewhere around ten years before that of the average risk in the population.

So, if we have agreed as a medical community to provide routine colorectal cancer screening to people at age 50, it makes sense to think about providing routine colorectal cancer screening to people with a first degree family history at age 40. There haven't been screening trials to prove that benefit, but a fairly compelling argument can be made, in part because the screening strategies that we have work just as well at 40 as at 50 and, in fact, two expert consensus panels have made that recommendation. You can get into conversations like should you do it for someone whose first degree relative had colorectal cancer at 80 or should you limit to people whose first degree relative was affected at a younger age.

But the point is that when you get into this discussion with primary care docs, you are talking about screening decisions that are the meat of primary care. You are talking about issues in making judgments about screening decisions that primary care deals with on a daily basis and you are also talking about 10 percent of their patient population because something like 10 percent of the population has a first degree relative with colorectal cancer.

So, you are talking about using family history in the practice of primary care in a way that has daily relevance to a primary care doc. And then you can start talking about what I think often comes up first on the radar screen for genetics and that is that whole continuum of family history, so that you have on the right the person whose grandparent had colorectal cancer at 80. Maybe that person doesn't need an early initiation of cancer screening.

The person whose mother in the middle had colorectal cancer at age 59 and that person probably should start colorectal cancer screening early and there is a lot of those folks in primary care practices and then on the far right -- I am not sure I am doing my lefts and rights here -- you have the high risk families.

These are the ones that from a genetics perspective we don't want to miss because these are the families with early onset, autosomal dominant inheritance, who may have FAP, may have HNPCC. The point is that if it is worthwhile to ask that first question about who has a first degree relative, you have already got an entre into something that in rare instances will lead to that high risk family.

You have shown primary care docs that you can identify high risk families within a context of an activity that has relevance to your daily practice. And clearly, as you have this discussion, it is very important to be clear about prevalence. Ten percent, somewhere between 5 and 10 percent of

people have a first degree relative with family history of colorectal cancer.

We are not sure what the prevalence of HNPCC is, but it is almost certainly under 1 percent and FAP, of course, is 1 in 8,000, 1 in 10,000. So, those high risk families are useful to find, but they are extremely rare.

That is part of the sort of truth in disclosure as we talk about the importance of genetics issues. And then, of course, we do want to talk about the issues in high risk families and those include opportunities for genetic testing, test limitations, the importance of testing an affected family member first because of the limited sensitivity of testing, the kind of prevention strategies that we think about, including very, very early onset of screening in high risk families and, obviously, again, a discussion about potential duty to disclose.
These issues get demonstrated in a primary care education project because we want primary care docs to be very cognizant of the kind of issues that kick in, very cognizant of what kind of issues need to be raised in genetic counseling and we suspect that many primary care providers with full awareness will choose to refer those patients. But we have created a larger context that makes it easy for them to get into the discovery process and understand why it is important.

I will just end there as an illustration of how we are approaching curriculum development. Obviously, we will know more in another year about how the strategy plays out.

DR. McCABE: Thank you, Dr. Burke and Dr. Kahn.

Our next presenter is Dr. Joan Weiss. As a nurse consultant in HRSA's Bureau of Health Professions, Dr. Weiss works with schools of nursing, health care institutions, foundations, and federal agencies to promote understanding of national nursing and health needs, issues, trends, and resources.

Among other issues, she is currently working on a genetics initiative in nursing, which we will hear about today. She is also involved in planning efforts for issues ranging from public health nursing and geriatric education to pesticides and border health. By training, Dr. Weiss is an adult and gerontological nurse practitioner with specialty practice experience as a cardiothoracic and vascular nurse practitioner.

She received undergraduate and graduate degrees in nursing from Temple, Catholic University and the University of Pennsylvania. Dr. Weiss will describe some of the efforts being made to incorporate genetics into nursing education.

DR. WEISS: Thank you and thank you for this opportunity to present activities the Division of Nursing is doing in the area of genetics. Before I start to talk about what we are doing in genetics, I would just like to give you a brief overview of the Division of Nursing.

First, I would like to start off with the mission. The Division of Nursing is the key federal focus for nursing education and practice. It provides national leadership to assure an adequate supply and distribution of qualified nursing personnel to meet the health needs of the nation.

The strategic goals of the Division are to increase access through improved composition and distribution of the nursing workforce, to increase diversity and cultural competence in the nursing workforce, to enhance nursing workforce data and analytic activities, to improve the quality and outcomes of nursing education and practice and to provide public information and technical assistance relating to the nursing workforce.

Our work in genetics relates to the strategic goal to improve the quality and outcomes of nursing education and practice. Programs that are in the Division of Nursing, include the Advanced Education Nursing Program, the Advanced Education Nursing Traineeship Program, the Nurse Anesthetist Traineeship Program, the Nursing Workforce Diversity Program and the Basic Nurse Education and Practice Program.

The purpose of the Advanced Education Nursing Program is to prepare advanced education nurses through the enhancement of advanced nursing, education and practice. Advanced education nurses are nurse practitioners, nurse midwives, nurse anesthetists, clinical nurse specialists, nurse educators, nurse administrators, public health nurses and any other nurses that receive a master's or doctoral degree.

Advanced Education Nursing Programs include master's and doctoral programs, combined RN master's programs, post nursing master's certificate programs and certificate nurse midwifery programs in existence on November 12, 1998.

The Advanced Education Nursing and Nurse Anesthetist Traineeship Programs pay for all or part of the cost of the tuition, books, fees and reasonable living expenses for master's and doctoral students. These programs are formula-based programs.

The purpose of the Nursing Workforce Diversity Program is to increase nursing education opportunities for individuals from disadvantaged backgrounds, including racial and ethnic minorities underrepresented among registered nurses in order to increase nursing workforce diversity.

Types of projects that are included with this program are pre-entry preparation activities, stipends and scholarships and retention activities. The purpose of the Basic Nurse Education and Practice Program is to enhance the educational mix and utilization of the basic nursing workforce by strengthening programs that provide basic nurse education.

We also have a National Advisory Council on Nursing Education and Practice and the mission of the council is to provide advice and recommendations to the Secretary and Congress on policy matters related to issues of nursing workforce education and practice improvement to meet the health care needs of the nation.

Now I would like to talk about some academic programs. There are actually four academic programs that offer advanced education, advanced nursing education, in the country. They are Rush University, the University of Washington, the University of Cincinnati and the University of Ohio.

The University of Washington is currently funded by the Division of Nursing. Funding began in 1998 and will end in 2001 and Rush University was funded from 1993 through 1997. The program at Rush

University is available at all graduate degree levels. They have a Master of Science in Nursing Program, a Nursing Doctorate Program and a Doctorate of Nursing Science Program.

Students enrolled in the Master of Science Nursing option are required to complete 55 quarter credit hours of studies for the nursing doctorate and also for the Doctorate of Nursing Science. They are required to complete 85 quarter credit hours of studies if they answer following their baccalaureate study or 30 quarter credit hours if they enter following their master's preparation.

At the MSN or doctoral level, ND level, the students may pursue the genetics focus within either a clinical specialist or nurse practitioner track. At the doctoral nursing science level, the emphasis of study is on nursing research and knowledge development in genetics.

They received a total of $682,338 and as a result of that funding, they enrolled 37 new students between 1993 and 1997 and graduated seven students. Since funding has ended, they have been enrolling three to five new students per year and between 1998 and 2000, they graduated five students.

DR. PURYEAR: Joan, are all those projects in genetics?

DR. WEISS: Yes. All of these programs are in genetics and they received funding from the Division of Nursing for all of these, for genetics at Rush University.
Graduates of the Rush University Genetics Program are employed in primary care settings and they incorporate genetic assessment, counseling and management into their practice. Complex cases are referred to geneticists or to genetic centers. In this past year, they developed two Web-based courses and these are the theoretical basis of genetic health and advanced principles of genetic health. These two courses are -- they are science courses and are required by students in the program. But this spring they decided to put the courses on the Web and offer them to students, graduate students, and undergraduate students who are not enrolled in the program.

Four graduate students enrolled for this course, theoretical basis of genetic health, and one undergraduate student enrolled and all of them have done really well. The advanced principles of genetic health will be offered this summer semester and they are still continuing to enroll students on-line. So, they didn't have a number of students who will be -- but they expect to have a pretty good turnout.

The University of Washington program, this is an Advanced Practice Genetics Program. It was started in 1998. Students are required to complete 38 to 44 credit hours and the purpose of the program is to educate advanced practices nurses to meet the health care needs of populations with or at high risk for genetic disorders.

They received, to date, a total of $597,901. They enrolled ten new students and graduated one student in this program.

The University of Cincinnati, this program -- I am just letting you know about it. It has not received any funding from the Division, but it is out there and it is a 60 credit hour master's of science and nursing dual major. This program can be completed with any other nursing major at the University

of Cincinnati or it can be completed after any other nursing master's is achieved.

The focus is on -- it focuses on maternal child nurses, but is flexible to allow nurses in other areas to pursue the genetic focus.

The University of Iowa also has a genetics nursing program. Again, this program is not funded by the Division, but it is out there. It is 47 semester credit hour master's of science and nursing program that focuses on providing nursing care to individuals, families and communities with known genetic conditions and/or birth defects.

This program can be combined with a nurse practitioner track or a community health program. Their practice settings include pediatric metabolic clinics, genetic counseling programs, familial cancer assessment and management teams, public health departments, private genetics testing labs, prenatal care programs and specialty clinics.

Now I would like to talk a little bit about what is going on in regards to national nursing organizations. First, I would like to talk about the American Nurses Association. In 1992 and 1998, ANA did a study whereby they looked at the extent to which genetics was included in nursing curriculum on undergraduate and graduate levels and found that there was little or no genetics content at the undergraduate or graduate level.

This is in keeping with what we at the Division hear from our constituency. In the early nineties, ANA did a study of nurses and they looked at nurses in relationship to information they received and communicated on genetic testing. This study looked at the way nurses were immersed in genetics without necessarily having been trained in genetics.

This study provided the beginning work from which ANA joined the American Medical Association and the National Human Genome Research Institute to form the National Coalition for Health Professional Education in Genetics, NCHPEG, which Dr. Guttmacher will talk about a little later.

Currently, ANA has two representatives to NCHPEG.

The next association I would like to talk about is the American Association of Colleges of Nursing. This organization is currently not doing anything in the area of genetics, but they do have a representative to NCHPEG.

Finally, the International Society of Nurses in Genetics, this organization is a nursing specialty organization dedicated to fostering the scientific and professional growth of nurses and human genetics. Its vision is caring for people's genetic health. Its mission is to foster the scientific professional and personal development of members in the management of genetic information.

Its goals are to provide a forum for education and support for nurses, providing genetic health care, promote the integration of the nursing process into the delivery of genetic health care services, encourage the incorporation of the principles of human genetics into all levels of nursing education, to promote the development of standards of practice for nurses in human genetics, to advance nursing research in human genetics and to provide a forum for a dialogue with others.

So, basically, this organization is working in the area of nursing education, nursing clinical practice and nursing research. The International Society of Nurses in Genetics in conjunction with the ANA have published standards of practice for nurses in genetics. The position paper is entitled "Statement on the Scope and Standards of Genetic Clinical Nursing Practice."

The last thing I would like to talk about this morning is a collaborative initiative with the Division of Nursing, the Maternal and Child Health Bureau at HRSA, the ELSI program at NIH and the National Institute of Nursing Research at NIH.

This initiative, we are gathering information from nursing leaders in genetics throughout the country at a two-day conference and we would like to identify gaps in nursing, particularly nursing education and practice and see where nursing should go with future initiatives. So, we are waiting -- we will be having this meeting on September 28th and 29th of this year and pending the recommendations, we will go forward with our genetics initiative.

Thank you very much.

DR. McCABE: Thank you, Dr. Weiss.

At this time, we are going to take a 15 minute break. We will resume here at 9:50. Members and presenters should proceed to the alcove. Those of you who received the menu, please take it and fill it out and turn it in there.

The restaurant bar is serving coffee for members of the public. Staff at the meeting registration desk can also provide information about cafes in the local vicinity. So, please be back at 9:50.

[Recess.]

DR. McCABE: Thus far, our presentations have focused on efforts initiated by or in collaboration with the government. We will now hear about an effort undertaken in the private sector by the American Society of Clinical Oncology to address the need for enhanced provider training in the specialized training in the specialized area of clinical cancer genetics.

We are pleased that Dr. Jeff Weitzel is here to discuss the clinical cancer genetics education efforts underway at ASCO, to incorporate new knowledge about the role of genes in cancer.

These efforts primarily are for ASCO's membership, but also for a broader audience of allied health care professionals. In addition to his work with ASCO's Task Force on Cancer Genetics, Dr. Weitzel is the director of the Department of Clinical Cancer Genetics and the Cancer Screening and Prevention Program at the City of Hope Comprehensive Cancer Center in Duarte, California.

He is board certified in clinical genetics and medical oncology, as well as in internal medicine and hematology. He directs the City of Hope Cancer Genetics Education for Primary Care Providers Program, which is supported in part by funds from HHS and NCI.

Dr. Weitzel is also a clinical associate professor of preventive medicine at the University of Southern California School of Medicine.

DR. WEITZEL: Sorry for the delay. To err is human, to really foul things up requires a computer. Thank you for the invitation. I am very pleased to be here as a representative of the American Society of Clinical Oncology, but also as a medical oncologist and geneticist, who uses genetics in his everyday practice.

My current focus is as a cancer geneticist or an oncogeneticist. You can provide many new terms for that.

What I have on my title slide is "The Role of Professional Societies in Clinical Cancer Genetics Education and I hope to let you know that there is an important role for the professional societies, as well as for individuals within those societies to utilize the resources that have been laid out there, both from the HRSA, the Maternal and Child Health Bureau and from the NCI and cancer education realm.

Also, I am going to lay out what some of the differences are in cancer genetics, as a small subset of genetics overall and in a sort of new mold that Dr. Burke started out to outline and I am going to continue with.

This is the front of the City of Hope, and when I first went there -- they are known for cancer as a specialty in treatment, but what they didn't realize is that at the front of -- their emblem is a man and a woman holding a baby aloft. I can think of no better sort of image for genetics than that alone.

The other reason I used this slide as an introduction is because all of us who work in cancer genetics and respect genetics as a profession understand the need of a team approach. One of my colleagues, who is my very close -- and works very close with me is Deborah MacDonald, who is a clinical nurse specialist in genetics. So, as Dr. Weiss was just alluding to in terms of training, she did a master's degree in maternal and child health with a specialty in genetics and has been involved in cancer genetics for some time.

She is also the immediate past president of the International Society of Nurses in Genetics. Also, I employ two genetic counselors in addition to Deborah McDonald, one of who is Kathleen Blazer, who is a board certified genetic counselor from the California State University program in North Ridge, one of the counseling programs that just recently received its full accreditation out in California.

We actually serve as a training site for that counseling training program.

Now, basically what all this is about is begging the question of were you born that way. I again want to mention what Dr. Burke mentioned earlier this morning that people are impacted by our public perception and by the media. You can't pick up a book or a journal these days without reading about something that is going to explain personality, temperament, life choices. In this case, we are, of course, talking about cancer.

So, the first thing I am going to make is a premise and sort of to outline why I think there are roles for different health care professionals within genetics, is that cancer is a complex disorder. Complex issues arise in genetic predisposition testing and proficiency in genetic cancer risk assessment requires cross disciplinary expertise.

Now, as I mentioned, it is a multi-step process. A lot of these slides I am going to use are also from the ASCO curriculum that we have created for teaching oncologists and other health care professionals about cancer genetics. But basically we have to identify at risk patients, provide pre-test counseling, provide informed consent, selected it all for the right test, disclose results in person. These are all basic principles of genetics in general and then I think one of the places where there is a big difference and where oncologists have a significant role is in the post-test counseling and follow-up care. How do you take care of patients at high risk for cancer?

Now, there are a number of ways to go forward from this. I think I have fashioned in a way that helps me to understand a little bit more about how genetics integrates into oncology and what are the cancer risk assessment domains that are relevant. First, there is the state of cancer genetics knowledge base, an ever-changing base; the state of mind. I think this is one of the areas where cancer genetics is, indeed, unique, as compared to perinatal genetics, for example. State of technology, an ever-changing field, and state of the art in terms of management, another changing -- rapidly changing field and fortunately in a positive way.

Over 20 cancer associated syndromes have been identified in the last five to ten years. This is just a partial listing. Of course, starting with familial retinoblastoma, a pediatric oncologist, Alfred Knudson, which all of know about right now because of his two-hit hypothesis in cancer genetics, the ones I would comment that are most relevant now are the familial polyposis, hereditary non-polyposis colon cancer, hereditary breast and ovarian cancer.

It is a long list and getting longer and I think it is part of integrating genetics into practice. So, the state of knowledge is also that we are seeing an ever-expanding role for cancer genes, tumor suppressor genes, oncogenes, DNA repair genes. The list goes on and the basic science field feeds us continuously.

There is emerging knowledge about gene-gene and gene-environment interactions, where clinicians are at the interface. Age specific penetrance estimates vary by population and by mutation, adding layers of complexity to the process and in oncology -- and this is, again, a unique feature, I think, of cancer genetics -- understanding the epidemiology and natural history, the diagnostic techniques that are used.

What is the utility of mammography? What is the utility of MRI and management strategies, as I mentioned? They are changing and the oncology perspective is invaluable in this regard. Now, one of the things that we have learned is that germline mutations, which is what a lot of this conference is about and about genetic testing in general, are present in the egg and sperm, are, obviously, heritable and cause cancer family syndromes in a small proportion of cases.

However, just as importantly, we have been barraged with information about somatic genetics, which is acquired genetics and as clinicians, we are called upon to understand the difference. So, hence,

another need for education.

A good example is that Her2/neu is a gene amplification. It is an acquired alteration in cancer cells associated with poor outcome and chemo resistance. There is a targeted treatment available. I don't know anybody who hasn't heard of Herceptin.

It is important for us to -- and physicians are called upon to know the difference between the two. I have had patients come to me and say my mother had Her2/neu in her tumor. I want to get tested for that. Obviously, this is an acquired abnormality, not an inherited one.

We have had a long history of genetics in cancer and in hematology, in particular, the diagnostic and prognostic value of specific karyotypic abnormalities in leukemia; the Philadelphia chromosome, one of the earliest examples of a genetic correlate to disease, acute promyelocytic leukemia in the 15/17 translocation involving the retinoic acid receptor.

Finally, very recent data talks about tumor microsatellite instability, a somatic marker of an inherited colon cancer syndrome that actually has prognostic significance and, thus, may be ordered by clinicians as a prognostic test, rather than a germline test because people, it seems, have a survival advantage if their tumor arose because of this phenomenon.

The interest in genetics has expanded for some time and it has been in the public purview. I use this example for the discovery of BRCA1. First off, of course, came studying families and pioneers like Mary Clare King, who is a genetics specialist, a Ph.D. geneticist, have been collecting these families for decades and, in fact, it was in 1990 that Jeff Hall and her group first published and established that there was a single gene trait on a single chromosome, chromosome 17, that could account for a proportion of these hereditary breast and ovarian cancer families.

Now, that was phenomenal news because up until that point most individuals thought that cancer was too complex and multifactorial to have a single gene trait associated with it, with the exceptions of some of the pediatric syndromes. But it took four years to narrow that region with an international consortium until finally in the genetics meeting in 1994, the BRCA1 gene was cloned and announced as being cloned. And that really started off a fear of considerable public interest, even before that and also the beginning of, if you will, some of the more common cancer genetics era for practical risk assessment.

Now, accompanied by that, of course, was the publicity and as part of that publicity becomes the second point I wanted to make about the state of mind. This is from the cover of Newsweek in 1993 before BRCA1 was cloned.

It says Joan Cunningham had breast cancer. Her daughter, Julie, had a preventive mastectomy. Will Alexandra be spared? Now, these are the kind of emotional pleas that are out in the public and certainly women who have experienced the strong family history of cancer come to the table with a serious issue already.

Marcia Grant, one of our nursing researchers at City of Hope, identified that among women, who

survived breast cancer, their most common concern was what is my daughter's risk. So, state of mind, previous cancer experience within the family, risk perception and risk tolerance, experience with death and dying, all of these top three are elements that oncologists have considerable experience in.

Life events might prompt somebody to come forward and previous experience with the medical system or personal cancer experience all color a person's interaction with this system. And, again, oncology perspective is invaluable to understand their perspective.

State of the art in management is changing. I know that Dr. Burke chaired the ELSI Guideline Committee and published that in JAMA a few years ago, talking about consensus guidelines for management. But these are changing. The National Comprehensive Cancer Network has recently published guidelines that allow us to integrate the management aspect and the evaluative aspect of cancer genetics. There is emerging surveillance technologies and surgical approaches.

Recently, data presented at ASCO and at the American Association of Cancer Research cited the efficacy data for prophylactic mastectomy, as well as emerging data on the efficacy of oophorectomy in hereditary breast and ovarian cancer. And chemoprevention, probably the most brave new world of cancer prevention, is starting to show significant benefit and there are major national trials in which oncologists have a major role in enrolling patients.

So, in the risk assessment realm, what is my risk for cancer is the commonly asked question, but there are different ways of quantifying cancer risk and one of them is empiric cancer risk models, based on population studies, which are one that is not necessarily been in the common realm of a perinatal geneticist or somebody who is a standard trained geneticist in the past, although it is something that is incorporated into risk assessment models.

However, a forte of a geneticists background is, of courses, Mendelian risk and Bayesian modification of risk, estimating the probability of being a mutation carrier, which is a common part of cancer genetics practice and then genetic testing, which provide gene specific cancer risk assessments.

Now, this is, again, part of the ASCO curriculum, but we are called upon to compare these models and to contrast them and let people know what the deficiencies are in each. For example, the Gayle [ph] model is an empiric risk measure about breast cancer, but it also includes things like age at menarche and age at first child, both endocrine factors that may contribute to breast cancer, biopsies of the breast, which don't seem to be related to genetics at all; yet, it is incorporated in a model.

But we have to compare and contrast these in our new practices. Why? Because breast cancer risk is extremely high in these individuals. Second primary breast cancer risk is almost as high. So, it may impact on management decisions and ovarian cancer risk is also high and even if you haven't seen ovarian cancer in a family, this is a relevant issue.

Now, all of these are things that are evolved in the last five to ten years in studying these high risk families. Now, how have we learned cancer genetics practice in the past? I can speak personally of this because it is part of where we have come from. Most of the practitioners in the community

now and in the nation are and have been oncologists by primary training.

It is not inconceivable, given that their primary interface is with cancer patients and where we have to sort out some of this history. The hard way is the way we have learned it, by self-directed studies. So, most of the people like Barbara Webber at the University of Pennsylvania, others like her, who are oncologists and learn genetics as a second specialty but without the benefit of formal training, hands-on experience.

I constantly see on our list serve at the National Cytogenic Counselors, of which I am associate members, that many of us are starting out and have to learn from the group as a whole how to deal with cancer issues; gleaning the literature, which is ever richer, and formal fellowship training.

Now, do you do medical oncology, clinical genetics or both? I chose the latter pathway and in the question and answer period, I would be happy to tell you my experience in that and how I think that that might be bettered.

Educational resources that are there now, and a lot of them have been cited, so I am not going to go over them in detail, but there have been American Cancer Society national conferences on cancer. I am, obviously, going to talk about our ASCO curriculum. NSGC has put on numerous short courses, starter packs, flip charts and other supportive mechanisms.

The ONS curriculum has come forward for nursing and ISONG, as I mentioned, they have been quite involved, as well, and were mentioned by Dr. Weiss.

Then there is also -- of course, you are going to hear from NCHPEG today. So, the Task Force on Cancer Genetics for ASCO was first convened in 1996, when commercial testing for BRCA1 and 2 first became available through Myriad Genetics. They were charged with the responsibility for developing a curriculum, teaching materials and a plan to implement teaching through a series of meetings for oncologists, nurses, genetic counselors and other appropriately trained health care professionals that recognized the need and moved forward with a task force that was made up primarily of people who were already practicing cancer genetics and at the fore of the field.

In May 1996, the ASCO published its first policy statement on genetic testing for cancer susceptibility. Within that statement, as for many other professional societies, like the American Society of Human Genetics, they affirmed a commitment to providing cancer genetics education so that oncologists may more responsibly integrate genetic counseling and testing into the practice of clinical and preventive oncology.

They outlined guidelines for cancer predisposition testing and endorsed efforts to strengthen regulatory authority for laboratories and providing cancer predisposition testing and endorsed efforts to strengthen regulatory authority for laboratories and providing cancer predisposition testing, certainly a realm of this committee, and endorsed efforts including legislation to prohibit discrimination by insurance companies or employers, all things that directly impact on our ability to deliver this care in the community.
These are an example of the guidelines that they issued for testing. So, many of the things you are considering today, ASCO published in 1996 and also trying to consider how to classify these different

groups of tests.

Here they said that these tests will result in a change of medical care and should be considered as standard of care in medical management. And I don't think it is arguable that familial polyposis is a good example of that, medulla thyroid cancer in multiple endocrine neoplasia type 2 and on and on, although retinoblastoma and Von Hippel-Lindau are extremely rare.

In a second category, they put in tests that were of possible medical benefit, but were uncertain at that point. The hereditary nonpolyposis colon cancer genes, the hereditary breast and ovarian cancer genes, I think it is fair to say the second item, at least, and possibly the first are moving fairly quickly into standard clinical practice, as we understand more about the limitations and how to move forward with the risk estimates.

So, the education activities continued and in May 1997, they created a resource document that was again published in the Journal of Clinical Oncology that was created by the Task Force, intended as a topical framework to promote formal instruction on the assessment and management of familial cancer risks in training programs and in CME courses, recognizing, as all of you do, that there are deficiencies in training.

Dr. Burke pointed this out significantly in the primary care field. In June, the first train the trainer workshop was held by ASCO, attended by 275 individuals, held in Chicago. Most of these individuals were oncologists, equally divided between oncologists, there were geneticists, genetic counselors and nurse geneticists.

The goals were to train clinical cancer specialists and health care professionals to develop regional training courses, essentially the formal type of effort that the primary care group is talking about doing now and is actually implementing. In 1997, we started that process within the setting of oncology.

Now, in May 1998, the first ASCO genetic satellite symposium was held at the ASCO annual meeting. It was impressive, I have to tell you, because it is hard to get people in genetics, but we had over 500 clinicians attend that first all day symposia. It utilized a working draft of a new curriculum that ASCO had developed.

In the summer of 1998, a refinement of this resulted in the publication of a curriculum, which I can show people afterward if they are interested, but it is available. It is a 300 slide set with lecture notes in a CD ROM format for training programs. More than a thousand copies of the curriculum have been sold.

This is the front cover of it. It was some lovely art work, but it talked about cancer genetics and predisposition testing. The modules, which I am not going to go through individually included all of the following subject areas and I want to point out more importantly, include ELSI issues, testing process issues and laboratory methods issues, all things that are perhaps greatest gaps in knowledge for oncologists.

Now, in November of 1998, they did another Fall education conference and in March 1999, an

update for the train the trainer workshop. It was attended by 225 trainers from across the country, many of them for their second time. It was designed to further update their skills and to give them skills in how to organize conferences regionally.

In 1999, a satellite symposium was again held at the ASCO meeting, again, 500 clinicians signed up and participated in the entire meeting. Now, we have used metrics to try and measure the impact of our efforts. Pre and post-seminar questionnaires were used to measure the attainment of specific knowledge. We even followed up long term retention of knowledge among our trainers by looking at the six month time point.

Overall, for those at the conference, there was a 50 to a hundred percent increase in the correct response rates immediately after the conference and gratifyingly improved scores were durable when looked at at the six month time point; for example, the example of what a missense mutation means in the context of disruption of gene function.

Ultimately, we wish to measure the impact on practice patterns and patient outcomes.

Now, to move on, we have expanded this realm into other forums. So, American Society of Hematology invited ASCO to present a joint forum, which I was a participant in in December of this year at a major meeting, again, two sessions, several hundred participants in each of the meetings. And in May 2000, just finished, was the state of the art, a clinical cancer genetics course that we held at the ASCO meeting, that held a progressive series of sessions, one on each of four days of the meeting, each attended by at least two to four hundred attendees and focusing on current state of the art, inviting national and international speakers.

So, our future endeavors, and where we are heading is in the realm of a self-education module, which, similar to the MKSAP education, which is Medical Knowledge Self-Assessment Program, a preparation for boards in oncology, we have created ONCOSAP [ph]. A number of the Task Force members participated, and basically this is based on the curriculum, whose text, questions, explanatory answers in the CME format, available in print and on CD ROM. That is going to be released in August.

Additional courses are planned. Fall education conference in the satellite symposium at our next annual meeting. These are intended to provide continual updates for clinicians. One option, also for preparation for a possible proficiency exam being developed independently by the Institute for Clinical Evaluation -- now some of you may have heard before I came here that that was one of the issues we would be focusing on, but I need to impress upon you the importance of the fact that this is an independent effort from ASCO.

ASCO did provide some financial support as an unrestricted grant to develop credentialing and proficiency examination ideas, but it is, indeed, independent of ASCO. So, I can only make a couple of comments. One is that there is a question writing committee being convened, which will comprise a 120 best answered questions. This is outlined on the ICE Web site, the Institute for Clinical Evaluation.

There is broad eligibility for clinicians and mid-level practitioners. The issue is one of proficiency and

competency, not of who is going to be the provider. I think that these are issues that we have to answer in a workforce way.

Education resources that are now available also include clinical genetics with a focused cancer experience at Memorial Sloan Kettering. Dr. Offitt has recently had a T32 funded fellowship, which is a traditional genetics tract, but with a focus on cancer genetics, which is, I think, a very welcome change.

There is also Cancer Prevention Control Fellowships at the NCI and I am on the Study Section G at the NCI. So, I would like to put a plug in for Interdisciplinary Cancer Research Training Programs, which are a new venue for looking at exactly this kind of cross disciplinary training need.

For my own part, we have extended and taken our own program to Southern California and beyond. And, in fact, I have a Cancer Screening Program and a Cancer Education Program, both targeted to our Cancer Center and to primary care physicians. So, I am thankful, indeed, for the support from Maternal and Child Health Bureau. So, I have utilized many of the resources you have heard about today from the Title V funds to R25 Cancer Education Grant to the NCI, all invaluable resources as we further the education efforts.

ASCO has 13,000 members. Thirty percent of them are in academic medicine, 55 percent in medical oncology and a number in other subspecialties. I want to point there are four pillars. We are not in credentialing. We are involved in prevention, research, treatment and education. I think that is an important point to remember in our efforts to further this. I think many professional societies have an important role in educating them and I do, indeed, think that ASCO has taken a lead in this.

I want to end there and just -- I use this slide often as a closer for most of my talks when I am teaching clinicians. This is called the Golter [ph] Gate. It is in the gardens at the City of Hope. It says, "There is no profit in curing the body if in the process we destroy the soul."

So, all of us, who are clinical oncologists and geneticists and provide cancer genetics as a practice do believe that counseling is a critical role in this effort. I applaud all of your efforts to make this a fact as well.

Thank you.

DR. McCABE: Thank you very much, Dr. Weitzel.

Our next presenter is Mr. Tim Baker of CDC, who will describe CDC's activities in integrating genetics into the training of public health professionals. Mr. Baker is deputy director of the CDC's Offices of Genetics and Disease Prevention. He is responsible for developing policies and programs that advance the integration of genetics and public health and for effecting public and private partnerships associated with CDC's strategic plan in genetics.

During a 28 year career at CDC, Mr. Baker has initiated several national programs to integrate scientific and technological advances into public health programs, including the AIDS information services.

Mr. Baker is a graduate of East Carolina University.

MR. BAKER: Thank you.

The challenge that CDC has attempting to meet and then will help doing collaboration with all the other organizations in this room --

DR. McCABE: If we could please have it quiet for Mr. Baker's presentation.

MR. BAKER: -- will be how do we integrate genetics into the training of the public health workforce. There is a couple of key emphases. You hear this from many voices, but all from Muin, as well as the challenge of how do we integrate what we are doing in genetics, just genetic knowledge into the various public health activities.

I want to go through four areas of emphasis to set the tone for this discussion. The first is the public health functions and essential services, which are the foundation of what public health does. It is important to begin with that frame of reference because that basically is what we are trying to utilize as the framework for plugging in relevant and important genetic discoveries.

Secondly is this is based on constantly changing roles of public health professionals. I am sure those of you who work in public health in the audience know this is really a dynamic environment. Development of organizational and individual competencies is the beginning point. We have heard some discussion about competencies already, but competencies is basically determining what it is you want the workforce to be able to do and from that developing the content and training necessary to get there.

And finally, where does genetics fit into all of this? That really is an answer that we are trying to shape and will continue to shape I guess for most of the rest of my career here.

This public health functions activity began with or was really tightly structured in the Institute of Medicine report, Future Public Health, 1988, in which there was an identification of the assessment policy development and assurance needs around public health. Now, these were further clarified by the large working group of public health professionals, who got together to say this is what we think in public health that report means to us and try to translate those functions into the essential services.

Basically, what do they, the public health leaders of the country, believe are the essential services necessary to sustain and protect the health of the public across the various dimensions of health policy and health practice. It is a very complex array of activities and it requires a constant focus on what are the roles that are changing, what is the organizational competency, what is the individual competency among the disciplines that are involved.

Organizational competency is an interesting challenge because basically it is an effort to say what makes an organization work. Dr. Tuckson can probably reflect on some challenges, as he ran a large public health department, and what is it that makes a competent organization and how do you

sustain that, particularly as a lot of challenges are coming your way from developments in science.

Instead of staying spread out, I want to try to focus in specifically on the scope of what are the essential services, what is it that is going on and trying to move forward in training the public health professionals that are charged or meeting the challenge of implementing and responding to the services and, finally, what is our specific activities we are trying to do to shape genetics into that process.

The CDC Task Force on Public Health Workforce Development was done in collaboration with mainly outside organizations, outside of CDC, in collaboration with HRSA, to look at what is the status of that workforce that we are trying to train, estimated to be around 500,000 people throughout the country and primarily state and local and community health departments.

How is you affect a lifelong learning model that is built again on these essential services? I am going to use the essential services in just a moment, highlight where we see genetics currently fitting into that, but from the broader challenge, how do you develop a lifelong learning model that is capable of absorbing and inserting into that learning process emerging infections and bioterrorism and genetics and every other thing that comes along that requires an integration of that new scientific knowledge into the core health policy and practice in the country.

The competencies for each essential service that we are going to talk about was really the focus of that. So, it took these ten essential services and said what are the knowledge skills and abilities necessary that got a core to that and then within specific disciplines of functional areas, what kind of disciplines -- what kind of competencies are needed.

The outcome measures that were identified have really been put forward now and Michele mentioned it in the Healthy People 2010 document, which focused on the public health infrastructure and identifies the kinds of core competencies necessary across public health organizations to affect and accomplish the essential services.

The wheel, as we have come to call it, is an image of presenting the ten essential services and basically the ten essential services are an amplification of the core functions, as I said earlier. Now, those core functions are assessment policy development and assurance you see around the outside of the wheel and within each one of these quadrants are color coded the components of those essential services that are relevant to that.

Without belaboring that, this is a very long report, as you can imagine, that went into describing this, but essentially there is an assessment process that consists of monitoring health and diagnosis and investigating all kinds of disease in public health. We looked at how do we put forward a definition that includes genetics in that context and used that definition here.

It is placing genetics in the context of that assessment role for public health. As you go around and look at policy development, the policy development challenge is how do you inform, educate and empower the community and professionals, how do you mobilize community partnerships and develop relevant policies by using that knowledge and making sure that it is available in practice.

The policy development focus, as you see on the side, for developing these standards and guidelines with stakeholders to promote the effective use of genetic information, this is a very important role because this really becomes the cut point between what we know and don't know, as we have come to know and love as a term, how do we build that into the policies and standards within the various organizations throughout the country, that are trying to affect and sustain the health of the public.

Then as you make the transition into the assurance role, which is the real implementation, this becomes the interface then that has really changed the most, I guess, in the past ten years as public health and health services, clinical services have become both distinguished, sometimes in competition, as managed care came in and there was a shift in resources and public health moved out of care delivery. But now the challenge is how do you affect this policy relationship in which there is an interface where protecting the health of the public goes hand in hand with the clinical services and the health financing and the health policies and the assurance, maintaining particularly the quality as you see around up at the top where you evaluate what works and what doesn't work.

That is going to remain, I think, always one of the essential services of the public health. In the center, there is a system management function, which basically says there is an information infrastructure. There is a heart of informatics and data that is essential, as you have heard from my colleague for years, you know, data is the basis of driving a lot of these activities. But this hub of data, the system management level is an important focus that we are always going to protect and the research focus in the center is systematic investigation, taking what we know and testing against known burden of disease, known distributions and populations and principally trying to find out what are the interventions that work.

This is the backdrop for where, when and how does genetics fit in. It is not a question of if. It is a question of when, where and how does it fit into most of these essential services for most of the people participating in those roles in accomplishing those essential services.

You see on the left, I have tried to associate the essential services with Muin's comments yesterday, which were from GenTap in which the challenge we are also trying to meet is how do we tease out the knowledge that we have on an ongoing basis, what we know and don't know from lab public health and make that available within the construct of these essential services and through the training programs that we are going to try to promote.

CDC is continuing -- we started, have been doing this for the last couple of years now and starting our own training programs and there was a -- we have had our own courses, where we brought in 50 or 60 people at the time and raised awareness. We have had a lot of collaboration in the schools of public health that Michele referred to earlier in trying to move forward with formal curricula.

We have recently had a very focused scientific training course that Muin and his staff put together around human genome epidemiology, which we may take on a worldwide tour if things continue to unfold the way we are hearing. We recently had our show starring Wylie and Muin with a nationwide distance learning program that was co-hosted with the University of North Carolina.

Dr. McCabe also mentioned -- reminded me that we have a couple CD ROMs that are coming out

that are -- one is being done by Joe Henderson from Dartmouth that focuses on communications around genetic testing and one that Karen Steinburg has been working on around breast cancer and genetic information around breast cancer, a lot of different products.

I didn't intend to put a list together of all those activities. We can get those off of Web sites and so forth that we have there in the office.

I did want to focus on how do we take these initial efforts and we recognize it is going to take a long time for us to train the public health workforce at 50 people semi-annually. I am looking forward to finding the additional resources and economy of scale to get there.

Last year, CDC trained 664,000 people, spending about $55 million. So, in the context of doing that, we said there has got to be -- we wanted to continue these small sort of inoculation kinds of training that we are able to do within our resource. We need to graft onto this bigger process, which is the challenge we are meeting. There is an overall workforce training strategy that CDC is undertaking. It is competency-based. It is based on years of study, publications that builds from the essential services report, by reports about the future of public health that have been -- they are in the literature. We can give you a list of them.

The focus on the competency and then content and curriculum, learning system, incentives to ensure competency, including credentialing, the evaluation of the impact of that training and you see most notably assuring for national support, that to ensure this lifelong learning model across these disciplines.

The visual images, the intersection between these genetics competencies, such as NCHPEG has been working on and others through the years, which are primarily health care delivery-based with the public health competencies that we are reflecting here. And as Wylie said earlier, there is this intersection between primary care and genetics. In many ways, we are looking at the same way, what is the intersection between public health and genetics. What is that nexus of those two competencies and how they complement and reinforce one another.

So, how are we fitting this in? We are undertaking a corollary to that process we described for overall training of the public health workforce. Let me go ahead one and then back up. We are doing that by assembling six public health working groups and those public health working groups are going to be structured by functional areas and it follows more or less some work done by Robert Wood Johnson and by workforce teams in the past. We are going to be assembling a group of health official, administrators, program directors, another group of clinicians, a group of educators, counselors, social workers, epidemiologists, data specialists, laboratorians, environmental health directors.

And the charge to these working groups are basically to come together and say given our role in the future, given our current role, given the competencies we are trying to develop to build into this learning model, this comprehensive workforce development strategy, where and when and how do genetics fit into those roles we see for our disciplines.

Further, given that, what are the core competencies that are going to emerge from that and how can

we then use that in training? Let me back up.

Then we are going to -- we are planning to have the full group meeting of this august body in August of this year in Atlanta. They will be looking at assembling that initial draft, initial structure of where genetics fits into the role in public health, across the disciplines. We intend to have a core -- a final report on the core competencies by the end of May and this is -- we fully intend it to be an iterative process, as we have all learned in working in competencies.

This first draft is going to be at the very least, at the very probably most, a working draft that is going to acquire a lot of broad input and reaction, a lot of cross pollination with other efforts, some mentioned here, some going on at the public health world.

And then we foresee that leading to our ability to answer where do genetics fit into the changing role of public health professionals. What is that competency they need, how to begin to develop the training necessary to get there?

DR. McCABE: Thank you, Tim.

Our last presenter of the morning is Dr. Alan Guttmacher. Dr. Guttmacher is senior clinical advisor to the director at the National Human Genome Research Institute. His two main areas of responsibility are educating health professionals and the public about the use of genetics in clinical medicine and working toward the incorporation of genetic medicine into the nation's health care system.

Before joining NHGRI, Dr. Guttmacher was associate professor of pediatrics in medicine at the University of Vermont College of Medicine. While there, he helped develop a new medical school curriculum that made genetics an underlying theme throughout all four instruction years.
Dr. Guttmacher is a graduate of Harvard College and Harvard Medical School. He completed a residency in pediatrics and a fellowship in medical genetics at the Children's Hospital of Boston and Harvard. Dr. Guttmacher will describe NCHPEG and GROW, two innovative public/private initiatives, established to facilitate the dissemination of information on genetics and to enhance genetics knowledge among health professionals.

DR. GUTTMACHER: Thanks, Ed. It is a pleasure to be here and to really give you two different talks. I think they are linked only by the power point really. They are in some ways two distinct topics. So, let's move right into the first of them, which is the National Coalition for Health Professional Education Genetics. You have already heard several references to that this morning. People said, well, Alan will get to that.

I hope during this talk to answer the two questions that occur to me, must have occurred to you during the morning. Many of you will have wondered, the important question is it NCHPEG or is it NACHPEG. Others of you will have wondered, no matter how you pronounce it, what in the world is it. I hope to answer both of those.

First of all, it is NCHPEG. That is the authoritative -- we have had a study group study that and after I won't tell you how much money, we have decided that it is NCHPEG. Now, the National Coalition

for Health Professional Education in Genetics, let me give you something about its history. It says something about how much genetics is a changing field. The only genetics that you get away with throwing up on the top of slide, history and go back all of four years.

But in 1996, NCHPEG was really initiated by three organizations, the American Medical Association, the American Nurses Association and the NHGRI. It has continued to meet over that period of time, but in 1999 got a three year grant from the Robert Wood Johnson Foundation, which is enabling NCHPEG to gear up and I think be much more -- even more productive than it has been in the past.

At this point, there are over a hundred member organizations. They are in a handout that I think the members of the committee received in your briefing books. The one thing I would stress about the 109, I believe it is, organizations at present is they represent a very wide array of health professions. It is not simply physicians, nurses. It is a broad array of health professionals and NCHPEG clearly tries to incorporate many different kinds of groups into what it is doing.

Its mission statement is that NCHPEG is to promote health professional education and access to information about advances in human genetics to improve the nation's health. In terms of a philosophy that helps NCHPEG meet that mission, clearly it is a collaborative effort. It is an idea of bringing under one umbrella, one tent, a number of very different kinds of health professionals and very different kinds of organizations so they can collaborate together to accomplish things.

Clearly, it is not just the magic of having many different people cooperate, but to do it in an interdisciplinary fashion so that people coming from very different kinds of disciplines and backgrounds can be of help to each other in doing things and particularly to enable disciplines to learn from each other whether those have been successes or mistakes that others have made, but to learn from each other rather than simply reinventing the wheel over and over again.

The major goals of NCHPEG are to integrate genetics into the knowledge base of health professionals and students, both; to develop educational tools and information resources to facilitate health professional integration of genetics into practice of health care and to strengthen and expand the community of individuals and organizations committed to a coordinated national genetics education effort for health professionals.

I thought in terms of describing briefly for you what is the real work of what NCHPEG, well, it seemed that the logical way to sort of organize that was around the five working groups that NCHPEG has established. The first is the Family History Tool Working Group and what that group is doing is developing criteria for evaluation of existing family history tools. There are many of them out there. The question is how does one really decide which ones are worth using, which ones are effective.

The working group is establishing criteria for evaluating these various tools. Then it is also trying to develop a tool, which is appropriate to all disciplines for effectively and efficiently obtaining and transmitting family history; in other words, a universal kind of family history tool that could be used across disciplines.

The next working group, the Information Center Working Group, which Tim is one of the co-chairs for,

is developing information platforms for communicating about NCHPEG-related issues, both within and among member organizations and with external organizations and individuals, to let the world know what NCHPEG is about, not so much to publicize NCHPEG as to make the products of NCHPEG available to a wide variety of folk. It has a Web site, which is being sort of tweaked up in a major way this year at WWW.NCHPEG.ORG.

There is an Operations Working Group, which overseas governance issues for the organization and I am very happy to say is playing a key role in the present process, which is going on, of hiring NCHPEG's first executive director. Largely due to the funding from the RWJ Foundation, NCHPEG now is able to fund hiring a full time executive director.

There is an Education, Certification and Licensure Working Group, which is working to increase appropriate genetic content and certification and licensure examinations of all health professional disciplines, which is something I think this group is particularly interested in and we are particularly savvy about how difficult it might be to accomplish that. If you think within any one of these disciplines, whether you talk about medicine, nursing, occupational health or whatever, the idea of trying to really get pertinent and appropriate genetics content into licensure and certification examinations is a difficult task.

It is obviously very important, though, because as many of us know, part of what drives behavior in health care is licensure and certification. If one can get a high amount and a high quality of genetics content into licensure and certification exams, then we may find many curricula suddenly springing up to teach people those things they need to know to get licensed and certified.

There is a Core Competencies Working Group and this group has been working quite diligently over the last several years and has produced a set of core competencies in genetics that are felt to be central for all health professionals. I believe you received this morning a handout, which lists the core competencies, which I will speak a little bit about more in a moment. These core competencies have been endorsed by NCHPEG's Steering Committee and have been submitted for publication.

The core competencies are organized around knowledge, skills and attitudes. There are a large number of each. I would point out that in terms of the skill section, some of the skills that are listed are universal ones, which are felt to be necessary for anybody who is a health professional in 2000 and others are for those who would hold themselves out as providing genetic counseling services only.

So that there are different categories certainly of skills that are needed, we feel, and they vary by exactly how one is advertising one's skills. It does not say anything about what the different certification processes might be, which I know is an open issue at the moment, but talks really about competencies and which competencies are important.

As you can imagine, when you have many different disciplines trying to sign off on universal competencies, there is some great debate and discussion about are they too broad or are they too ambitious or are they not ambitious enough, et cetera, et cetera. But this is a core group that everyone felt eventually they could sign off on with the idea that it will be out there for various disciplines to modify and use in ways and probably change in ways that will be particularly relevant

to their disciplines. But we felt it was important to say no matter what one's expertise, training, licensure, et cetera, that if one is going to practice genetic medicine, there are certain kinds of knowledge, skills and attitudes that one needs to possess.

So that, I think, is a particularly beneficial product already from NCHPEG. So that is all I am going to say about NCHPEG right now. We can do more in the question and answer period.

Then let me say something quickly about Genetics Resources on the Web. Genetics Resources on the Web is a very different activity in some ways, though informed in several ways I think from our experience with NCHPEG. One of the ways we were informed by the experience with NCHPEG was to realize if you come up with an organization, you should think about the acronym before you come up with the organizational name. So, we came up with an acronym. We like GROW and then we figure out a name for it. So, it is Genetics Resources on the Web.

Now, the history of GROW is even briefer than the history of NCHPEG. This goes back all of less than a year, when there was a decision last year that there ought to be a one-day conference to bring together various groups that were interested in sort of human genetics on the Web. So, a conference was called -- actually people were invited last July and much to our surprise it turns out if you call a conference in July for the middle of August when you assume everyone is on vacation and you invite 26 different organizations to come to the conference, 28 of the 26 will show up.

So, it says something about everybody should schedule conferences in August because everyone you invite will show up, but even people you didn't invite will show up because nobody else has conferences in August.

At that conference, which was really just to bring together people for a one-day sort of session to talk about common issues and common interests, it seemed to work so well that in the afternoon the idea that this should become a kind of standing group was born. So, GROW was sometime in the afternoon, Francis just sort of announced there would be this organization called Genetics Resources on the Web and everybody that was there was welcome to keep coming.

GROW had its second meeting this March and will have its next meeting in November, all held at the NIH here.
The mission of GROW is to optimize utilization of the Web to provide health professionals and the public with high quality information about human genetics, especially those aspects of human genetics dealing with health.

Now, a logical question is why get another genetics organization. There are a plethora of them already. The reason for this organization, the reason for the original conference, really there are several reasons, but a key one was that the Web is, obviously, an increasingly important purveyor or human genetics information. So,, it has become increasing important to encourage that information on the Web about human genetics be of high quality and meet the needs of all users.

It was also recognized that many organizations have been devoting significant human and financial resources creating a human genetics presence on the Web and, therefore, there is a need to minimize unnecessary duplication of effort. That infers that there might be some necessary

duplication of effort, that having more than one thing on the Web about the same topic might actually be useful.

But on the other hand, having a thousand things on the Web about the same topic might not be. So that there was a need to minimize unnecessary duplication of effort for the sake of both the organizations that are making that effort and of the potentially confused poor Web user. There was also the recognition that there was a need for a forum to encourage sharing useful knowledge and also one that would foster collaborative efforts among the organizations mounting such Web sites.

Finally, there was a recognition that the pool of creators of quality content in human genetics, especially human medical genetics, is a rather limited pool and that for the sake of the folks in that pool, as well as for the sake of quality on the Web, one could only dip into the pool so many times. So, if there was a need to minimize unnecessary duplication of effort, both to make the people who could write this content be willing to continue to do so and also to make sure the content would be of high quality.

I would stress, as you might imagine, for a group that is less than a year old that this is clearly a work in progress and although I am going to tell you about GROW, it is clearly still being refined.

Now, GROW is a non-organization organization of organizations. You may wonder what I mean by that. I may wonder what I mean by that. What I mean by that is that there are no bylaws. Since there are no bylaws, there can be no officers. Since there are no officers, there can be no office. Because there is no office, there can't be a staff. Because there is no staff, there can't be any stationery. Because there is no stationery, there is no need for postage and because there is no postage, there is no need for a budget.

GROW is somewhat unusual in that all of these are true for it. It is really a kind of collaborative -- it is a little bit like -- I think, like Mickey Rooney and Judy Garland meet genetics on the Web. We are all going to get together and camp out together and see what we can do. In fact, it has worked about as -- better probably than MGM musicals, I think.

There are several type of participant organizations within GROW and, roughly -- though several of these organizations really wear more than one hat, they are site providers; that is, they are organizations whose Web sites contain significant quality educational content about human genetics. GROW does not intend at this point to really include organizations that have huge Web sites, of which, you know, they sort of mention genetics, but Web sites, whether they be huge or small, that have a fair bit of content about human genetics.

There also are some organizations involved that are content providers. That is national organizations who represent membership, who create quality Web content in human genetics. So, whether they have Web sites that have a lot of information on them or not, it is obvious that, for instance, the International Society of Nurses in Genetics should be at the table, so that various kinds of organizations representing content providers.

Then, finally, support providers, federal and philanthropic organizations, who have a demonstrated history of support of human genetics. In terms of what that means at the first couple of GROW

meetings -- there are a couple of slides here, I will show you, just a list of the GROW participants.

You will see there are several dozen and they are a fairly wide swath of types of organizations. To achieve the mission that we talked about before, GROW's specific goals at this point are to create and maintain a Web site, whose search engine searches effectively across all GROW participant sites. I will come back to that concept in a moment, to help determine user needs and encourage individual organizations and collaborative approaches to meet them; so, to figure out what is it that users or potential users of the Web in terms of human genetics, what are their needs and are those needs truly being met and also to foster communication among participant organizations through periodic conferences and e-mail-based list serve and other useful means.

There are a couple of working groups that GROW has established and that have been functioning since last year, a Search Working Group and an Assessment Working Group and, again, I think that is probably the best way to tell you something about what the organization is actually accomplishing.

The Search Working Group is providing guidance for making GROW participant organizations' Web sites more visible in external search engines. One of the questions was, you know, most people that use the Web, they go to Yahoo or some such search -- some of them are search engines, others are portals, et cetera, et cetera -- and then type in something about genetics. It turns out that there are some technical things one can do to tweak your site to make it more prominent on these kinds of search engines.

So, part of what the Search Working Group is doing is simply providing some technical expertise to various organizations within GROW, to help them make themselves more prominent on such external search engines.

Then also, I think, importantly, in some ways perhaps more importantly, the group is working to develop an effective GROW-based search engine that would search simultaneously across all participant sites, the idea being that if we have several dozen organizations that have sites that we recognize as having quality content in genetics, wouldn't it be wonderful to be able to go to a specific search engine that searches those sites and those sites only, that one could type in whether it be Hirschsprung disease or colon cancer, whatever, and see what the Genetic Alliance, what the CDC, what all the different groups represented here have on their sites about this, sort of a one-stop shopping for information about human genetics.

There is a beta version of that, which is being worked on and I think that our hope is that sometime this year, that will be available to the public and will be quite helpful. There are a lot of design questions involved here. One of them, for instance, is do you design it so that it is somewhat specific to the user? That is, ideally you might have a search engine, which works somewhat differently if you told it I am a high school student trying to do a paper about Hirschsprung disease versus if you are a primary care provider wanting some information about Hirschsprung disease versus if you are a geneticist wanting some specific information that the search might do different things for you.

Our hope is eventually to have it that kind -- to allow that kind of search. The Assessment Working Group is developing guidelines or minimal standards or some other tools for evaluation of participant

sites, to help the participant sites really figure is our site working. How do we know that? Is it doing a good job of what it is trying to do?

Also, to help GROW recognize, well, gee, what kinds of sites are doing a good job, what kinds of sites should be involved in this GROW search engine, for instance. And there are various kinds of standards that one can use. If you want more detail about that, I will be happy to talk with you about it during the Q&A session.

Finally, the Assessment Working Group is also identifying unmet needs of potential users. We are really trying to look at what is out there on the Web at present. What are the needs of various kinds of potential users? So, to try to find those niches, which have not been occupied yet so that individual organizations or perhaps collaborations of organizations within GROW or elsewhere might be able to need those needs.

Other GROW activities include twice-yearly meetings held at the NIH, which include presentation of Web sites, discussion of issues of common concern, informal networking opportunities and simply further defining what exactly GROW is and should be. Then there is a list serve amongst members to facilitate communication.

The near future for GROW, GROW is coming to grips with exactly defining membership criteria, participant criteria, however one wants to label it. There has been discussion about whether for profit and not for profit should coexist equally in this organization or how that might work, those kinds of questions. Getting the search engine launched sometime this year, welcoming appropriate new organizations, yet trying to remain informal and functional.

One of our concerns for GROW is that it has worked very well, having several dozen organizations and if suddenly the number were to double, for instance, how do you really have sort of cordial, informal conference amongst those groups. The near future otherwise, I think, is still undefined and being developed as we speak.

So, I think that is it and we are on to the roundtable, if I understand.

DR. McCABE: Thank you, Alan.

Could all of the presenters from this morning come to the front of the room, please, and cluster around the mikes there, so that we can have the roundtable discussion.

While you are gathering, I will start off with a couple of points. That is I think it was at our first meeting, Elliott Hillback suggested that the major service that we could perform in this arena, looking at strategic planning, would be to serve as a catalyst and I think the term was to "convene a summit" of the various organizations working on education to evaluate a broad level of activity here and, perhaps, to outline some sort of grand plan.

It looks like a lot of stuff is going on, but it has not really been brought together by any overarching group. So, I wanted to go back, since that had been raised before by Elliott, remind everyone of his comments and start off the discussion with consideration of a way of trying to get everyone together,

but also trying to see if one could develop a grander plan rather than just a meeting.

Any thoughts on that? Elliott?

MR. HILLBACK: I think one of the frustrations that those of us in industry have tried to deal with is to look at the other part of the whole approach of delivering better health care and running labs, we interface with a lot of physicians who are frustrated by their own lack of knowledge. So, we raised the issue early on of how do we look at the whole system and not just look at one part of it in labs, but look at the whole system and figure out how we improve it.

A number of us have been involved with various programs. AMA put on some programs and I was invited to go teach and enjoyed that, but they had a hard time getting anybody to come. This was a meeting in New Orleans a few years ago. So, in discussing with many of the people at the table, I think there is a lot of frustration that everybody or a lot of people perceive the need, but getting it moving has been somewhat difficult.

So, there are a lot of interesting programs here and I would love to just hear whether the group that is here feels that their frustration level is going down and whether we have momentum or not. From that, I am sure we will get an interesting discussion going.

DR. McCABE: Anyone from the roundtable have any comments on that?

DR. BURKE: I actually think the issue of what I call buy-in, discussion, dialogue, is extremely important. I think there may be some encouraging signs. Media hype does drive things to some extent. For example, at the GPC presentations at annual meetings for family medicine and general internal medicine this past spring, there was intense interest in our general internal medicine meeting. It was a standing room only kind of presentation. That may be an indicator that things are starting to get on the radar screen.

But, to me, this speaks to a tremendous need for dialogue, rather than the genetics community sort of speaking at other communities and saying here is what you need to know, here is what you need to think about. In fact, it is a joint problem-solving exercise. A huge bolus of technology is rolling our way and there needs to be a sort of collaborative discussion.

So, my sense is that one of the most important things we can do now is identify stakeholders and figure out how to have those collaborative discussions that figure out joint solutions.

DR. GUTTMACHER: I think Wylie really made the points that I particularly wanted to make. I might just elaborate on them a bit because I completely agree with her. I think the buy-in is a very important question. That was really, I think, the frustration that Elliott was primarily speaking about.

I, too, see some changes of that in the last couple of years. I think part of it has to do with things being more prominent in the media. Part of it has to do with health professionals being occasionally driven by embarrassment, not wanting the patients to come in asking questions that they can't answer and partly because health care providers want to do the right thing.
And I think that we have for some years found with trying to integrate genetics into a wider array of

health care providers, some frustration on the part of providers about don't teach me stuff about, you know, in ten years, is it really going to be helpful, et cetera, et cetera. I want things that are going to change the way I practice tomorrow morning when I walk into work.

We now are at the point where we are beginning to have those kinds of deliverables and I think health care providers are sensing that so that there now really is more of the buy-in, I think partly because of that.

I think there is also the question about once we have that buy-in, how do we do all of this, which can be a frustration. I think many of us feel we have sort of a window of opportunity here where we are beginning to get the buy-in. We have some deliverables we can provide, but also that we have a little bit of time until this really hits clinical care in the huge way it will within a few years so that the next few years are key in this.

And I think the fact that we are seeing many different kinds of efforts is really pretty good because it is not going to be one size fits all, one national program that is going to educate health professionals or the public about genetics. It needs to be a multi-pronged, I think, sort of grass roots approach that, you know, we hit people with this in many different ways and many different places, whether they be providers or consumers or health care.

I think that we are beginning to do a fairly good job of that, but clearly we need to be spending more time and resources doing that.

DR. TUCKSON: I just want to ask you and others of you as you make your comments on this window. You are saying there is a window for a few years before it hits clinical care, but all the discussion we had yesterday and are having about the introduction of new genetic tests, it seems to me that the window is already there. I just wonder -- or am I --

DR. GUTTMACHER: No, I was trying to say that there is a window, I think, until it hits it big time. It is hitting it somewhat now. No question that it is hitting it now. I think it is, but different areas of medicine -- clearly, in oncology, it has hit it much more quickly, sooner than it has in, for instance, heart disease, but in primary care it is making more and more inroads all the time.

DR. PURYEAR: I just want to emphasize one point that Alan made and that I was going to make in terms of grass roots involvement. The success of the -- and I am highlighting the Genetics in Primary Care project because I think that is where certainly our bureau has done the most work. That came after a lot of work. We had a series and NIH did, too, a series of projects that focused on primary care providers, both nurses and physicians. But then, again, we also had a meeting on -- this was done with the help of -- I mean, this became the entry point of the Bureau of Health Professions bringing together all residency directors, deans, from across the country. Francis Collins came and spoke.

That group came -- some of them came kicking and screaming to that first meeting and, you know, wanted nothing to do with genetics, not understanding the importance of it. But even so, made recommendations that allow us to go on with the Genetics in Primary Care project. So, I think it is nothing -- I mean, I think part of the problem with the AMA meeting was it was geneticists speaking to instead of having some of that coming up from the grass roots or being recognized by primary care

physicians and looking at genetics through a primary care lens.
That is certainly what we have been trying to achieve within the Genetics in Primary Care project.

DR. WEITZEL: Well, I can certainly speak from the perspective of oncology and I share Alan's comment that it has already hit oncology by storm in many ways. I think the interest in the curriculums that we have been offering has been self-sufficient or self-evident and we have had, like I said, standing room only crowds at each of the last two annual meetings and the curriculum, which surprised all of us -- we had a very good group of people put it together and it sold a thousand copies. Many of them have gone to training programs around the country because it really covered the whole waterfront; cancer genetics being just the front of adult onset disorders, partially penetrant.

All of the complexities that we are going to have to deal with as we go forward are really front and center with cancer immediately. So, we are going to learn a lot from this process, I think, beginning. But there is an interest and the efforts of the Maternal and Child Health Bureau and others to educate primary care physicians -- and I sometimes include oncologists in that realm and one could contest that, but often times a cancer patient's last physician is an oncologist, unfortunately.

So, we often have a huge intro into families and families where cancer risk is an issue, but certainly there has been interest and an effort in all of the individuals in the oncology community who practice cancer genetics have essentially done, like the GROW opportunity -- we came together as a loose coalition to begin with. We are formalized as an ad hoc task force. I know that ASCO intends to give us permanent committee status shortly. So, as a professional society, they clearly have roles in this regard, too.

DR. KHOURY: Actually, I would like to amplify on some of the themes I heard this morning.

I guess maybe just to reiterate some of what I heard and maybe I will throw this for discussion. The theme that came around many, many times from Wylie and Dr. Weitzel and Tim and others is that when there is this intersection between genetics and whatever group you are talking to, be it oncologists, primary care providers or public health people, it seems to me that the best way to get at that group is to talk their own language.

So, for public health we start with the wheel, the public health essential services, with primary care physicians, what they do the most, and I guess the thing that struck me is that that theme is so recurring, that unless you have that dialogue, starting where people are, you are not going to break the new ground, basically talking at them versus with them and trying to lead them gently.

I think that underlines what Alan said about the relevance of, you know, you come and teach me -- and we have done that at CDC, multiple times. We have gone to epidemiologists or health departments and talked to them. They go back to their own business basically because they don't see the relevance of what they can tomorrow morning when they wake up and go to work.

I think this august body here can really make some good recommendations for all these groups and come up with a sort of a grand plan of action or recommendations to HHS to begin that process of integration.

I just want to elaborate on two themes that struck me, which I have said before in multiple settings. The emphasis on single gene disorders, which is sort of the traditional mantra of medical genetics, is now expanding so much that I don't know how much of the current efforts that are being presented around the table go beyond the single gene genetics disease model to the use of genetic information, which includes pharmacogenomics, includes a number of multi-gene things, along with environmental factors, which leads me to the thing that I suggested to some groups before.

We are not talking about medical genetics anymore or public health genetics. We are talking about genetics in medicine or genetics in public health. I even suggested to the American College of Medical Genetics they change their name to the American College of Genetics in Medicine at one of the meetings.

So, integration is a two-way street, but you have to start where people are and I guess the question I have for people around the table is how much efforts are going on to go beyond the traditional world of genetic disease into genetic information and how genetic information can be useful to cancer or the primary care or public health professionals?

DR. McCABE: Anybody from the panel which to respond to that?

DR. PURYEAR: How relevant what Muin -- to talk about the relevance, what Muin said, to actual primary care organizations it is -- after Dr. Weitzel, after Jeffrey speaks, if Norman or Gene could speak to what Muin said.

DR. McCABE: There is a mike in the audience you can use.

DR. WEITZEL: Well, certainly I presented partly in my presentation the issue that, for example, what I call somatic genetics, acquired genetic changes is already being used in clinical perspective, the concept that deletions of the long arm of chromosome 18 have prognostic value in colorectal cancer was published in The New England Journal several years ago. It is actually out there available as a diagnostic test from Lab Corps and individuals were using it, some incorporating it into their practice, the idea of using micro-satellite instability as a marker of prognosis is there.

Her2/neu, as I mentioned, is already -- it is part of the -- in fact, there are debates about the best measurement for it and it is part of the vernacular. So, we are already having to deal with it at the level of clinicians and to teach them about that. I think that this isn't something that we are -- we are looking forward to it, of course, but it is already here in some ways. I don't think drug resistance has reached that realm quite yet in terms of common parlance. But, clearly, these others are. So, oncology is dealing with that now, in addition to the single gene trait diseases.

I think the limitation of most of the complex genetics is the practical value of the advice that you might give an individual. Even if you find a moderate risk gene that has a two-fold risk, how does that meaningfully impact on somebody's decisions about prevention or care? That is the most difficult part is integrating those things into care in a way that makes sense from a practical perspective.

DR. McCABE: We will have comments from the audience then, please.

DR. RICH: Gene Rich. I am from the Genetics in Primary Care project.

As I have gotten involved in this, I have come both from the perspective of a general internist, who spent 15 years being a general internist in academic health centers and now five years as chair of a department of medicine, chairman of a department of medicine actually at a school that has quite a history with respect to medical genetics with Creighton University and Henry DeLinch [ph], and now considerable work being done in the genetics of osteoporosis by Haney Recker [ph], et al.

For those folks that are coming from the genetics perspective, I have emphasized repeatedly and I think the last speaker pointed out the importance of being -- of understanding the perspective of the health professionals. I have emphasized repeatedly that academic primary care professionals, particularly general internists in departments of medicine, have become sensitized to being repeatedly lectured to by the specialist of the day regarding their inadequacies in that particular area of pathophysiology.

We have observed with increasing cynicism over 20 years the emergence and then decline of fear boutiques at our academic health centers, where we would have the TMJ clinic or the Alzheimer's clinic or the prostate clinic or the chest pain center and this would be the popular concern of the day with a specialist, who has deployed resources to try to attract patients for that.

Clearly -- and this group recognizes genetics does not represent that kind of advance, that it does not represent a transient opportunity for specialists to carve out a piece of the curriculum that will then be pushed aside by another specialized interest carving out a piece of their curriculum. This represents a fundamental change in our understanding of human biology and the application of biomedical science at the bedside.

I think, therefore, it remains extraordinarily important for the scientists to be working carefully with the specific health professional disciplines in working with clinician educators in those disciplines to specify exactly how this remarkable advance in our understanding of human biology should be applied in those particular clinical settings.

DR. KAHN: Representing Genetics in Primary Care project, it is going to be easy for me to support what Dr. Rich had to say. I will be brief.

It is also easy to support what Muin brought up. That is basically what we are about. We are not about trying to create a workforce of medical geneticists, not that that isn't necessary and valuable to the overall scope of medicine, but what we are talking about is integrating genetics into the practice of medicine, into the primary care practice of medicine.

We anticipate that the genetics revolution is going to be every bit as big as the antibiotic revolution. Francis Collins has a great comment that all of you know that with the possible exception of trauma, everything is related to genetics. Therefore, everything that a primary care physician is going to do is going to be related to genetics. That is really what this project is, a demonstration project, a start, and we certainly hope that there will be more like it to help us integrate genetics into the practice of clinical medicine, particularly at the primary care interface.

DR. McCABE: Kathleen.

DR. REED: Just some observations and comments. I think it is directed mainly toward something that Wylie brought up, a question, and that was you mentioned the aspect of primary care on one end and genetics on the other and the exchange of information beginning.

How much work has gone into leap frogging over that so that the recruitment process is really bundled. In other words, there is a packaging that goes on to bring that information so that it is not just being integrated, that it is actually being presented as a bundled package. That is one aspect.

The other is I heard a dyad, I heard the linkage between genetics counselors and primary care physicians. What I am not hearing is the emphasis on lay informants, what we would call lay informants within the community. I bring that up because there is enough time, ahead of the curve, to integrate public members in communities, who have an incredible amount of information, who at some point downstream are going to have to come in because of the training for genetic counselors.

Many of the genetic counselors of the future are not going to come out of the scientific community, as much as they are going to come out of the community into genetics to be trained. I bring that because there are family designated archivists, genealogists and what is referred to in term of art as keepers of the family line. So, I am asking if there can be at least a thought about in this education model, a triad, which is the genetic counselor per se, the primary care physician, but also community lay informants that may be brought into the process.

Again, I know it is early, but I bring that up because at some point downstream, it will be there.

DR. BURKE: Thanks very much for those comments.

I want to say first of all that the idea of bundling, if I am understanding what you are saying what you are saying correctly, is a very important one and it is one of the reasons that we in our RFA have asked that respondents to the RFA bring in a team. That team -- one of the things we are looking for in our teams is already a collaborative relationship that exists and can be built upon in order to create a sort of comprehensive approach to education.

The second point that you make, I think, is an extremely important one and one that we have had a little bit of discussion with, particularly with representatives of the Genetics Alliance, that is the potential that there are individuals from the community, representatives from the community, who might be a tremendous -- play a tremendous role in the education process. We have had a little bit of discussion. I think we need to have more about -- in the process of identifying local resources, that those local resources are not only genetics expertise, but they are also advocacy organizations and others who can speak to the need of diverse communities.

What I think you are also referring to, which I think is a tremendously important point, is that as one interacts with families and sometimes with communities representing certain disease burdens within a community or certain community interests, that is part of good health care delivery is being sensitive to the needs of the family and interacting with the family.

That is certainly something that has received some discussion, can always receive more discussion.

DR. REED: Let me close by simply saying this. I have brought this issue up with one particular organization, just to bring, you know -- and others, but, for instance, there is an African American Historical and Genealogical Society. They really know where the folks are and they already deal with pedigrees.

So, the issue of interest in some of the people going back to be trained and knowing the sort of insiders' role, they are very much interested, but that kind of linkage is the bridgework that if that contribution can be made to identify, also bridge people, people who can come into this room and feel comfortable, but can go into communities and feel comfortable and go back and forth, if we can identify those people as well, then much work can be done.

Thank you.

DR. McCABE: Tim, you wanted to follow up on that?

MR. BAKER: Obviously, that is one of the things very close to the heart of public health as we develop and mobilize the community in state-centered capacity. Through the years of working on HIV programs, preventable disease and working within communities and through communities, that is one of the core areas.
I think emphasizing the importance of the complementary nature of many of the programs we are talking about here, because that is an audience, it is a part of the audience that we in public health are trying to address that complements the clinical medical specialty and the primary care role here.

It is, as Kathleen knows, best done by the people in the community that know the community. How do we share the body of knowledge we are talking about in a way that is relevant to the care provider and that gets in the proper dose to that community leader so they can validate it, first of all, second of all, get it to people in a way they can use it.

That is this whole evolving notion of what we know and don't know that we deliver through these various channels. I am glad to say with Alan and -- you know, we talk a lot in GROW and NCHPEG and various technologies about how do we develop a common information system and set of resources that we all share and then we utilize the strength here of the various organizations and professional community leadership to get that content out of those systems and into those delivery channels so they can get to the people who can use it.

DR. McCABE: Alan, you wanted to follow up on that?

DR. GUTTMACHER: I think I want to follow up on a couple of things that have been said. One is to make explicit, as a card carrying medical geneticist, make explicit something that might have been implicit in what is being said by several of us, which is we engage in this dialogue and when one goes to talk to primary care groups, for instance, the idea of not saying something, but there is dialogue there. It is not just to the primary care groups, but to medical genetics and I very much appreciated Wylie's group of a couple of slides that talked about primary care looking through a genetics lens

because we really are talking about thinking genetically. That is what we are talking about.

That is so important, but it is also important and makes medical genetics so much better to learn to look through these different lenses. It has been a fascinating -- again, Wylie brought up the question about these different cultures intermingling. It has been fascinating -- cancer genetics, since that has been the one place where maybe genetics has been integrated the most -- to see these two different cultures. I mean, within medicine, there may be two cultures that are no more different than the clinical oncologist and the medical geneticist.

To see these two groups work together, they really both learned, I think, a lot from each other and this dialogue, I think, just to make it explicit, works both ways.
I would also want to point out one thing. What we are discussing, you know, I am very appreciative of the fact that the title of this is the SACGT, that it is not the Secretary's Advisory Committee on Genetics but the Secretary's Advisory Committee on Genetic Testing.

At the same time, I would like to make explicit, which, again, I think is sort of implicit here is that, you know, genetic testing is kind of the stalking horse in some ways for medical genetics. It is the nose that is getting under the tent kind of thing. If we talk about those kinds of things that encourage health care providers to want to know about genetics, genetic testing is one of the driving forces behind that because when they think about what am I going to start using, what do patients start asking me about, it often is genetic testing. So, I think that the degree that we can use genetic testing as a way to sort of encourage people to think about wider and other applications for genetics, that is very important.

We are still challenged, though, with the question of the provider saying, well, this genetic testing stuff is great, but tell me how it is really going to impact what I do in the office tomorrow. Why am I going to do this genetic test, et cetera, et cetera, not only how, and they often, unfortunately, don't think about the question about how am I going to do it, but that is obviously, a chance to talk about that as well.

DR. LANIER: This was suggested in some of the comments that were made this morning, but I wanted a little more discussion about the fact that there are at least two groups of clinicians who are out there in primary care. One group are the people that are in training or in school currently, that I think these curriculums would reach most easily, but then there is another group of people that are beyond that formal phase of their training, who are in practice, who may be more difficult to reach. I think even with that second group, there are subgroups of people who are seekers of knowledge, who clearly believe in evidence-based medicine, and continually improving themselves.

They will be the easier people to reach in terms of the curriculum that you are developing. But how do we get at these groups of people who it is not through lack of interest. It is that they are overwhelmed by the body of work there is to be done on a day-to-day basis. How do you get an awareness, an increased knowledge among those people, who perhaps are at least as important as any other group?

DR. McCABE: Alan.

DR. GUTTMACHER: I think it is a very important question, but actually I disagree with you in that I

think it is more difficult to get it into undergraduate medical curricula, for instance, and undergraduate nursing curricula, et cetera, than it is to the folks out in the field because I think the folks out in the field are beginning to get some appreciation of how important this is. When you think about it, a lot of the efforts we are talking about are for training those people already out in practice.

It has, in fact, I think, somewhat surprisingly, perhaps, proved more difficult so far to really get this into the curricula of professional training schools and that is because deans, et cetera, are so used to being barraged all the time by everybody saying, you know, this is the era of infectious disease, this is the era of immunology, this is the era of whatever and so what, genetics, you know.

So, I think that it is difficult to get into each of those and requires a sort of different strategy in some ways, but I think if anything we have more effective models so far at integrating into the education in terms of continuing education, rather than education in professional schools. There obviously are exceptions to that, but it is a challenge in each area.
DR. McCABE: Jeff, can you comment briefly and then we are going to move on.

DR. WEITZEL: Sure. Just the comment that actually our patients are driving the clinicians to learn. They come in so well-informed or misinformed from the Internet, from other sources of information, from the media, that they are, in fact, asking their physicians about this. I think the major barriers I see is I have had many clinicians say don't get genetic testing because you are going to lose your insurance. You have heard that theme before. That is in spite of the health insurance -- you know, a number of acts that are out there. So, I think there are a number of issues that become barriers, but our patients help to drive the clinicians to the table and there has been a surprising amount of interest among them.

DR. CHARACHE: I wanted to ask about the issue that Alan Guttmacher just touched on, which is moving back one step and getting into the area of medical education.

I wondered what groups are doing in terms of developing teaching models that can be adapted. As an example, in year two, the students walk through pathophysiology and pathology by body system and they get infection in every body system they come to. I don't know why they can't get myocardiopathy when they hit the heart and hemochromatosis when they hit the liver and make this an integral part of the medical education process.

I am wondering what approaches are being used by the groups thinking of modeling, to develop strategies that can introduce this into medical schools?

DR. KAHN: I think that I may help a little bit in this area. We have just announced a contract to develop a resource manual for -- a faculty resource manual for the development of curriculum. One of the areas we have asked the contractor to look at is genetics. We have listed a number of other areas as well.

But this will be across the four years of family medicine education and often in many schools of medicine, family medicine is the provider of the first and second year. Along with that, we have asked that the Ambulatory Pediatric Association and the Society of General Internal Medicine work with that group so that there will be a primary care approach to the genetics information in the early

years of the curriculum.

I can't tell you how it is going to turn out yet, but at least it is an effort and we are hoping that this faculty development along side it is -- those two things will work together.

DR. WEISS: I would also like to agree with Dr. Guttmacher from a nursing perspective. The deans are absolutely overwhelmed with the amount of new information they have to include in undergraduate and graduate curricula. Once you have the buy-in of the deans, you also -- it would be easier if you had the accrediting bodies also have genetics as one of their criteria.

In addition, you need to have the licensing bodies buy-in because it -- this content if not being included on the examination the graduates are taking, there is not as much concern to have it into the curriculum. So, it is really a three-pronged edge here. You need to have the licensing bodies. You need to have the accrediting bodies and you need to have the deans.

You also need to have the faculty because not all faculty have expertise in genetics. They may know their area that they teach very, very well, but they have to go that one step beyond to become competent in genetics in the courses that they teach.
All of it is a very complicated problem here. Also, with the nursing community, this is what we hope to start to look at in September when we have our genetics conference and then maybe come up with some ways to help faculty and deans begin to integrate content into curriculum.

DR. BOUGHMAN: There is hope. The AAMC, in fact, at their conference in the spring spent some time on genetics across the curriculum, not unlike infectious disease. Some of us have been hanging out that window of opportunity for a long time and Jim Hanson may have been hanging out there longer than I have, but after having chaired the first conference for the Genetics Services Branch on genetics in nursing and social work education in 1978, we -- what goes around comes around, I guess -- I would like to focus us for just a minute on what we, the SACGT, need to do, like what is our task here.

But I would like to capitalize on the way Ed started remembering Elliott's comments at our very first meeting and I would suggest for your thought, at least, over lunch or whatever, that we might take a comprehensive strategic plan type approach to this report, if you will.

I have been involved in a recent very comprehensive strategic planning process and I think this model might work, where we have an introduction that talks a little bit about some issues in the literature. And then the needs and the current programs are merely mentioned, but, in fact, included as appendices each in a one page summary background paper, if you will, or we could make it two pages, but that the body of our report take a strategic planning approach that would have major goals, each goal with objectives and possible strategies that the Secretary might consider.

I am hearing several other things that I have been jotting down here. One of the areas of major goal would be the genetics training in health care professionals at the curricular level and then during the professional training CME workshops and so on, the actual increasing of the genetics workforce itself, in other words, programs, fellowships, the full-blown genetics professionals, the building of additional interdisciplinary efforts, both based on Wylie's conversational and buy-in emphasis, as well as formal

programs out there and then the development of public educational models, including the buy-in of the lay informants and the alliance and others, just some of the major areas that from this comprehensive plan would be the overarching goals and then we could address them in objectives and strategies.

DR. McCABE: So, what you are proposing, Joann, is that we begin to think about another task beyond the one that we will complete today and finish up and have to Dr. Satcher within the next two weeks or so.

DR. BOUGHMAN: That is right. This would be like the next step, but the activities that I have been involved in recently in the State of Maryland, a slightly different level, at least that I am used to, where you gather background, these very short background papers that address an issue or a needs assessment or whatever, would allow the committee to, in fact, garner in a formal way some of the summaries that we have heard today. We could acknowledge some of these programs that are started but then in our assessment and our comments we could add weight or oomph to some of these and focus for the Secretary.

We could have members of our audience and other interested parties that wanted to follow this format, we then could vet these papers and these short summaries and, in fact, get some of these really important concepts incorporated into this report that, in fact, I think is our next task.

DR. TUCKSON: Actually, that is a -- Joann really has gotten to where I wanted to go, but before I can get there, I need to ask the panelists to help us. I mean, you have each made very good and really appreciated presentations. I need you to step back away from the work that you are proud of and those of you in government, we need to -- on behalf of the Secretary, since we are the committee advising her -- deputize -- immunize you from the narrow confines of your reporting structure, your command and control structure, to ask you is there a crisis in this training of health professionals at this moment, given the realities of the window, however you assess it, that requires governmental leadership at this moment, action by the Secretary that we ought to recommend or are you comfortable that the work that you are doing and the collaborations that you see in the private sector and in the public/private collaborations that you are a part of, is it handling the problem?

So, before I can get to Joann's point, I need to know from you is there a problem that we ought to prominently say to the Secretary, you have to take leadership and deal with this or is it being handled okay and are you comfortable?

DR. McCABE: And I would ask you to be brief because we are going to need to wrap this up soon.

DR. PURYEAR: Yes. There is and I alluded to it actually. For instance, the head of our agency, Dr. Earl Fox, actually has proclaimed for fiscal year 2002 that genetics is an important and emerging issue and it is one of his budget priorities. However, at the same time, the Department doesn't recognize that. When I said that for fiscal year 2001, the health professions budget has been zeroed out for primary care in nursing, I mean, that is dramatic and those funds that we have been using to do this small Genetics in Primary Care project are being threatened.

I mean, to even think about expanding that and doing the kind of -- if you look at the example of HIV,

where there was a huge concerted effort to educate the health care professionals and there was a significant amount of funds that were directed towards that. We don't even have anything equaling that. So, that is just with primary care.

If you go -- when I said there were very few funds for allied health professions and public health professions and it is even more dramatic there, because to be able to even specifically target special kinds of competencies, those professions depend very much on federal funding, compared to nursing and primary care, you know, it is even less money.

So, there is a great deal of need and especially when you compare it to -- and I am sorry, NIH -- when you compared it to the amount of money that we have given to research, the amount of money that we are giving to educate the public, because that needs to be part of this, and to educate providers is just a drop in the bucket.

DR. McCABE: Wylie, Joan and Tim and then we are going to have to wrap it up.

DR. BURKE: I will speak both as a member of the panel involved in some of these educational activities and as a member of the committee.

I don't think we have a crisis, but I think we will have a crisis. We have a huge amount -- we know there is an expanding amount of genetic technology coming toward providers. That technology is going to offer many testing opportunities, so focusing on our role in genetic testing. And, quite frankly, some of those testing opportunities are going to be good and some of them are going to be bad.

Some of them are going to have very narrow applications of great value, but if expanded to broader applications would lose their value or potentially cause harm. I think it is an important element of the translational process to have an educated health professional group that is able to make those distinctions independently. That is, we will certainly take advantage of consultation from a genetics community but have enough understanding of those issues to be able to make good judgments in the initial sort of triage phase of the process.

It is a -- like any other new technology, a huge technology, the providers need to be prepared for it.

DR. WEISS: The Bureau of Health Professions has identified genetics as a priority and the Division of Nursing has also identified genetics as a priority going with this initiative. It really is important for nursing because there is little or not genetics content in curriculum on an undergraduate or a graduate level. With everyone in education feeling overwhelmed, many faculty have teaching responsibilities, practice responsibilities and research responsibilities. They need to start someplace and, hopefully, we will be able to help them with our initiative. But, yes, it really is crisis level for nursing.

DR. McCABE: Tim, you will have the last word on this.

MR. BAKER: I like that.

Is there an urgency? Yes. There is a definite urgency in public health. The question is what is the

scope and the current status of that urgency. It is an evolving need. The challenge we have been trying to meet initially I would characterize as an awareness raising, reaching all the audience and say get ready. We have to have a set of competencies of just take the initial knowledge, but get ready for the more knowledge as you engage in all these various competing priorities.

You heard some of the discussion I had about other training activities and there is bioterrorism and a variety of things are hitting the various audiences we represent as public health. What is your next stick. Get ready for that and then we are trying to build that knowledge.

The laboratorian, the Maternal and Child Health director, says I got it. Give me as much training as I possibly can get because I know I have got to get ready for it. The environmental health directors are saying why are you bothering me, you know. And then we start talking about asthma and how might this be useful in asthma programs in the future and they say okay, now I will sit down at your table. That is the kind of level we are at. We have no reason -- if we want to start comparing resources, we have got no resources. So, we have to get serious about modulating this in a way we can ramp it up as this knowledge becomes available for these different audiences in a way that is sustainable and takes advantage of everything we are doing here to build, as you know, the public health community to be a resource to everyone else.

DR. McCABE: Thank you very much.

I want to thank Michele for organizing this and thank you very much to the panel. I apologize. I had a list of members of the committee, but if we want to eat lunch, we need to move on.

Perhaps we will have some additional time to discuss this later in our meeting.

It sounds to me, though, that there has been a proposal that this be one of our next tasks. I know that Elliott had said from the outset that education was one of our primary goals. It sounds like Reed endorsed this and I am seeing a lot of shakes of the head around the table.

The structure that Joann proposed is one that we could discuss later in the meeting as a way to progress with this, but I think --

DR. TUCKSON: Ed, I am not sure that -- by the way, I think I have endorsed it. I think what I am sort -- what I am trying to figure out is -- and we can -- as we discuss it later is what is the role that we are calling for for the Secretary versus what is the role for the private sector or do we call for the Secretary to have the private sector start taking care of business.

DR. McCABE: Well, I think that one of the things that we have heard is that in the overall scheme of things within HHS, education is an area that has not prospered. At least if we can move that forward and increase -- even if it is not at an emergent level immediately, propose that we need to put a structure in place to deal with it so that it doesn't become an emergent problem.

Elliott, did you have a comment?

MR. HILLBACK: I just want to make the additional comment that as we go forward, I hope we don't

just consider the medical community, but I believe the public education is one that we have to deal with because it -- the mistakes, the errors, the fear -- the word "fear" is a real word out there and I think we have an opportunity to try and limit that and it helps the whole system. Again, as long as we can help the whole system, I think that is what we are here to do.

I just want to make it is different to some degree than the practitioners, but it is a similar, related problem.

DR. McCABE: Well, we may want to involve some of the foundations because the March of Dimes, some of the other foundations are very involved in public education as well. We will need to discuss later whether we are going to keep those separate, which I think would be an artificial separation or bring them together.

I also want to be sure that we do not short change the public comment because that is a very important part of this meeting. Signed up for public comment today, we have Sharon Robinson, who is the administrator for the American Board of Medical Genetics. She runs the American Board of Medical Genetics, but I am not sure what her title is. Sharon has asked to comment.

MS. ROBINSON: Hi. I have never done this before, so I am a little nervous. So, bear with me.

First, I want to make reference to a letter from Haig Kazazian [ph] that was in your blue folders. It was addressed to the American Board of Internal Medicine, Dr. Steven Wasserman, that presents the formal ABMG position for the certification of clinical cancer geneticists. We want to make the following points.

It is not the training and the education of the non-geneticists in cancer genetics information that we are objecting to. ABMG as a board is addressing board certification issues and related program accreditation. Many geneticists are involved in a variety of training programs and it is the claim to certification that ABMG clearly objects to because we feel it will confuse the patients.

I can read excerpts from the letter, but you all have the letter in front of you. So, if you have any questions for me, I would be glad to answer them.

DR. McCABE: Any questions for Sharon?

[No response.]

Thank you very much.

Do we have any others who would like to comment or raise questions?

Yes. Please identify yourself.

MS. ESTERBROOKS: I am Susan Esterbrooks [ph]. I am a genetic counselor. I work for the Center for Human Genetics at Duke. I really enjoyed listening to the talks today about moving education of primary care providers in genetics.

As a genetic counselor, one of our largest roles is as patient advocate, and we like to see our patients getting appropriate genetic services. One of the things that I was picking up and gathering a picture of what genetic counselors do from listening to the talks, though, seemed to be very defined to me. It seemed to be genetic counselors are the prenatal counselors. They work in genetics clinics. They help with pediatrics and it is a very defined role.

Then you are talking about primary care and you are talking about providing genetic counseling services and making sure that the social issues and the non-directive counseling and all that is addressed in primary care and I feel like you have a population of professionals that is already trained in that particular area that is willing to move into that area.

We have gradually expanded ourselves into cancer genetics, into other specialties as the need became available. Clearly, from what everyone is talking about here, the need for genetic services in the primary care setting is clearly established from all those talks today. I want to urge you to maybe increase some funding to transition genetic counselors into the setting.

Most genetic counselors are willing. We are definitely qualified. We are probably the most qualified people at this particular point to be functioning in this setting. Mostly, we are limited, like I said, by funding. We have reimbursement issues. We have licensure issues. If we were able to bill for services, we would be able to transition into that market a lot easier and to fill a lot of the immediate need that is there.

Thank you.

DR. McCABE: Thank you.

Any questions?

[No response.]

Any other comments? Yes.
DR. GITSCHIER: I am Jane Gitschier. I am on the faculty at the University of California at San Francisco. I am going to talk to you later today about a different topic, but I just want to really emphasize this issue of the lack of genetics training in the medical school curriculum and the culture that goes into fostering that lack of genetics education.

I do teach the medical students at UC-SF, which is one of the most well-recognized medical curriculums in the United States. It is a source of continuing frustration to me that the faculty don't support genetics. In fact, our curriculum is in the process of undergoing a very large change from traditional subjects, such as biochemistry, anatomy, to an organ and systems-based curriculum, which is going to come into effect next year. So, this is really an anecdote, but I think you should know about it as probably representative of the medical school philosophy throughout our country.

In this organ and systems-based curriculum, there is a prologue, which will include in it aspects of biochemistry, protein structure, et cetera, a short prologue that will then move into cardiovascular

systems and then pulmonary, et cetera. I said, well, where is genetics in this curriculum and there was no genetics in this curriculum and the man who was responsible for really spearheading this curriculum said we will just stick it in somewhere.

The geneticists at UC-SF got together and said here is what you need to do, but there was absolutely -- it was not a point of discussion. We were not allowed to mention DNA in the prologue. We are allowed to talk about proteins, et cetera. DNA cannot be introduced there. I am sorry I don't know all of you but maybe as Ruth pointed out earlier, we did say, yes, you are going to talk about cardiomyopathy. You are going to talk about the genetics of asthma or whatever when you come to pulmonary. You need an example in each one of these sections of genetics because we feel that this is the whole core of our medical problems are genetics often.

So, anyway, we have got a huge mind set problem on the faculty and we don't even require genetics as a course that our medical students have to come in with. You can take either anthropology or genetics. This is ridiculous. Can you imagine a medical student coming in without organic chemistry?

So, I think we need to emphasize this to the accrediting boards, that genetics is really important and you are not going to be accredited unless you pick up on this. Our school emphasizes primary care education. They want to train more people for primary care. Yet, the mind set of the faculty is that genetics is not important. Something has to be done.

Thanks.

DR. McCABE: Thank you.

Wendy, if you could make a brief comment, please.

MS. UHLMANN: I just wanted to say I really enjoyed the presentations this morning and that as efforts are developed in terms of education, I think we need to make sure that we are at the conferences where primary care providers are. I think it is very hard to ask people to go to additional conferences. Physicians have the exact same problems that we do. They have enough meetings per year already and it is very hard to tack on something different. So, I think it is going to be key to integrate into existing meetings and to get genetics content there.
I also am very excited to hear about the efforts of GROW because I think that a lot of physicians -- we turn to the Internet and if it is not there, you don't act on it. I think it is very key to get as much information as possible that will be user friendly to primary care physicians that would be available there.

DR. McCABE: Thank you.

I think we also need to think beyond some of the models we have for teaching. In my somewhat circuitous trip to Washington from L.A., I sat next to an individual who is very involved with the Internet and works for one of the major providers and he was telling me about ways that he is involved in educating people all over the world with virtual classrooms. It was really quite intriguing and, yet, seems from his perspective, there is voice, there is vision, he can interact directly with these

individuals, but it doesn't involve travel.

So that we may need to think beyond some of the fairly time intensive ways that we exchange knowledge right now.

Very last comment.

DR. TRAXLER: Just a very brief comment on the genetics counselors. This is the only recent workforce we have done and if you are interested, please download it. It was done by the director of the University of Illinois Center for Workforce Studies, who is a general internist. So, it is from an outside person. It is not done by a genetics counselor, but somebody who has been looking at the health workforce for a long time.

It is only 25 pages, double-spaced. Download it from the Web site of the University of Illinois at Chicago. It is the only workforce study which I am aware of.

DR. McCABE: Thank you very much.

Again, I think it has been a very stimulating morning and I want to thank everyone for your planning and participation in this effort.

We are now going to take an hour for lunch. Members and presenters should proceed to the Alcove Room. For the public, the hotel has lunch in the restaurant upstairs and staff at the registration desk can help you if you wish to eat outside of the hotel.

We will return here sharply at 1 o'clock.

[Whereupon, at 12:03 p.m., the meeting was recessed, to reconvene at 1:05 p.m., the same afternoon, Tuesday, June 6, 2000.]

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

DR. McCABE: Let's go ahead and get started.

We are going to talk about informed consent in genetics testing research involving family information. At our meeting in February, we briefly discussed the genetic research study conducted at the Virginia Commonwealth University, VCU, that had been cited by the Office of Protection for Research Risks, OPRR, for failing to comply with human subjects regulations.

According to OPRR, the investigator and the VCU IRB failed to consider that family members of twins to be surveyed in the study were human subjects, whose informed consent needed to be obtained or waived by the IRB. Although the issues raised by the VCU case are much broader than genetics and genetic testing, we thought it would be important to learn more about the decision and how it affects or applies to research involving the development and use of genetic tests.

We have asked OPRR to explain the regulatory requirements regarding informed consent of family members to be sure our understanding of the requirement is clear. We will also hear perspectives of several patient advocates in the research community. And then we will have an opportunity to discuss the issues together.

Our goal for this session is to enhance understanding of the regulatory requirements for consenting family members and how they apply in research involving the development of the genetic test.

Before we start, I again want to remind presenters, as I did this morning, to please try to keep within the time allotted for your presentation. We have much to accomplish in this session and the Q&A periods are very important because they allow time for follow-up questions and clarifications.

We will begin with a brief presentation from Dr. Penchaszadeh, who will explain how family information is used and the development and interpretation of most genetic tests.

DR. PENCHASZADEH: Thank you.

Genetics research is a family affair from the beginning and has been so ever since the rediscovery of the Mendel laws at the turn of the last century. So, what I am going to do very briefly is to outline for you, you know, the major types of genetic studies and the major goals of genetic studies and how family information is used in genetic research, leading to, among other things, genetic tests and applicable to medical care. Next slide, please.

We could conceive of genetic studies, different types or different goals. One of the types and/or goals is to define the natural history and the phenotype of medical conditions and this has been done by studying -- by following individuals and families, individuals within families, with effective genetic diseases. You know, as I said, since the turn of the 20th Century, you know, interfamilial and intrafamilial variability has helped, for instance, uncover genetic heterogeneity. I could cite examples, like with Marfan syndrome and mucopolysaccharidoses, way before we learned even the biochemical defects, let alone the molecular defects much more recently.

Family studies helped define the phenotype and the natural history of the diseases. Then prospective linkage and gene identification brings us much more closer to over the past 20 years, I would say, we have seen an explosion of knowledge of the use of family studies to map genes and to identify genes. Huntington's disease is a clear example. Whoever reads the scientific literature on Huntington's disease will see, you know, huge family pedigrees that have helped map initially and eventually clone the gene.

The example of BRCA1 and 2 was mentioned earlier today in those large collections of families and that researchers have been following for many years until the technology enabled the mapping of BRCA 1 to chromosome 17.

Genotype/phenotype correlation also requires a conjunction of gene and family studies. I can mention perhaps the example of cystic fibrosis is a good example to see how the enormous variability and heterogeneity in gene mutations has been followed to try to come up with some

correlation within genotype and phenotype.

Eventually all that transpires into the development of genetics tests, where we have to follow affected individuals within their families for -- to determine specificity, sensitivity, to rate the value of the tests. Next slide, please.

Now, what type of family information is required for any of these studies? You could have -- we have put here only, you know, very general type of information but, of course, it will be targeted according to specifically what condition you are studying and what are your hypotheses. Of course, general health status of family members, presence of any particular disease, if it is the disease that you are targeting for study or any type of birth defect. Family aggregation of birth defects has been one of the main tools to detect genetic factors in birth defects.

Empiric risks are developed from epidemiological study of families with conditions such as cleft lip and palate, congenital hip dislocation and so on and so forth. Of course, you are interested in cause and age of death of deceased family members and you are very interested in specific family relationships, whether it is a first degree relative, second degree relative and so on and so forth.

This type of information has been very -- has been essential, I would say, in pointing to genetic factors in medical conditions. Next slide. Now, the study of families affected with genetic disease or condition has proven to be of great value in all those factors that we have mentioned here, ability to more quickly identify disease-related genes and mutations. I already mentioned the example of Huntington's disease and BRCA 1 and 2 genes.

I could list, you know, hundreds of gene discoveries over the past ten years that have been -- would not have been possible with a study of small and large families.

Opportunity to understand disease, etiology and pathology in order to develop treatments is also something that perhaps the example of cystic fibrosis is one that comes to mind, knowing the precise gene defect and the precise protein that is affected in this disease is enabling -- you know, has enabled already to develop a better treatments based on their knowledge of the pathology and eventually we hope may be amenable to gene therapy.

Understanding inheritance patterns also requires family study and this, in turn may help understand some of these disease patterns, such as Fragile X and many other triplet amplification conditions where before the study of these families, one could not -- the doubts about specific modes of inheritance were hampering a good knowledge on which to base among other things genetic counseling and risk assessments.

All these translate into opportunity of developing diagnostic or predictive tests as the least of several hundred available genetic tests that we were mentioning earlier today these tests. Next slide. Now, of course, in order to screen for families or recruit families for genetic studies, you know, you have to follow a number of steps. I am not going to go through the particular issues of ethics and informed consent in human research because I understand this will be addressed later by other speakers, but, of course, you want first of all to ascertain whether -- you know, which of the families have had the disease or condition that you are interested in studying. Of course, you have to explain the goals of

study and risks and benefits of the study, ask if they wish to participate in the study.

You have to obtain informed consent. Informed consent is not simply a paper that has to be signed by the research subjects, but it involves a whole process of explaining all of what is there in No. 2, explaining goals, benefits, risks and so on. After which and only after which you enroll individuals in the study. You start collecting family history, draw the pedigrees, you know, if your research study will involve tissue sample and specific tests, that is what you will be doing and it is essential to have proper follow-up and feedback to research subjects on any development of different types according to the rules of the game, according to what were the specific issues addressed at the beginning of the study. Next slide.

Now, of course, addressing specifically the issue of development of genetic tests, once disease-related genes are identified, you may need more study on other affected individual in the families to obtain the relevant data for gene phenotype correlations, as I mentioned early, identify range of mutations, clinical manifestations, determine differences in expressivity, mutation frequency, et cetera, in different populations. Next, please.

You know, we are concerned specifically with development of genetic tests, but the development and application and application and implementation of particular genetic tests is a corollary of all the steps that we have been mentioning in this presentation, for which you will need more precise study and determination of sensitivity, specificity. Next slide, please.

Finally, I want to stress that the sentence with which I started this talk in saying that genetics is a family affair because you cannot study genetic diseases outside the context of families and, of course, family history is probably one of the most important things not only in research but also when we come to clinical settings and determining who needs what. As a health care provider, probably one of the first things that you start in meeting a new patient is getting proper family history, which will be important not only for the appropriate use of genetic tests, but to make an accurate interpretation, a risk assessment for diagnosis and courses of action of medical treatments or medical interventions.

I think this is all what I wanted to say so far. So, I will close now and there will be questions afterwards. Thank you.

DR. McCABE: Thank you, Victor.

I think we will move on with the presentations, and there may be questions that come up later unless somebody has something urgent right now.

Next, we are going to have OPRR discuss the VCU case. Dr. Cohen is associate director for education in OPRR's Division of Human Subjects Protections. In this position, Dr. Cohen is responsible for coordination of the National Program of Educational Workshops, the development and dissemination of educational materials and the development of on-line training materials.

Prior to joining OPRR, Dr. Cohen served for 20 years in the Office for Research at SUNY-Albany, where he was responsible for ensuring that all research activities at the university were in

compliance with federal regulations.

Dr. Cohen received his Ph.D. in experimental psychology from Northern Illinois University in 1974. Dr. Cohen will walk us through the regulatory requirements and clarify how they apply to research along the lines described by Dr. Penchaszadeh.

Dr. Cohen. (Pause). If we could, we need to plug you into the mike so we can get this on the record.

DR. COHEN: I bring you greetings from the soon to be former OPRR. As many of you know, I hope, we are being moved out of NIH to the Office of the Secretary and at some point imminently, could be now, we will be in the Office of Public Health and Science under Dr. Satcher. We will be known as the Office for Human Research Protections. I still haven't got it yet. We are not exactly when that is going to happen, but it will be happening fairly soon.

A couple of things I want to clarify in terms of OPRR's position and the whole situation with Virginia Commonwealth. The first thing I want to clarify is that the specific study, the family history study, the twin study, was not in and of itself what caused the suspension of VCU's assurance. I really want to make that very clear because we hear that all of the time. You shut down VCU because of this study. That just isn't the case. OPRR would never, ever -- well, I shouldn't say that -- except for the most egregious circumstance shut down a facility or suspend an assurance based on a single study.

What really happened was that the investigation that was prompted by this study, by complaints about this study, uncovered systemic problems with VCU's whole program for the protection of human subjects. And that is what is caused the suspension of VCU's assurance. That is true in all of the other cases that OPRR has taken action like that. It has always been the result of systemic problems, not any individual specific problem, not any individual specific study.

So, that is the first thing I wanted to say. The second general point I wanted to make is that the issues that were raised in the study, the twin study at VCU, were not new. One of the other things that we hear all of the time is what has changed, why did you come up with this new rule, this new interpretation. That is not the case at all. The regulations have always required the same kind of review that we encouraged at VCU.

I am going to walk through the regulations and where that is, but nothing has changed. There has been no interpretation. There has been no new change in the regulation. What probably has happened is that many, many, many researchers, many, many institutions have ignored, ignored the implication of what the regulations say about who is a subject in this context. That is the problem and this is the first time that OPRR has made a specific action based on that, but nothing has changed in terms of the regulations and there is no new interpretation of the regulations.

So, at this point, let me walk you through it. Has everybody got the handout? Is there anybody who didn't get the handout? This handout that I provided, we are in the process -- yes, this is the one, called "The Involvement of Secondary Subjects..." This is something that we are preparing as guidance for IRBs and we will be posting this on our Web site as guidance in the near future.

I would appreciate your feedback on this. Do you think this document as it is written is helpful?

Because that will give us some feedback.
You notice the term "secondary subjects." This is something that we have sort of started using as a shorthand. It isn't an official term. It doesn't appear in the regulations. It is just something that we have been using as a shorthand. We struggled for a long time to come up with some easy way to refer to these subjects without going into a whole long string.

So, a secondary subject we are defining as when an investigator obtains information about an individual for research purposes from someone else without direct contact with the individual. In other words, that is why we are calling it a secondary subject. They are not getting information from that individual. They are getting information about that individual from somebody else and that applies directly to family histories, where you have a proband. You have the person who has volunteered to be in the study and provide information and that person gives information about his or her family members. The family members we are calling secondary subjects.

Now, the first issue here -- and we have prepared, in addition to this statement -- what we have here is a series of questions that an IRB and an investigator even before the IRB, the investigator needs to walk through these questions and then the IRB needs to walk through these questions to determine the involvement of the secondary subjects. So, the very first question is are the secondary subjects human subjects at all. And to answer that question we have to look to the definition of human subjects that occurs in the regulations.

By the way, if you are not familiar, the regulations are 45 CFR 46, what is called the common rule. Now, the regulations are very specific, that in addition to the traditional interaction, intervention with subjects, the definition of the human subjects includes a living individual about whom an investigator conducting research obtains identifiable private information. So, the first question that has to be asked is the research obtaining identifiable, private information about the secondary subjects.

Now, to be identifiable, it means that the identity of the subject has to be readily ascertained by the investigator or associated with the information. What we are saying is that that identity has to exist somewhere. If the information that is being gathered
-- if there are no links, it is totally unlinked and there are no identifiers whatsoever, then it is not human subjects research. But if there is a link, even if the link isn't with the data, it is coded, but the link exists, so that it could be ascertained, the identity of the individual could be ascertained, then it is identifiable data.

In most studies, particularly genetic studies, you have the identity of the proband and if you have the identity of the proband, then you know -- and you are getting information about his mother and his wife and his sister, you know who they are. That is readily ascertainable from knowledge about the proband -- who is the identity of the proband. So, in those cases, that would be identifiable data. Private information is in the eye of the person, not in the eye of the researcher or the IRB. It is what the subject, the person could reasonably expect will be maintained privately.

Any information that subjects could reasonably expect to be kept private is private information. So, if you give information to motor vehicles, we don't assume that is private information. We assume that that is publicly available. However, when we give information to our physicians, when we give information in a hospital intake, when we give information in other settings, that is considered private

information.

And I think when we are talking about family histories, that is probably the crucial question. Is the information that you are obtaining about the secondary subjects private information? Is it information that those individuals could reasonably expect will be kept private? If the answer is "no," then they are not human subjects. We are done. We don't care from a human subjects point of view.

If the answer to that question is "yes," then the secondary subjects are human subjects and now this is where we get into another sort of misconception. The other thing that we hear a lot, well, if you are saying these are human subjects, then we can't do this research unless we get written informed consent from all of them. That means we can't do the research. You have told us we can't do our research.

That isn't the case either. The regulations give a lot of flexibility, a lot of flexibility in how we treat or how we deal with human subjects. Once we have established that an individual is a human subject, then we have a whole other series of questions that we have to ask with regard to how we deal with that person, how we respect that person's rights and welfare.

So, the next question is does this research, the information you are gathering about the secondary subject fall under 45 CFR 46. The requirements of 45 CFR 46 apply to all human subjects research, except a list of what is called exempt research. So, the key element for this kind of research, the key question is is this exempt and it is Exemption No. 2. There is a list and they are numbered. Exemption No. 2, the question is: Is the information recorded with identifiers and -- they have capitalized that because it is an "and" not an "or" -- and disclosure places the subjects at risk. And the exemption specifically lists what kind of risk we need to look at. To quote it, it says, "The research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability or reputation."

So, there is a whole range of health information, which would not fall under those categories, would not fall under those types of risks, which are, for want of a better word, innocuous. No one could be harmed even if that information were divulged. So, that is the next question.

Would disclosure of this information place the subjects at risk? The answer is "no." Then this research is exempt from 45 CFR 46. The requirements of informed consent and so forth do not apply or do not have to apply. This is an institutional decision. However, they would be considered -- they would be eligible for exemption. If the answer to either of these -- to both of these is "yes," then the research requires IRB review. It falls under 45 CFR 46 and requires IRB review. Now, the next question is what kind of review and the regulations allow for two kinds of review, review by a full IRB or what is called expedited review, where one individual or the chair or a designated one or more individual members from the IRB can review the research. Why is this important? Because if it does qualify for expedited review, you don't have to wait for a convened IRB meeting to make this decision. This decision can be made through an expedited process by the chair or one or more IRB members. So, it expedites the process.

The question is is the research more than minimal risk or -- and this time it is an "or" -- or does the research involve procedures not on the expedited review list. There is a list of categories of research

that is eligible for expedited review. So, if it is more than minimal risk, it can't be eligible for expedited review ever.

If it is less than minimal risk and it is not on the list, it is not eligible for expedited review. And what is minimal risk? That is the next question. The definition of minimal risk in the regulations is the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during a performance of routine physical or psychological examinations or tests.

So, now we are in the question of is this information typical health information that would be gathered during a routine, not an intensive, but a routine test, physical test, physical examination. Now, again, this is ordinary life, routine tests, not very invasive. Usually, routine physical examinations, medical examinations do not get at really in-depth, intrusive questions, but they get at general health questions. So, again, if the information that you are gathering falls in this category, then it may be eligible for expedited review.

Now an important point to make about expedited review. Expedited review is not review-like. All the requirements, all the regulations apply equally to expedited review and full review. It is just who does it. That is the only difference. It doesn't have to go to a full convened meeting of the IRB. It can be done by one or more people designated by the IRB.

The next series of questions has to do with informed consent. And the question is do you need to get informed consent and do you need written documentation of consent. It is very important to remember that these are two different questions. Informed consent and documentation of consent are two different questions. One follows from the other, but they are not totally linked.

So, the first question in deciding whether you need informed consent is is the research more than minimal risk. If the research is more than minimal risk, as we just talked about, then you always need informed consent and you always need written documentation of consent. So, as soon as the information you are gathering about the secondary subjects falls outside of that range of minimal risk information, then you need informed consent and written documentation of consent.

But if it is minimal risk, if it falls within the minimal risk, then the next question is would the waiver of informed consent adversely affect the rights and welfare of the subject. Now, that is a very subjective question. It is not a black and white. There is no formula. It is up to the IRB to decide whether the subject's rights and welfare would be adversely affected or could the research practicably be carried out without the waiver? In order to waive informed consent, basically you have to be saying there is no other way we can do this research. If we have to get informed consent, we can't do the research.

If you can do the research while getting informed consent, if you can get informed consent and do the research, then you must get informed consent. If the answer is "no" to either of these questions, then the IRB does have the authority to waive the requirement for informed consent.

If the answer is "yes," that informed consent is required, now that brings us to the next question, do you need written documentation of informed consent and the key question here is does the research involve procedures for which written consent is required outside the research context.

I think this brings us back again to routine ordinary health information gathering. If this is the kind of information that is routinely obtained without getting informed -- written consent from subjects -- doctors don't usually get written consent from the subjects when they do a physical, when they get general health information about them. I have never had to sign a consent form when he asked me about have I ever had measles, have I ever, you know -- had mumps. You never get written consent for that.

So, that kind of information would not generally require written documentation of consent. I am not saying it doesn't require consent but it doesn't require written documentation. So, you will see here -- this group here, this is the troublesome group. It is the research that gathers information about secondary subjects, which is more than minimal risk, which presents more than minimal risk to those subjects if it gets disclosed. If the information were to be disclosed, the subject will be placed at more than minimal risk, then, yes, you do need informed consent and you do need written documentation of consent.

And my response to the people that react negatively to that is duh. If someone is gathering information about me that could put me at risk, I want to know about it and I don't want it done without my permission. We will hear some stories about that in a few minutes. But I think in terms of respecting individuals and the respect for other human beings, that we owe them. We also owe them if they are being put at risk to get informed consent from them.

To go back to my original point then, just because -- if we determine that secondary subjects are human subjects, that does not automatically mean that we must get written informed consent from each and every one of them, that IR -- investigators and IRBs need to work through these questions to determine whether that written consent is necessary.

Then if it is, determine how to obtain it. Thank you.

DR. McCABE: Thank you, Dr. Cohen.

We are going to move ahead and we will hold the questions for the roundtable because I want to be sure we have plenty of time for each of our speakers to present.

We are very pleased to have with us today three individuals, who will share their perspectives of patients and family members on this topic. I will take a moment to introduce all three now.

Mr. Richard Curtin has a particularly keen appreciation for the issues raised by the VCU case. He is the father of twins, one of whom was invited to participate in the survey research study at VCU. Some of the questions in the study raised deep concerns for Mr. Curtin and he is here today to help us understand those concerns more fully.

Mr. Curtin is a senior financial analyst with the Department of Defense. Mr. Curtin entered federal service in 1974 as a management intern at the National Institutes of Health, a position he earned through a national competition. He continued at the NIH in a position on the NIH Director's immediate staff, Don Fredrickson's staff, and worked on the development of the guidelines, decision

documents and environmental impact assessment that were required before Congress would permit NIH to fund recombinant DNA research.

Mr. Curtin graduated from Rutgers University and has master's degrees in human genetics, as well as business administration and public administration.

Ms. Sharon Terry is the president of PXE International and vice president for Consumers of the Genetic Alliance. Together with her husband, Patrick, Ms. Terry founded PXE International after their two children were diagnosed with PXE. The organization fosters research and policy, as well as support for members of the public.

In four years, PXE International has grown to include a 17 lab research consortium, 48 offices worldwide and a database of thousands of affected individuals. Ms. Terry graduated from SUNY-Stony Brook with a degree in geochemistry and has a master's degree in theology from Assumption College.

Our third speaker is Dr. Vicky Whittemore. Dr. Whittemore is executive director for operations of the National Tuberous Sclerosis Association and director of NTSA's Center Without Walls. Dr. Whittemore has been associated with NTSA since 1987, when she became a member of the board of directors.

In 1994, she was appointed vice president for medical and scientific affairs. Dr. Whittemore is a graduate of Iowa State University, received a Ph.D. in anatomy from the University of Minnesota and held fellowships at UC-Irvine and the Karolinska Institute in Stockholm.

Mr. Curtin, would you please proceed. Thank you.

MR. CURTIN: As Dr. McCabe mentioned, I am the individual who filed the complaint which led to the suspension of approximately 1,100 research projects at Virginia Commonwealth University earlier this year.

I want to thank the committee for inviting me to present my perspective on this controversy. It has been my experience that many of the people critical to the OPRR actions in this case never really took the time to learn the details of exactly what occurred.

Let me take a few minutes to explain how the Virginia Commonwealth University situation developed.

I am the father of twin children born in Virginia. In September 1998, my teenage daughter received a questionnaire entitled "The Virginia Twin Study." I have a background in the development of survey instruments and I immediately realized that this questionnaire was offensive, poorly designed and could easily result in a erroneous conclusions.

Some of the problems included (1) its size; 25 pages of incredibly detailed questions. The typical respondent simply is not going to take the time to respond carefully and accurately to such a long questionnaire. No. 2, the absence of any informed consent literature. No. 3, the inclusion of dozens of questions, which required the respondent to have a level of medical knowledge that most

respondents would not have.

For example, my daughter would have no idea whether my seizure is grand mal, petit mal, prolonged psychomotor, temporal lobe, complex partial or epilepsy. Any response she provided to this question would be worse than useless. It would be misleading.

No. 4, last, but certainly not least, 176 of the questions on this survey instrument asked the respondent to provide detailed medical information about every other member of the immediate family. I cannot understand how any researcher would feel that she has the right to ask my daughter to diagnose and report other family members as suffering from abnormal genitalia, depression, infertility, alcoholism, schizophrenia, abnormally long or strong menstrual periods, other diseases of the female genital tract, sperm abnormalities or low sperm count.

These are just a sample of the questions that the respondent is being asked to report for all other family members. My daughter should never have been giving the opportunity to decide whether or not her entire family would participate in this study.

I immediately wrote to the principal investigator and later to the chairman of the IRB requesting that in the future separate questionnaires be sent to each family member. This was really important to me personally. All I asked, the only remedy that I wanted was to get rid of the columns in the questionnaire that said "Father," "Mother," "Siblings." All I wanted them to do was include within the package a separate questionnaire for the father, the mother and each sibling.

I realize that sending multiple questionnaires would increase the cost of collecting the data. It might reduce the response rate, but it would also have two very significant benefits. The database would be more accurate and all respondents would have volunteered to participate.

The response back from the principal investigator was insulting, but at least she wrote back to me. The chairman of the IRB just ignored me. Since it was clear to me that I wasn't going to get any satisfaction, at least to my satisfaction, from VCU, I filed a complaint with OPRR. And a year later, OPRR concluded that the internal controls for the protection for human subjects at VCU was so inadequate that the 1,100 suspensions were necessary.

At first, I could not believe that my complaint led to such drastic actions, but then I filed a couple of Freedom of Information Act requests to get the correspondence that went back and forth between OPRR and VCU. After reading this correspondence, my disbelief turned to asking why didn't somebody close this operation down years ago.

I refer you to the addendum in my prepared statement, which contains a list of 19 deficiencies cited by OPRR. This list clearly reveals a history of disgraceful performance by this IRB and the failure of this IRB to adequately respond to the OPRR requests for information and corrective actions. Let there be no doubt about it. These suspensions were well deserved and were the direct result of the IRB to do its job.

This issue has taken up a lot of my time during the past half year and I have formed some very strong opinions in reaction to what I have learned. I would like to use my remaining minutes to voice some

of these opinions.

This genetics research community has been given a large degree of autonomy to self-regulate its activities. Unfortunately, the community has proven itself not up for the task of responsibly exercising this autonomy. When an error is discovered, the initial reaction is to cover up. When an outsider begins to ask questions, the reaction is to stonewall and when a mistake is fully uncovered, the reaction is to attack. This strategy will no longer work.

A trust gap has developed and others are now rushing in to ensure that this gap is closed. This community has lost control of its fate and I don't think it even realizes it yet. Last month, I was contacted by a producer from NBC News in New York City, who is developing a proposal for a one hour show focusing upon human subject research. Folks, this lady I spoke to is not doing a show showing the great work you are doing.

Right now, incidents, such as those that occurred at Tufts and Penn have received relatively little publicity. But can you imagine the public reaction if the circumstances of these deaths are reported on a show such as "Dateline."

As my involvement in this controversy has deepened, I have become more and more aware of widespread failures at every level of the scientific community. There has been a failure of leadership. The VCU situation offered an excellent opportunity for the leadership of this community to step forward and denounce a truly deplorable situation. Instead, the leadership responded with hyperbole, demagoguery and attacks on OPRR's actions.

I am also surprised at the lack of attention the leadership has paid to the June 1998 Inspector General's report. At a congressional hearing held just last month, the Deputy IG testified that few of the recommended reforms were enacted and the congressman who convened the hearing accused the department of foot dragging and failing to be proactive in reforming the program.

The congressman then issued this ominous warning. There seems to be bipartisan agreement that this is unacceptable. I don't understand how the leadership could have allowed this situation to deteriorate so badly.

There has also been a breakdown in the IRB concept. GAO and the IG have clearly documented that the current structure is inadequate for accomplishing the tasks assigned to the IRBs, but I am more concerned about the inherent conflicts of interest, whether actual or perceived, that are built into the IRB system. I am amazed I even have to mention the impropriety of a researcher participating in an IRB review of her very own project.

There has been a failure in the ranks of individual researchers. What are people supposed to think when they read about incidents such as those that occurred at Penn, Duke, Tufts, Harvard and Baylor? Let's be very clear about this. The disturbing thing is not that a mistake was made or that someone died during a clinical trial. The general public can accept the fact that there are risks associated with this cutting edge clinical work, but what the public cannot accept is a researcher who intentionally commits acts of noncompliance with federal guidelines and covers up these instances of noncompliance and covers up unfavorable research results.

In their defense, researchers have argued that these rogue scientists make up only 1 percent of this community but it is the 1 percent that defines in the public's mind the attitude and behavior of the genetics research community.

Then there is the really disturbing question. What actions have the other 99 percent taken to stop those 1 percent. I cannot help but believe that there were members of this community who were aware of what was occurring at Penn and Tufts, but they remained silent.

Also in their defense, researchers have complained that the human subject guidelines are confusing and I have no doubt that this is true, but you are highly educated people. If you are going to accept federal money, you have to accept the responsibility for understanding and complying with the constraints attached to that money.

Let's be honest. Do you really need a clearly written regulation to know that you should not participate in IRB review of your own project and isn't it obvious that a death during a clinical trial must be immediately reported to someone? Knowing the right thing to do usually is quite easy. But doing it may take some courage. There is a growing perception that the genetics research community does not possess this kind of courage.

So, what are some of the solutions? No. 1, you have to upgrade OPRR. It is very apparent that NIH has done its best to minimize the effectiveness of OPRR by underfunding it and understaffing it. Clearly, OPRR has been treated as the proverbial stepchild within the NIH family. OPRR should become more of a resource to the IRBs and researchers. For example, people should be encouraged to submit questions about the interpretation of guidelines and OPRR should issue advisory opinions, similar to the way GAO issues Comptroller General decisions to guide federal agencies and the way that the Federal Aviation Administration issues bulletins to airlines.

The OPRR advisories should be posted on a Web site and should be required reading for every scientist and administrator involved in human subject research. The IRB structure and process must be revised. Paying for the IRBs and paying for the training of IRB members should not be left to the research institutions. These costs should come right off the top of the extramural funds appropriated to the agencies issuing the grants.

The conflict of interest issue must be resolved. My suggestion would be the creation of a new structure consisting of a network of IRBs across the country, with no IRB being associated exclusively with any single research institution. Each IRB would have a permanent, full time, professional staff and would provide a formal education program resulting in the certification of administrators and scientists. These certified individuals then would form ad hoc teams to perform the IRB functions for the institutions within the designated geographic area of that IRB.

Finally, 1 percent of the rogue researchers, they must be punished. Let's be realistic. This research community is so decentralized that no amount of oversight by OPRR and the IRBs will be able to completely cover all the projects in all of the approximately 4,000 research institutions receiving federal funds. In an ideal world, the real force behind the system of compliance would be the individual scientist and administrators located at these institutions. But the recently publicized

incidents make it appear as though the public cannot rely upon this kind of self regulation.

Therefore, I suggest that the quickest, least expensive and possibly most effective way to improve compliance is to severely punish acts of noncompliance. Since the probability of getting caught is so low, the penalties for noncompliance must be certain and severe.

For example, a principal investigator who fails to file a timely and accurate adverse event report might be precluded from applying for federal funding for a year or might be suspended from the current project for a year.

I realize that these opinions are harsh and I want to once again thank the committee for the opportunity to express them.

DR. McCABE: Thank you, Mr. Curtin.

Ms. Terry.

MS. TERRY: I would like to talk about informed consent in genetics research, genetics testing research, from a couple of perspectives actually. My role is as administrator of PXE International, which is an organization I founded, as Ed told us in the introduction, because my two children were diagnosed with pseudoxanthoma elasticum, a rare disorder. And so, I am also the parent of affected individuals.

In addition, I am the participant in several research projects, having donated skin, various tissues, blood, that sort of thing, and then epidemiological data. And then I also function at some points within my own organization as a researcher, most recently having contributed to the discovery of the gene for PXE, which was published this week in Nature Genetics. Next slide.

We really have dual concerns as lay advocacy organizations and those are that we promote and accelerate research. It is very difficult for a lot of lay advocacy organizations to have research done on their disorders. So, one of the primary concerns of organizations is that research be promoted and accelerated.

In addition to that, though, is a really strong concern that the risks for participants in research are minimalized and that we make sure that we can guarantee in some sense that they are as minimal as possible.

As a practical application of that, I thought I would talk a little bit about what my foundation has done. It is similar to many of the other organizations under the auspices of the Genetic Alliance. PXE International seeks to do many of the things that Victor shared with us in his introduction. We want to find the gene, find mutations, do genotype/phenotype correlations, make available genetic testing and look at interventions, pharmacological or genetic.

Probably one of the best experiences I had kind of bringing things together myself for doing this kind of thing in my own organization was working with the American Society of Human Genetics Consumer Issues Committee that the Genetic Alliance and ASHG work on together. And one of the

things we discussed there was the fact that the research culture and that of the participants is in some sense converging and in other senses diverging and that as long as we respect each other's agenda and find a place where we comfortably overlap, we can have very productive and wonderful relationships.

One of the things that we, therefore, do is call ourselves participants in research rather than subjects and look at it in a collaborative kind of sense, rather than a kind of top down sense. Next slide.

Informed consent, therefore, is part of a collaborative process and the Genetic Alliance has fostered that for many years. Part of that whole process is the collection of whatever data or sample it is is justified. So, there is a real reason to do whatever the collection is. There is a thorough consent process that is not just the simply signing of form, but, in fact, a lengthy process that is ongoing and longitudinal in a lot of ways and that maintenance of privacy and security be a very critical issue throughout the process.

So, when we keep informed consent in mind, that is the kind of informed consent we mean.

We believe that research participants and others are equally vulnerable and we really see this kind of in two ways and we need to really balance the need of several groups when we look at this issue. And we are both for the vulnerable for the risks and for the benefits. So, for example, I may consider that there is a risk to my children if they give some information, but on the other hand, there are benefits they receive through the research and in addition to that, there are benefits and risks to the others, the society or other persons with this particular disorder or even people outside the realm of my particular disorder because of the information that looking at rare diseases or other diseases will give to the society as a whole.

So, we really want to look at balancing the common good, the rights of the individual and not really kind of looking just at the benefits and risks to the research participant, but looking at it more globally.

So, we look at family information and I will give a concrete example of that in a minute, but we are really operating under the premise that an individual's genotype is information and it is passed from parents to offspring and it contributes to but does not define phenotype. So, in some sense we are looking at it more broadly, realizing that the genotype that we all have is really information not material or something that we have actually physically gotten, but in a sense contributing to who we are but not defining who we are. So, it is only a part of the whole.

So, family information is really critical to translating genetic information into testing and other useful services. Without family information, I don't see how we could translate genetic knowledge. By itself, it really is not very useful. It can't be done in a vacuum. So, things like pedigrees, epidemiologic studies, natural history studies, those sorts of things are really critical to translating information like our just discovering our gene will really not be beneficial to the people affected by the disorder until we are able to look at other ramifications.

In one bit of research that we are doing that I could share here that might be illustrative is an epidemiological study and the study is a research questionnaire we have developed over a year. It is 44 pages long. It is several hundred questions and we have had returned about 500 out of a

thousand. So, we have a very good return rate on this questionnaire, a very motivated audience.

In this epidemiological study not only do we ask for information about the primary participant but also about the affected status of the relatives. That is really critical information for us because we need to know mode of inheritance, penetrance, expressivity, characterization of the carriers, expression and that sort of thing and we are not able to do that unless we do have information from what I guess we would call the secondary subjects.

When we are looking at this epidemiological study we are really looking at that we want minimal risk to the proband, to the person answering the study and also to anybody else who would be impacted by this study or any of the secondary subjects.

We also want safeguards in place. So, both of those things would be very important, those two elements. Our study has IRB approval. One of the issues for the IRB was what sort of information would we have in terms in terms of identifiers on the secondary subjects. We don't have identifying information on the secondary subjects.

In addition, because we have no identifiers for the non-consented individuals and because we in principle would not do this, we also would not contact the secondary subjects.

So, if someone does say, well, my grandmother also has this disorder, we instead send another questionnaire to the individual asking the individual to deliver it to the grandmother. We run a risk there in that there will not be follow-up. There is no way to follow that sort of thing up and then perhaps there won't be any compliance in that case, but that is as far as we feel we can go because we really do want to protect the identity, privacy and confidentiality of the secondary subject as well.

So, in summary, we believe that family history is an integral part of an individual's health and that it is critical that it be included with no identifiers in medical histories, pedigrees, epidemiological studies and natural history, with all of the protections in place that can be afforded at this point. Because PXE International holds all the identifiers for all the blood, tissue, data that is collected, researchers are given only coded samples without access to the code. That is held within our foundation and we believe that, therefore, we act as a good firewall between the researchers and the subjects in the research and are certainly trying to advocate for both advancing the research but protecting the subjects.

DR. McCABE: Thank you, Ms. Terry.

Dr. Whittemore.

DR. WHITTEMORE: Thank you.

First, I would like to thank the committee for inviting me to be here today and add to my bio that I think the reason I was invited here is not only because I work for and with the National Tuberous Sclerosis Association but also my family is impacted by that disease.

My nephew was diagnosed with tuberous sclerosis in 1985. So, it is because of his having this

genetic disease that I became involved initially. Then many years later, when my son was diagnosed with tuberous sclerosis, I was also diagnosed. My sister continues to this day to have no clinical signs of the disease.

So, I have worked with the organization for 13 years and the two genes for this disease were identified in 1993 and 1997 with funding from NTSA and NIH in a little bit of a different model from what Sharon described. I served as the liaison between the researchers and the families and collected families for the studies. Once we had the families and the informed consent, we passed those families with identifiers along. And I will come back to that in a little while.

As Victor said, we are all part of a family and the dynamics within a family can be very complex. So, that is why we served as the contact with the families. In some cases, we also did have a genetic counselor involved, but we felt that the families trusted us as the organization and as the lay advocacy group where they were able to get their information, get their questions answered and decide whether or not they would become involved.

There were some people who had such a fear that their rights and privacy would be violated that they chose not to participate and if that was their choice, there was no further contact with them.

The issue at hand today is informed consent and should family members about whom you collect only medical history information for research purposes be considered human subjects and, therefore, require informed consent? What I have heard today and I think the way that we have handled this is that when we are in contact with an individual, primarily it has been the mother of a child, who is diagnosed with tuberous sclerosis.

We will ask them questions about the family history and very often we find that because tuberous sclerosis can be so different from one individual to another, even within the same family, it often takes probing and asking some questions for them to think about the fact that there may, in fact, be a family history of the disease.

So, for example, my nephew is very severely affected with tuberous sclerosis, but my son only has seizures and white, hypopigmented macules on his skin. It took really us thinking about our family to realize that my grandfather had periungual fibromas and my mother has some very subtle signs, that if we hadn't really stopped to think about it, we would have totally missed in thinking about was this a familial case or a spontaneous mutation.

This is very often the case that we find when we are talking to families. So, in collecting, when we first started these studies to do the linkage studies, we were looking for multigenerational families and without being able to ask those kinds of questions with the contact person, which was not always necessarily the affected individual, without being able to ask those kinds of family history questions, we would not have been able to do the studies.

We only asked for a waiver of consent or did not obtain consent from individuals participating if we could not contact them. So, for example, in a family where we had the contact individual and they provided consent for themselves and their child to participate in the linkage studies, if they then gave us further family -- or indications that there were other members in the family that were affected, we

either asked them to contact those members and have them call us back, which many of them did or we were given permission to contact those family members directly.

And again, there were only 5 percent of the individuals that we contacted out of, I believe, 400, who said they did not want to participate. Of those, there were only a very small number of individuals in the families that we could not track down. But, again, the way this works then is that the information provided to the researchers was only provided once we had informed consent from all participating members of the family and did not pass on any information from a family member, who had decided they did not want to participate.

So, we felt that the clinical information that we were collecting did put those secondary subjects at minimal risk. However, we took the step to contact them and obtain informed consent. If there was an individual, who could not be contacted and we tried and the family tried, the clinical information was left in the family history and in the pedigree. But we felt again that it was putting that member at minimal risk.

There were no identifiers then connected to that information and it was important because the research could not have gone on without that.

I think a difficult area that we have run into recently is wherever appropriate the subjects are provided with additional information about the study and it has become difficult for us to go back to some of the individuals because of regulations put in place by certain institutions. So, for example, families that were entered way back, say, for example, in 1987, as part of the linkage studies, now that we can identify what gene their family has and, in fact, the specific mutation, there are some institutions that will not allow us now to give that information back to the family.

We are in the process of developing the diagnostic test. It is not developed yet. So, we are having to link the research labs to a CLIA-approved lab so that the research findings can then be confirmed in a CLIA-approved lab and then those findings given back to the family. It is appropriate and necessary that we do that but it has also frustrated some families because their expectations were that from the research studies they would get that information back and they are now not understanding why they have to give new blood samples and come back through a CLIA-approved lab.

But we have learned a lot, obviously, in the years since we started these studies in 1987 and I think that what lies at the bottom of our concerns is that private information about an individual might be used in some way that it is harmful to that individual and that information provided for a research study will be provided without that individual's permission.

So, I think, you know, there are really two things that need to be provided and one is legislation that prohibits the use of genetic information or, for that matter, any medical information to discriminate against an individual and keeps that information private.

And, secondly, the infrastructure to handle medical information including genetic information with the assurance that it is private and the information will only ever be used with the permission of the individual.

So, I thank you for allowing me to provide my comments and look forward to answering any questions you have.

DR. McCABE: Thank you, Dr. Whittemore.

Again, I think we are going to proceed and then have questions during the roundtable.

Now we will hear a prospectus from the genetics research community. Dr. Jane Gitschier is a member of the board of directors of the American Society of Human Genetics and serves on its Social Issues Committee.

Dr. Gitschier is a professor of medicine and pediatrics at the University of California-San Francisco, an investigator in the Howard Hughes Medical Institute. Before joining the UC-SF faculty in 1985, Dr. Gitschier was a postdoctoral fellow at Genentech in San Francisco.

Her current research interests are in the areas of inherited disorders of copper transport and the molecular basis of syndromic retinitis pigmentosa. Dr. Gitschier graduated from Pennsylvania State University in engineering science, earned a master degree in applied physics from Harvard University and a Ph.D. in biology from the Massachusetts Institute of Technology.

Dr. Gitschier. Do you want to move around, maybe you could trade with Sharon, where Ms. Terry was sitting, one over there. It just might be easier for people to see.

Thank you Jane.

DR. GITSCHIER: Okay, may I have the first slide. Why am I here? I am a member of the board of directors of the American Society for Human Genetics and I am here to speak in regard to the question of whether individuals about whom only medical information is given by a relative should be considered a research subject in a study of human genetics.

Who is the American Society for Human Genetics? Our membership includes medical geneticists, molecular biologists, genetic counselors, laboratory practice professionals, such as those who run DNA testing labs, lawyers and ethicists.

And I should say that this organization is really the premiere organization for researchers studying human genetics in the world.

Now, what is the position of our society on this question? ASHG supports a waiver for such individuals as research subjects on the basis that such research poses no more than minimal risk to the individual and does not adversely affect his or her rights and welfare.

And we also support it on the basis that it is impracticable to carry out such research without a waiver. I would like to say that what I am going to describe now represents, I would guess, 80 or 90 percent of the research cases that we have in the American Society for Human Genetics; namely, an individual researcher often studies a disease, which is a single entity or a disease, which is a

member of a class of diseases, like, say, cancer genetics or neurodegenerative disorders.

So, it is these types of protocols that I want to address specifically. What is an example of the problem? Okay. Here we have a mother and father with a little boy, who is starting to lose developmental milestones. He is starting to not be able to walk properly. He is starting to not be able to speak properly. Maybe he has seizures. Okay? They come into the neurologist. The neurologist does a physical exam and the neurologist -- most neurologists are really thinking people and they want to know more. They want to know if there is anybody else in this family who suffers from a problem similar to that that he has found in the little boy.

But imagine a situation where you are not allowed to know about any of the other members in this pedigree as regards their medical history unless those individuals are first contacted by the mother and the father and then they are asked to contact the physician or the geneticist studying this case.

So, here we have a situation then where the little boy is affected and, lo and behold, the mother, indeed, has a brother, who suffers from many of the same physical conditions as the little boy. So, the researcher or the neurologist, often they are the same person, they say, ah ha, this looks like a case of X-linked inheritance to me. But I am studying or my neighbor is studying an autosomal recessive condition of nerve degeneration. So, this person is or is not appropriate for a particular research protocol. That decision can be made right away, simply by interviewing the parents, rather than going through a very protracted and possibly not possible procedure of getting informed consent from all the other family members.

So, this is just one simple example of what is encountered and it goes without saying that this kind of information is absolutely crucial for making a diagnosis for this little boy and with a diagnosis comes therapy, comes information about what clinical course this patient might have. It is also needed, as you can see, in this illustration of the sister, who is now pregnant. She wants to know am I going to have a child that is affected with this disorder and does she want to make any decisions about termination of this pregnancy, if the fetus is carrying the affected gene.

So, there needs -- in many cases there is an urgency for knowing this genetic information. So, clearly, I hope this illustration shows you that it is impracticable to require informed consent from all the members of this family in order to collect one very simple piece of information; that is, is there anyone else in your family who has something, which we can piece together with what your boy has. Okay. We are not asking about an entire history of cancer genetics in this family or heart disease. We are asking very specific questions that are pertinent to the diagnosis and care of this little boy.

Now, how do we define minimal risk? I wish I had had this flow chart that Dr. Cohen gave us today prior to this talk. I used the ones that are on the Web site and the ones I have been made familiar with through an IRB, which is a different flow chart.

So, let's just think about some of the risks that are associated with being a human subject in a research protocol at a university or an institution, medical institution. Now these run the range from drugs, devices being implanted in individuals, different behavioral regimes, surgical procedures and even gene therapy.

So, the IRB looks at a case of a geneticist doing a study on, say, a neurodegenerative disorder and looked at these secondary subjects and say, well, what is the risk to a secondary subject compared to these medical risks and the IRB says, well, there is no medical risk.

In fact, the risk for these individuals with these other procedures as well as the individual who is the secondary subject all boils down to one common risk, a non-medical risk, which is a risk to privacy. So, that is really the crux of the issue.

So, the question we need to answer is how does the risk to an individual about whom medical information is obtained from a relative -- oh, wait a minute. I answered that question.

So, what are the risks to privacy in the United States? Now, these are just some of the things I came up with in the last week and these are risks we are all aware of and if you think about it probably for 15 more minutes, you can come up with another 20 risks I haven't thought of.

But medical records, your blood and biopsy samples that are in the hospital or in a laboratory somewhere, your insurance and pharmacy records, psychiatric records, your police and FBI records, credit card use and credit history, your investment records, everything you do over the Web or the phone or through the mail in terms of ordering, your driver's license, car registration, membership and contribution to organizations, your participation in phone or Web surveys, which, let's face it, have an identifier attached to them, government life event records, birth certificates, marriage certificates, immigration census records, your income taxes, social security records, security clearance for governmental and other agencies, employment performance evaluations, your school and university records, the use of the Web and the e-mail and even the U.S. mail.

Now, all of these things have risks of privacy associated with them and I would argue that -- so, the question is how does the risk of privacy for the individual about whom medical information is obtained from a relative in a research setting compare to the risks to privacy from these other means.

It would be my argument that the risks are truly minimal. In fact, this is, in fact, what the IRBs throughout the country agree with. Okay? Now, what is common practice in human genetics in the U.S.? How do our protocols really operate?

What happens is the geneticist obtains approval for a research protocol from his or her IRB. The geneticist notifies physicians and patient support groups of their research interests in this particular disorder. The family members, the physicians or sometimes the subjects themselves will contact the geneticist. The family and the medical history is briefly recounted to the geneticist to ensure that the family is appropriate for the study. This was actually step No. 1 that was described by our first speaker.

Then the physician or family are sent blood collection kits, consent and assent forms, experimental subjects bill of rights. In the consent form will also be a consent for medical records. Depending what other things are needed that will all be spelled out in the consent form, which, of course, has to have approval through the IRB.

Now, how do I know that this is common practice in the United States? Well, I know this because over -- I started to have some soul searching about this as a matter of fact. I don't think we are quite all as arrogant as might have been previously alluded to and I was thinking, well, you know, is the really the right thing and is this what we -- you know, is this common practice or is this just something I am doing and nobody else is doing. So, in the course, the short course of time I had to prepare this, I contacted the other 15 members of the American Society of Human Genetics.

I said what are you doing. What is your IRB doing? What do you know about this? What do you think should be done and 13 of -- all but three of those people I was able to contact in the last week, all of those but three sent me their research subjects protocol and consent forms. I was able to review them all. I was able to talk to them, either directly or on e-mail about how they go about doing their research. It was absolutely consistent. The way I do it in my lab is the way it is done in labs throughout the United States.

Now, this is obviously a small sample of human geneticists, but it is the best I could do in the course of a week or two and I think it is probably pretty representative of what goes on in the U.S. and in Canada, as our membership really includes both.

So, then I talked to the head of our IRB and I asked what is the reasoning behind the decision of UC-SF's IRB to waiver human subjects for individuals about whom only medical history is reported by a family member. So, I wanted to get inside the brains of the people in the IRB to see what are they thinking about as they go through these flow charts to be consistent with federal regulation. What Sharon Friend, the head of my IRB told me, is that the risk -- they first consider that the risk -- whether or not the risk is only minimal and that the waiver will not adversely affect the rights and welfare of the subjects.

Second, that the study is impracticable without such a waiver and then, third, she considered what Sharon actually referred to earlier, which is something that I didn't even realize. They had gone into their thought patterns, which is that the potential benefit of the research to the group as a whole is far greater than the risk to any one individual. So, I thought that was quite good of them.

So, I assume that these are the same kinds of thought processes to go -- that IRBs throughout the country are making since they have quite consistently made the same set of rules. How does the IRB at UC-SF reach this decision? Well, we have a huge university. We actually have two identical but separate membership IRBs, 15 members each. Each IRB meets every other week and each IRB per week reviews 15 to 20 new protocols and looks at 30 renewals.

So, you can imagine, this is an enormous work load for people whose -- this is not their primary job. They are doing this because they are a member of the IRB, but it is just one committee that they are on, in addition to their day job. The protocols are triaged by the administrative staff at UC-SF so that the protocols can be complete before going to the IRB and so that they also kind of -- the administrative office will make a recommendation, in fact, to the IRB saying, well, here is what we think this protocol needs. Here is the kind of consent we think is needed by this protocol.

Now, I must say I had a lot of trepidation in coming to you and saying I have talked to my own IRB because I thought OPRR is going to be here and they are immediately going to go back to my IRB

and say you guys are not doing this right. Sharon said "no," you want to talk about this. I want you to talk about this.
She said what we need from the OPRR is education, education, education, not compliance. We need education. This is exactly the point of Sharon, I believe, earlier and it is made again and again. We need the OPRR to educate the IRBs and we, the human genetics community needs to be educated. I never even heard of OPRR six months ago, I am embarrassed to say, but it is true. I mean, I just go through my IRB. I had no idea who the higher god was that they reported to.

But I now am much more familiar with the whole process and much more aware. I think this is good. It has been good for me. I was also very concerned that the OPRR is now going to look at the front sheet of the ASHG journal and say she has interviewed these people. Now we had better go look at their IRBs.

Again, the other board members said to me don't worry about it. This is important. It needs to be said that this is what we think should be done.

So, thanks very much for your attention.

DR. McCABE: Thank you very much, Dr. Gitschier.

If we could have all the presenters assemble at the front. And Pat, I will give you the first question.

MS. BARR: Well, I just want to thank all the presenters, I think, for really informative presentations. One thing as a consumer I want to stress is that you heard from two advocacy groups with different models, but each one trying to work with the genetic and research community cooperatively and, so, I tend to like the word "partner" even better than a participant.

But I do think in their presentations they raised issues that IRBs are grappling with and in which there are differences of opinion. For instance, it is my understanding and our representative from OPRR can clarify this, that, in fact, if the foundation can link the information, even though it is is a one-way track to the researchers, the information is linked.

And the kind of discussion that I think we need to have is to say that this is not what the research participants or partners want and it is not what the researchers want. They do want protections but they seem to be content with the firewall sorts of systems.

I also think that we need to distinguish and think about the diseases that are, I guess, highly penetrant versus the diseases where their genetics connections and penetrance may not be high. In those situations the exchange of information and the discussion of information may be a greater risk.

I want to say that I agree with all of them about the balance of individual versus public and, in fact, we cannot improve individual health unless we have the public work done and the way that the two groups that described their methods were really operating was with a kind of if we looked at a commercial model, a premarket approval. They were going ahead and doing this and collecting the necessary data so that they could understand what the end result was going to be and they do it longitudinally and they keep doing it.

I guess the question that I have is for the representative of OPRR is the question of linkage and the sufficiency of keeping the information one way.

DR. McCABE: Dr. Cohen, if you would, please.
DR. COHEN: I think the issue is a little bit more complicated than that because as I tried to point out, there are a number of decision factors here. Linkage and identification is only one piece of the overall decision process.

Yes, OPRR's interpretation of the regulations is that, because it says that the information is accessible and that means accessible. If it exists, it is accessible. So, then the question -- so, yes, some of this information, for example, the information, the examples that were given, would be considered identifiable and still considered identifiable information. But that then then comes to the next question and that has to do with minimal risk.

And if the procedure -- given that it is identifiable information, if the procedures are adequate and the IRB has to look at what are the procedures to protect the confidentiality of the subjects, given that it is identifiable. So, for example, if the foundation in this, quote, firewall, unquote, has adequate procedures to protect the confidentiality of the subjects, to protect the information from being inadvertently released, to have steps that investigators have to take to gain access to that information, all of those things are routine standard procedures in terms of protecting confidentiality.

If those are in place, that helps ensure that the risk to subjects is minimal. So, it is not just whether it is linked. That is only one piece. That really only addresses the very first question as to whether it is human subjects research. Given that they are human subjects, because it is linked, then we get into the other questions and the primary one of that is risk.

DR. McCABE: Thank you.

DR. TUCKSON: On that specific point, both in your comments, as well as in Jane's last comments, we see this -- what is the effect of the Internet world and the co-mingling of this data and its ready accessibility? I have watched people sit with a computer terminal in a courtroom environment basically and just go through and prove that you can very quickly co-link the mail, the census data, information, so forth and so on.

Has OPRR specifically looked at the question of this new Internet interconnection of data and does that in any way change your level of concern for this linking of identifiable data?

DR. COHEN: This is an area that we are looking at because it is a very important issue and more and more research is being conducted on the Internet and data is being gathered on the Internet and data warehouses with bits of information are being pulled together about people. We are very concerned about that.

It goes back to the same question I was just addressing before in terms of what are the protections, the confidentiality protections that exist for subjects. A lot of those questions have to be is how are you storing the data? How accessible is that data through the Internet?

You know, there is a whole range of additional questions that the technology incurs or causes. So, those are all questions that the IRB has to ask when it is examining the risks to the subjects.

DR. COLLINS: I want to thank the panel for very thought-provoking presentations, all five of you and particularly I want to thank Mr. Curtin for bringing this attention to a lot of people's consciousness when, in fact, it hadn't really received that level of attention and you are doing so again today. I appreciate your doing that.
I wanted to ask specifically, though, Dr. Cohen, in terms of this flow sheet, which I think is a helpful way to help us think through the practical implications of this discussion. If you would walk us through, because this is what the IRB is going to have to do. Let's take a specific example. It would help me anyway if we sort of bring this down to earth. So, let's say I am a researcher, who is interested in trying to uncover the genetics susceptibility factors in bipolar illness, manic depressive disease.

Clearly, a condition, which has strong hereditary contributions, also one in which the diagnosis carries with it certain social consequences, which we may all rail against, but which are, in fact, part of our existing society, it seems. So, being identified with that diagnosis carries with it certain risks in terms of how one is treated. That is not going to be exceptional. I think there are going to be lots of pedigree research in the area of mental illness that will be of this same sort.

So, if I am a researcher, who wants to figure this out and I would argue and I would suspect few of you would disagree that it would be a good thing to figure this out, that understanding the genetic contributions to this illness would advance us in the direction of having something better to offer people with this condition than we currently do.

Presumably, I would set up a protocol and Jane has already sort of gone through what people often do here, where I would indicate that I am interested in finding affected individuals with a family history because I am not going to be able to do much, at least not right now. We will get there, but right now I am going to need people with a family history and ask them to come forward and then I would after, of course, having this whole protocol through my IRB, before I ever make this announcement, I would then with that approved consent form talk to the proband about their experience and, of course, this protocol isn't going to go anywhere unless I have the opportunity to validate whether or not there is a family history.

Now, already I could be getting into a bit of a bind here because in the process of asking about their family history, in order to figure out is this a subject who belongs in this research study at all, I am already doing something to inquire about private information about people not in the room, who have not given their consent.

So, that is sort of problem number one. Problem number two may be that a significant number of folks who would like to participate in this research are themselves in families where this diagnosis has been controversial and painful and they may wish actually not to let the rest of the family know that they are involved in such a research study because it protects their own privacy to keep that somewhat less of a public event.

And I can tell you from many studies of this sort, there are lots of people who feel that way. So, we are already in a bit of a pickle here in terms of how to apply your diagram. I guess what I would like is for you to walk me through your very helpful algorithm and now I will sort of switch and say, okay, I am in the IRB chair and I am trying to evaluate this protocol.

How do I take your algorithm and apply it to this situation and decide what is the appropriate and ethical thing to do in this circumstance as far as collecting family history information, without which this study is not going to go anywhere?

DR. McCABE: While you are doing that, Dr. Cohen, I might ask the other members, the other participants, to think about it from your own perspectives, too, as well, but Dr. Cohen first.
DR. COHEN: I think that, again, we keep coming back to the same basic question and that has to do with risk. That is always the key question when any IRB evaluates any protocol. So, the very first thing that the IRB has to do is get a very good handle on what are the risks to the probands and what are the risks to the secondary subjects.

That requires a lot of expert opinion to draw that determination. What are the real risks involved here, social risks, reputational risks, economic risks, et cetera? Because I think we are -- given the scenario described, we have already jumped down a whole lot of steps here because we are already assuming that there is a certain amount of risk, that these are subjects. The secondary subjects are human subjects, that there is risk involved. So, then we are really down to that question about consent.

If you follow the chart down, you go out of the chart at the minimal risk areas, the parts that are non-controversial, innocuous. That is where you can drop out at various stages, whether they are human subjects, whether it is exempt. But I think the example you gave probably blocks out almost all of those and we are in a situation where it is -- the decision has to be made in terms of informed consent and the risk to the subjects.

I think the answer -- first of all, once the real risks are established and one of the problems -- concerns we have with IRBs is they don't take the time to -- and they don't have the time, they need to have the time to really evaluate risk as accurately as possible.

But then the question of what you do then becomes more complicated and it is a challenge. By the way, I highly recommend particularly in a scenario like that, the investigator going into this knowing that this could be difficult, should be working with the IRB at the very beginning, not at the end. In other words, you don't wait until the protocol is all done, you are ready to go and then go to the IRB because that is going to be a problem.

They should be working -- the investigator should be working at the very beginning with the IRB and with the IRB staff. How can we do this research? I think in my experience there is almost always a way to do the research ethically. It requires some challenge, some thought, sometimes a lot of creativity.

For example, sociologists for years have been studying socially controversial issues, where they need to get information but they can't reveal the source of the information. There are a lot of

techniques out there for getting informed consent without revealing the source of the information. It may require, again, more challenge. It really comes down to this word, is it "practicable." That is again where there has to be a give and take and a working between the investigator and the IRB and practicable means you can't do the research, not it is more expensive, not it is going to take longer. Only if it is so expensive, you can't do the research. Only if it is going to take so long we just can't do it. That is when the line in practicable comes. And there is a lot before you get to that line. There are a lot of creative solutions that can be done before you get to that line.

I don't have them off the top of my head, obviously, but this is the thinking process that the investigators and the IRB have to go through and they should go through it as early as possible.

DR. McCABE: Francis, one follow-up.

DR. COLLINS: Does OPRR or OHSP have the intention of providing any additional guidance to IRBs beyond this flow chart mechanism? Because I am an optimist and while the IRB system is under enormous stress right now, I believe that most of the people participating in it are doing so with good intentions and good intentions will often get you places other than the road to hell, which is a good thing.

I think in this circumstance, they are the best hope we have got to sort of pull ourselves out of what is clearly a very complicated and difficult situation. But IRBs do not necessarily come to this with the level of information and sophistication about this kind of genetic study. In order to avoid a real patchwork of responses, which may be quite heterogeneous, they might appreciate having some more guidance from you all about exactly in this kind of a study what would you consider as a reasonable starting point in terms of, okay, this is minimal risk and is appropriate for a waiver and what isn't or is the flow chart here basically all you feel comfortable providing?

DR. COHEN: Well, there is a couple of answers to that question like every other questions. First of all, we considered this a start and what we are trying to do now, building on the VCU case, what we are trying to do, because the worst thing and the real problem are the IRBs and the investigators that don't address this at all. That is the problem. That was the problem at VCU. We didn't second guess the IRB at VCU because they made the wrong decision. We came down on VCU because they didn't make any decision. They didn't even consider the issue that these might be subjects. They didn't even consider the issue that the subjects might be at risk.

So, the very first thing, the most important thing we want investigators and IRBs to do is to recognize that this is an issue and to recognize that in many cases the secondary subjects are subjects and that these things have to be addressed. So, that is the first thing. We are hoping to do that first.

When we get to the more tough questions, there we do hope to do as much as we can to help IRBs, to provide as much information to IRBs. There is a limit to what we can do. Obviously, we can't do it all. We would like to work with organizations like these organizations here to help put together guidance, put together workshops, get communications out to investigators and IRBs, information about genetics research and the issues involved in genetics research, information about social risks and what are the impacts of various social risks.

That is our goal. We have taken education as our primary responsibility and the point that was made about education, education, education and not compliance, that is our goal. We take that very seriously. We do believe that the more education we can do the better the job the IRBs are going to do. But we also need help on that. We can't do it alone.

DR. GITSCHIER: I have two questions for you. I guess I would disagree that impracticable turns out to be just time or money issues. There is the issue of just non-response, which is a kind of a wild card. You don't know if somebody is going to come back and say "yes" I would really like to give you this information or "no," I mean, look -- you know, people don't -- it is human nature to throw to the side of your desk something that you don't feel an urgency to take care of.

Yet, for the family, the nuclear family, the immediate family who has a child with a particular disease, as in my example, they want -- they need action quicker than that. So, it is not really a time thing. You just don't know whether or not the other members of your family are going to come through for you. Okay? So, there is that. I think it is not really fair to just reduce it to time or money.

DR. COHEN: I wasn't trying to do that. Those are two dimensions.

DR. GITSCHIER: Okay. The second thing is -- one thing that I would appreciate is in terms of this issue of risk, there would be no risk if there were no identifiers. I think we all -- do we all agree with that? If there are no identifiers, there are no risk to an individual because you don't know who that individual is.

Now, that clearly in a genetic setting -- well, I guess we could imagine ways in which we could have no identifiers, but as Sharon was saying before, she was saying that, you know, other members of the family wouldn't have an identifier, but that is not really true. Just by being a father, a mother, a sister, a brother, they are identified in your study.

So, everybody has an identifier in the garden variety study. So, how would you advise the researcher to store that information so that it can be as private as absolutely possible so that there really are no risks? I mean, sometimes we have things written on little slips of paper that we put away in a file drawer and nobody knows it is there. Our stuff isn't on a Web site, but I think it would be great if you had a well thought out plan for this. Instead, it is the researcher always coming forward, well, here is what I think I am going to do. It is kind of like throwing darts back at the IRB.

They say, well, no that is not good enough. Okay. Well, let's try Plan B. You should have some directive for us so we could really say "yes," we feel that this is absolutely as private as we can be. Everyone would feel really comfortable with that, I think.

DR. COHEN: I can understand that. The problem is and the problem that we face is that every study is different. Every research setting is different. It would be, I would think, almost impossible for us to come up with guidelines that would be even a big chunk of the conditions that are out there.

Our main guidance, again, goes back to the investigators and the IRB should work together to come up with standards at their institution. You know, at their institute, at San Francisco, these are the things that -- you know, if you are doing this kind of research, these are the things you should be

doing.

Those could be done between -- a dialogue between investigators and the IRB. For us to say at San Francisco, this will work, but that may not work at Colorado because they have a different setting. They have a different type of computer configuration.

There are things out there -- there is technology out there that could be very helpful. I don't think investigators or IRBs are taking advantage of what is out there; encryption techniques, you know, firewalls and -- you know, the technology is out there. There is a lot more sensitive information that is being protected in the world than the type of information we are talking about and there are people, experts, devising systems to protect that information.

The level of protection depends on the degree of risk. This goes back again to getting a good evaluation of risk. The fact that I had mumps but didn't have measles when I was growing up isn't a very sensitive piece of information to me and I don't really care if anybody knows about it, but there are other things in my medical history that I do care about and that could come back and harm me and those things require much more protection.

So, you know, if you had that information on a scrap of paper in your drawer, I would be very uncomfortable, but if you had the fact that I had mumps and didn't have measles on a scrap of paper in your drawer, I wouldn't care. So, it does require a lot of thought beforehand.

A lot of these things can be worked out if the investigators and the IRBs work together. We will, again, try to do as much as we can in a generic way, but there are limits to that kind of generic guidance.

DR. McCABE: Before we go on to other questions from the committee, I would ask if anyone else on the panel had any thoughts on Francis's model.

MS. TERRY: I don't have an answer for it, but I have a question that arises when I think of the same sort of situation because even with PXE, I often get siblings who the rest of the family don't want them to talk about this disorder. The question I come up with when I am dealing with this situation is how much of our information is ours in the sense that when I decided to have children, I didn't ask my parents could I pass their genes and I got all my genes from them on to my children. So that information I felt free to do with what I needed to do.

So, in the same sense if my mother has breast cancer or PXE or has bipolar disorder, can I pass that information on because it is part of who I am because it is part of my genotype and may become part of my phenotype? Can I pass that on to a researcher in the interest of my own health without the permission of the parents? Because I do pass other information all the time without permission from the people who owned that information initially.

I don't have an answer to that. That is something I think about, though.

DR. McCABE: Again, before we go to the members of the committee, first of all, does anybody else on the panel have anything to comment on?

MR. CURTIN: Dr. Gitschier mentioned that one of the really important issues here is how we define minimal risk. To me, before you get to the question of how you define it, the really important thing to me is who is going to define it. Especially, going back to Decision Chart No. 1 that Dr. Cohen gave out, up above before it requires IRB review, there is a question that has to be answered there. Does disclosure place subjects at risk? Who makes that decision right there at the very top of the process?

DR. COHEN: Under the regulations, that decision is an institutional decision. The way the system works is the institution has to tell us who is going to make that decision.

MR. CURTIN: It is not the institution review board?

DR. COHEN: Now, in most cases it is, either the institutional review board, the chair or some combination thereof. What we look at when we evaluate who is going to make that decision is how knowledgeable are they? Are they in a position of conflict of interest? Who is going to make that? Is it going to be the person whose job it is to bring in the money to the university? That kind of question.

MR. CURTIN: I hope the committee can understand my discomfort when I get an answer like this. Okay? What I am hearing here is that very possibly the researcher who submitted the proposal is making the decision.
DR. COHEN: It is never acceptable for the researcher --

MR. CURTIN: The researcher's best friend, who is another part of the institution is making the decision. I don't feel comfortable with this at all.

Like I said before, before getting to how we are going to define minimal risk, I want to know who is defining it. I don't see anybody here in this group that shares my concern -- I heard about, oh, we are going to pass a law protecting this. I guarantee you any law that is passed will be subject to a national security exclusion. None of you folks share my concern about me losing my job.

I had a woman in the office two weeks. For 20 years she has worked in our office and then her parents, her Chinese parents relocated from the States to return to Taiwan, to retire and die in the old country and as soon as the Department of Defense found out about this, they took this woman's security clearance away, a 20 year career down the drain.

Nobody I see here around this table or what you call an institution or an institutional review board, I don't see anybody sharing my concern.

DR. McCABE: I would like to think about something that could come from this group as a recommendation. One of the things that I have learned is that with the movement of OPRR into the Secretary's office, out of the NIH and into the Secretary's office, one of the things -- and it was in the information that was in our briefing book is that there will be a public advisory committee to OPRR.

I think that one of the things that has come up is and I would agree that the research community, as well as the public, need more education about this because partly the public needs to know what

their rights are as well. I think that a lot have not until Mr. Curtin has brought it to everyone's attention.

But also, I think the research community, the IRBs, need education about this, much better than has been achieved. I would like to put on the floor for discussion by the committee whether this is something that we would recommend as the Secretary's Advisory Committee, be an issue that is taken up for discussion by the Public Advisory Committee to the OPRR and whether we think that is important.

DR. TUCKSON: Just before I can answer that, I need to get a sense in your mind as you lead us through this, when do we have to make these decisions and will there be an opportunity for us to reflect -- what is the time table that we are under?

Let me say to you, Mr. Curtin, that I really do appreciate your points, but I would urge you and I must counter in the transcript of these proceedings that whether we do or do not share your concern is not obvious at this point because we have not shared how we are reacting to your points.

I know for one that I would like to have the opportunity to think about this a little more. So, I would like the record to state that while you, I think, are legitimate in raising your issues and have done them very well and certainly have gotten my attention, please don't be sure you know how I am thinking.

Secondly, I would say that at what point, Mr. Chair, do we have a chance to reflect and come back to this or are we at a timetable that requires us to make some decisions at this moment?

DR. McCABE: No. This was a point of discussion for us at this time. The question is whether we want to pass on any advice basically through the Secretary's office to another advisory committee that will be constituted. So, we are under no pressure because there is nothing that we have been requested to do.

DR. BURKE: In direct answer to your question, it does seem to me that it would be appropriate for us to give some consideration before we have already identified IRB as an important part of oversight of genetic tests in the research and development phase. I would support Reed's comment that I think as we explore this issue, we really need time.

I also wanted to comment specifically on this issue of minimal risk and really appreciate Mr. Curtin's comments on who defines minimal risk because I agree that that is a crucial issue. We have heard that minimal risk is what a reasonable person would consider minimal risk, if I am understanding. And I don't know how we can get to a reasonable person standard without having appropriate community participation and being sure that there are no conflicts of interest involved in who is deciding for a given study what represents minimal risk.

So, I really appreciate your comments on that and it seems to me that is a very important issue that comes into how IRBs are constructed and then to the extent that we take up IRBs represents an issue that we should address.

I also want to make sure that I am understanding a point that was made about minimal risk since that

is such a critical determination at a certain point in the effort that one has to go through in getting informed consent from secondary subjects. And that is if I am understanding it correctly there are two elements that go into determining whether or not a subject is exposed to minimal risk or more than minimal risk and the first is the nature of the information. So, we all agree your vaccination records are probably not a concern, but I think we would probably also agree that your history of manic depressive illness could very well be a concern.

It sounds as though there is a second issue that comes into play and that is the nature of the privacy and confidentiality protections that are afforded by the research subject. So, that gets me back to very careful consideration of what that reasonable person's standard is and who is deciding whether we have met it because it is a complex evaluation of the nature of the information and the nature of the privacy protections that are in place around that information.

Is that understanding correct?

DR. COHEN: Yes. I think you have said it very well. That is exactly -- it is a combination of both of those factors. You need both of them to determine what the risks are. One of the problems in this is, I think, also a strength of the process. These are almost all subjective decisions, everyone of them. There are no formulas. It is not black and white. The question is how do we as institutions, as a society, want to make these kind of subjective decisions. The IRB model, where you have a group of people, who try to reach consensus on these decisions is one of the only ways we can come up to do that, but it requires a lot of effort. It requires a lot of time and it requires a lot of resources. That is the other question is where these resources are going to come from.

Let me say one thing in part to address Mr. Curtin's point and some of Dr. Collins' points. One of the problem that we at OPRR have and that we have lived them and, therefore, you live with -- I mean, if we have a problem, you have a problem -- is that these regulations were written, originally written 25 years ago and last revised in any kind of major way, 20 years, in 1981.

The things we are sitting around talking about now weren't even conceived of in 1981. The list of exemptions, which is where the point that you raise, that decision, institutional decision about disclosure of information, the list of exemptions was put in the regulations under the assumption that none of this research could ever conceivably ever possibly hurt anyone. Well, we now know that is not true.

If you will notice, it doesn't say anywhere in that list of exemptions, the term "minimal risk" doesn't even appear and that is a problem.

In the expedited review list, it says it has to be minimal risk, but not in that list. So, there are problems with the way the regulations were written and when they were written. The corresponding problem is how difficult it is at this point in time to change those regulations, which without some outside influence I would say are nil, unless Congress or somebody gets involved and produces some outside influence.

Those regulations are the regulations that we at OPRR and, therefore, you are stuck with and we try to make the best of it and try to work it out as best we can, but we have to live with the regulations

as they are written.

DR. McCABE: I know that others have additional questions and comments. Again, though, we have a time for public comment and I do not want to erode that.

I want to thank the panelists for your presentations, your very thoughtful and helpful presentations on this. I think per the discussion, we will be considering this tomorrow in the afternoon in terms of next steps. So, if anybody wishes to follow up on this conversation, that is when it will be occurring in our agenda.

So, thank you very much.

Again, it is time for members of the public to express their opinions, give comments or questions. You could make it to our presenters if you wish. I know that Nancy Buelow from the Alpha I Association would like to make a statement.

MS. BUELOW: Thank you.

The Alpha I Association would like to thank Dr. McCabe and the committee for their thoughtful deliberation on genetic testing. As someone with Alpha I, a genetic disease, I would like to personally thank the committee for their attention to and acknowledgment that, yes, genetic discrimination does, in fact, exist and it is not only a real threat to my family but to a large part of today's society. A pedigree analysis and family study would be very helpful to those with Alpha I since it is an adult onset disease.

The research of families and identifying asymptomatic Alpha family members could allow them to make lifestyle choices and medical management decisions that could in many cases extend and save their lives. Many Alpha I families are reluctant to become involved in research studies because of the great fear of genetic discrimination. We have several cases of genetic discrimination, as Dr. McCabe mentioned yesterday, that are documented with people -- Alpha family members that have gone on record.

Clearly, we do support research, but we must protect our family's genetic privacy because of the lack of federal legislation to do so. For this reason in January at the SACGT meeting, the Alpha I association publicly called for coded testing for asymptomatic family members of diagnosed Alpha I patients.

The Alpha I Foundation, the research arm of our community, has committed to structure and support a coded testing program in which genetic counseling will be an important component.

In closing, I would like to say that we believe that Alpha I is today's working model for all Americans when one's personal DNA is sequenced. The biotech frontier is the legacy we leave our children. We all need to be careful as we blaze this new trail.

Thank you so much for your attention.

DR. McCABE: I have a question, Ms. Buelow. I remember that there was a press announcement at the February meeting, but I don't recall the details.

In terms of the coded testing that you were recommending then, is that a linkable code?

MS. BUELOW: No. It is coded in that it is in a research bubble. The information is protected that we have no way for asymptomatic family members to be tested presently without that going on their medical record. So, this will like the one that Sharon Terry has.

DR. McCABE: But there would be a central repository --

MS. BUELOW: Yes, a research registry.

DR. McCABE: There is a potential link back to the individual then. Some of the -- in the HIV testing, there were some unlinkable codes so that the individual knew the code number, but nobody else knew the link back to that.

MS. BUELOW: No, this would be linkable, yes.

DR. McCABE: Thank you.

Any other comments from the public at this time?

MS. BENKENDORF: I am Judith Benkendorf and I am actually wearing my hat as a legislative fellow with the House Commerce Committee, sponsored by the American Society for Human Genetics.

I am very pleased to announce and bring to the committee hot off the press part of this multi-step to revamp IRBs and increase protections for human subjects in the United States to facilitate research, a bill that we are going to be introducing on Thursday morning that I have spent a lot of time working on. It is not perfect, but it is genetics friendly, I really hope.

You can certainly comment on it and react to it. There will be a press conference and I know Mr. Curtin is going to be speaking at it.

I can just give you a quick review of what it does. One of the things that it does is it protects all human subjects in the United States by extending the common rule, which right now only applies to federally-funded research, to all human subjects research.

It also talks about informed consent as a process and sets out the minimum content of what should be in informed consent. It ensures that all research projects in the United States go through IRB review. It has got very stringent disclosures of conflict of interest for both IRB members that have to go to the IRB and the institution, as well as to investigator -- from investigators to participants/subjects, including a perceived, actual or real conflicts of interest, proprietary or non-proprietary.

It modernizes and updates federal oversight, moving OPRR, of course, to the Secretary's Office. It

codifies that and takes into account some of the up and coming more high risk research, including human tissue research, gene therapy research, multi-site collaborations, international collaborations and, finally, adopts a number of the recommendations from the HHS Inspector General's report, which as Mr. Curtin told you in the two years since that report, I think, only three of the 11 recommendations were addressed. This includes mandatory education for all IRB members and accreditation and certification of IRBs.

The AAMC and a couple of private sector groups are taking the lead right now to begin some uniform education for all IRBs across the country. It also codifies NBAC so that NBAC can continue their work.

So, again, this is just a first step, but it is legislation that will be introduced with bipartisan support and I will leave a copy of the bill and specs for the committee so that can be passed out to you.

DR. McCABE: Thank you very much, Judy. I was going to ask when it was available if you would make it available to us.

MS. BENKENDORF: It is right here and I also have it in Web form, so I can e-mail it, so it can be e-mailed around.

DR. McCABE: Okay. Well, we will get that to Sarah Carr and she can make sure we have it copied for all the members of the committee. But thank you for coming and for that news.

MS. BENKENDORF: You are welcome.

DR. McCABE: We have time for another one or two very brief comments.

DR. HANSON: I am Jim Hanson. I am here for NCI.

I really just have a comment for the committee's consideration, and that is, I would hope that in whatever actions you take with regard to the issues just passed, that some attention be given to the problems inherently associated with trying to do large scale multi-institutional research in genetics and genetic risk factors, which is clearly to be essential to the study of risk factors for many common types of disorders where we think much of this is going.

I would make a similar plea for the consideration for the special needs of research involving children.

DR. McCABE: Thank you.
Our last public comment before the break.

MR. MERZ: I am Jon Merz from the University of Pennsylvania. I could go on at length, but I have three quick ones.

First off, I would just like to get it on the record that one of the problems with minimal risk is that it does two things as was discussed. It is basically the criteria for expedited review, but also is a criterion for waiver of consent. I think what happens as a practical matter is that chairs can make the

decision about whether or not this is minimal risk and then waive consent. So, instead of a full IRB ever making waiver decisions, it never goes to the full committee.

The second thing is one thing also to consider is the influence of state law on research performance of genetic testing. A state that comes to mind is New Jersey, which would ban the performance of a genetic test on someone even in research when identified them without consent.

The last thing is just to respond to the ASHG statement, which was essentially asking for default, like the NBAC almost, asking for a default that says genetics research, like other research, is minimal risk.

I think, personally, and this is my opinion, and it is backed up with evidence which I can present to you, is that the default should be that it is more than minimal risk, and the burden should be on researchers to prove that in any particular case, that they have adequate protections of people and of groups and the like, and of family members, to bring them below the threshold.

Thanks.

DR. McCABE: Thank you very much.

Thank each of you for your comments.

We will now take a 15 minute break. For members and presenters, there are refreshments in the Alcove Room upstairs and for the rest of you, the restaurant has coffee.

We will resume at 3:30.

[Recess.]

DR. McCABE: We are going to get started. I would have everyone go to Tab 3 of Topic 1: Oversight, page 3. We are going to Topic 1: Oversight, Tab 3, page 3. It is the summary that Susanne did -- as I almost dumped my water over -- it is the overview of issues raised in Public Comments. Apparently, it came to you later, so it may be in a separate file but it starts "Definition of Genetic Test."

And yesterday, we reviewed the comments of the members and the first two pages of the "Public Comments." On this page there is "Review of Tests Currently on Market," and then, "Additional Recommendations." My reading of "Additional Recommendations" is that we already have covered those in our prior discussion yesterday.

So all we have left are the two bullets at the top of the page. For those of you in the audience, these are available outside. So if we are speaking in code, please feel free to go get a copy of this so that you will understand what we are working on.

Regarding "Review of Tests Currently on Market," several concerns were expressed regarding review of tests already on market. A suggestion that the tests on the market that are approved by

FDA or that have reached standard-of-care status be exempt from further review and evaluation beyond CLIA requirements.

These were several comments from the public. Remember, yesterday we said those that are already on the market -- we took care of those that are already on the market, as well as new tests. So I think this has been dealt with, by my reading.
I am told that others agree with me that it has.

Anyone wish to visit this sub-bullet? Elliott?

MR. HILLBACK: I am not sure where to do this, because yesterday we talked about some of these things, and this next bullet below this one gets back to FDA.

DR. McCABE: Well, what I would like to do is complete all of these. If we have covered them, I want to wrap this up, hopefully within the next 10 to 15 minutes. And then what we are going to do is go to prioritization. So if they are issues related to this, bring them up now.

MR. HILLBACK: I think they are. I thought that the next bullet was going to get there, but I think that they are all related at this point, so maybe I should jump in.

It seems to me that, kind of looking at the next bullet, looking at this one, the next bullet talks about the fact that of all the public comments, there were a number of them concerned about FDA oversight. I think we did talk for a while yesterday about the complexity and the size of the issue in terms of the review process and everything else.

One of your points yesterday, Ed, was to suggest that having a little more time to think might be useful.

I guess, overnight, I have come around to a point that I would like to put out on the table for discussion and see where people go on that. And that is that, I think a lot of the reaction we saw from the laboratories and from clinicians that responded about FDA were responding to, really, a perception of FDA that is a historical perception, a perception that old systems would be applied. And we did have a sentence or two in our previous report that talked about FDA needing to find some other ways to act.

I guess what I would like to do is propose that we go back and look at the section related to the approval process, related to review of tests, and think about whether it is really most logical for us to leave in the two sentences that says FDA should be the lead, FDA should do this, versus going back and really saying, what is it we want to have happen.

I think the complexity that we have all been trying to deal with is, when we say we want FDA to do it, we sort of say, well, FDA do it, and you guys figure it out exactly how you are going to do it, and if you do it in the old FDA ways, maybe there are a lot of concerns, both on the committee and off the committee about now/future costs, availability, timeliness, and everything else.

So where I was going was to suggest that we look back at the paragraphs. What we really want to

make sure we get across, I thought, was that there was some sort of a premarket review process, and that there was a way that was flexible and reflected the variability that is there, the different kinds of tests that are there, the different risk factors that are there, that reflected orphan diseases, which we talked about yesterday, orphan tests, of which many of these tests are going to be, and that we really defined more clearly to the Secretary what it is we are looking for to have happen, and basically say to the Secretary, you have the staff, you have CLIA, you have FDA, you have CDC.

There are working groups that have gotten together to work on this. You need to come up with the new regulatory methodology system that uses the best of each group to do that. Some of the key factors would be
-- and we list them, including some sort of premarket review, but it is variable depending on X, Y, and Z -- some way to collect data from the market, as well as from the labs; some way to require, with quotes around it, that as we know more, to use Muin's phrase, to be able to say accurately what we know and what we don't know at any point in time; and that the real objective we have is that that be done in a way that is cost effective, that is not going to be the bottleneck -- it is 700 tests now, but what could be thousands and thousands of tests in just a couple of years; that we don't ask for a specific agency or a specific way to do things as much as what we want to get done, what we want the end point to be.

So this is where I wanted to go, and I don't know whether it is this point, or the next one, or the one from late yesterday, but I think it is a point I would like to see some discussion on.

DR. BURKE: I actually agree with Elliott, that I think it is very important for us to focus on what we have identified as the crucial issues. One is premarket review, and the other is the nature of the premarket review to be correlated with the nature of the tests, and that includes both characteristics of the test, complexity of interpretation, characteristics that suggest high scrutiny, and characteristics of the disease that is the orphan disease issue.

As we do that, however, I think we need to give some consideration to the who-decides question. And I would see us as having three choices. We went with FDA. We basically said FDA decides last time, because we received information that FDA was the agency with legislative authority to do this kind of premarket review.

So I think we need to take that seriously.

What Elliott is suggesting as an alternative approach to who decides, is, in essence, to punt to the Secretary. And I think that is certainly another possibility we could consider.

A third possibility that we might want to consider is that there be a collaboration between DHHS agencies and the kind of collaborative infrastructure that we see developing, and want to see developing, for data collection.

You know, I think there are pros and cons to all of those different approaches. I think we should separate very clearly, this is what we see needs to happen, and then, as a separate consideration, our thoughts on who should be involved in deciding the process.

MS. BARR: I agree with Elliott. And Wylie and I actually –. I have been thinking about this and I have been thinking about the collaboration. I guess I would move a step further than Wylie. I think it is a mistake for us to say, these are choices that we have thought about, because that puts us very much back to where the Genetic Testing Task Force was. These are the issues, and these are the possibilities.

I think it would be wiser for us to try and come up with a structured outline. After all, she has the freedom to modify our suggestions or to look elsewhere, but I think we need to be as clear as we can be.

The reason that I feel strongly about a premarket approach and a collaborative approach is because I think I have been convinced that we do need to give the patients and doctors access to these tests in order to ever determine their utility, and that what we want to do is make that hurdle not as difficult, get the tests out there, but somehow design, and this may be CDC, or CDC and others. How do you design a large cohort study where you are collecting the data. I mean, is the Cancer Registry the right model. It is a trade-off. If I want the test, as an individual, I am going to have to trade some of my privacy, so that we can understand what this test really means in the long run. And that is a choice each individual should be able to make on their own, given the appropriate information.

DR. CHARACHE: First, I do definitely want to agree with Elliott and with the thoughts that Wylie expressed, that it probably is not a good idea to focus on a single agency at this point, as opposed to saying what it is we need to have happen.

And I would like to add one other thought. I have been concerned about a single constriction in the hour glass that would block the ability to get tests out on the market, because it is not just 700 tests. If you have to look at all the different susceptibilities and sensitivities, specificities, and predictive value associated with each variation in the annealing temperature, or the master mix and what is in it, the magnesium concentration, what have you, we are really talking about thousands if we want to know the sensitivity and specificity of the test that is being used in a given laboratory.

So I think these issues should be addressed in terms of what is going to be in -- to, and what you are going to have specific clinical data, clinical validation on it.

But there is another thing I think we should call to the attention of this group that concerns me, that I was reminded of with Dr. Feigal's discussion yesterday, and that is that the strength of the FDA is that they have the knowledge base, they have people at the FDA who know how to do premarket reviews. And I think we have got to take advantage of that strength and that skill.

They do have legislative authority, but on the other hand, as a result of the FDAMA, which is the FDA Modernization Act, which was passed about a year ago, they also have very meaningful, from our perspective, legislative restrictions, things they are not allowed to do.

And I was thinking of this as I thought about the strength of some of the consortium approaches. If it were put under the FDA, we would almost have to be sure that it wasn't limited by some of those restrictions, and I will give you just one example. And that is, if the FDA now approves a test because the sponsor says that BRCA1 can be used to assist in the diagnosis or screening of familial breast

cancer, any other company can use that test to screen for any body site or any disease, and the FDA can't control it. That is called off-label use, and as a result of FDAMA, they can't prevent that.

So I think there are limitations right now if we don't add some issues that we want to be sure gets addressed, such as the FDA can address this off-label use, and they have the resources to do the reviews of this large number of studies we want reviewed and so on. I am very concerned, without a little more thought by the group, of just saying this one group, without other restrictions, will be the group responsible in and of itself.

So I would almost like to see perhaps this be able to support the FDA more by getting the Secretary to lead in removing some of these limitations to what the FDA is allowed to do with its knowledge.

DR. McCABE: Before we progress with that discussion, I think if we pursue this discussion, we will address all of the issues in these bullets and will have completed our tasks that we began yesterday.

The next decision is, then, we can go back to the written document and annotate that, or do you want to spend 10 minutes and not be constrained by the written document, and say, let's just think for a few minutes, what is it that we would want the process to do, and not feel that we are wordsmithing the existing document.

I see people's heads shaking. Do we want to do this on the PowerPoint so that we have it? Or, do you just want to spend some time thinking and then we can decide where we go with this list? Sarah and our staff will keep a list that we can come back to.

It was mentioned that we want premarket approval, that that is one of the points that we want to do. Is that right?

[No response.]

DR. McCABE: So premarket approval is one of the things.

DR. BURKE: Just to elaborate on that, I actually think, and I would ask Pat Barr to comment on this. I think there are two things that we are most interested in doing. One of them is premarket approval meaning that a test doesn't come to market without some review of its properties. I mean, in a simple sense that is what premarket approval is.

But we talked last time, and I think it is implicit in some of the discussion now, about the idea that we would have potentially a conditional approval, or a preliminary approval, after which there would be some form of, really, mandated data collection. And I think that speaks to Pat's concern about monitoring off-label use.

In other words, what I think we have talked about and I think we should be clear about, is, that for some tests, perhaps only the high-scrutiny tests, we are interested in the tests being made available under conditions that promote ongoing data collection, so that at a later point, perhaps specified in the initial approval, a more final approval could occur with the data , the knowledge accrued by the

data collection.

Again, I would ask Pat Barr to comment on that, if she could.

MS. BARR: Ed, would you like me to comment on that?

DR. McCABE: Yes, Pat, please.

MS. BARR: Well, I think that the two issues, for me, are transparency, which we have talked about over and over again, so that as we are collecting data, we have a way to present it. Another issue that I thought about is, that our current system of research does not necessarily assure that we will be getting the data in in an organized way, because of the incentives for personal publication and the creation of a uniform data set.

And so that, I think if we believe what Francis has been telling us, that medicine is going to be increasingly genetic, with the doctor presenting genetic information for patients, then we need to think about medical practice in a slightly different way, and think about public health slightly differently, and see if we can modify some of the models that we have had that have been successful, where people have been very willing to participate in data collection.

I don't know if I can elaborate any more than that, except that for me, the meaning of premarket approval to me is perhaps what Wylie is calling conditional. We will let you get that test out there, but in exchange for that we need a system that I think is government-sponsored, that will collect the data and analyze the data so people continue to get meaningful information.

DR. CHARACHE: I would like to urge that no test be permitted to be used for patient care in which the result is not interpretable, which is to say, I don't want a test out there if they can't say, this is what it means, and this is what we know about what it means.

I think then you collect your data, but you don't put it out conditionally when you can't interpret it, and all you put is your result is, we don't know what this means but it is $700.

MS. BARR: If I could clarify.

MR. HILLBACK: I think the point --

DR. McCABE: Wait a minute. Pat Barr is --

MS. BARR: I was suggesting that it doesn't go out until we know it has some value for some group. We are generally starting with high-risk families in common diseases, but we really want to know how it translates out in different ethnic groups or in different populations, and in order to be able to do that, many people are going to have to be tested.

MR. HILLBACK: I think I would follow right along. I think the problem that many of us have had for a long time is, and my favorite word, the iterative nature of these tests.

Again, to go back to the Genzyme CF test, we are now up to 86 mutations after nine years of having that test out, but we started with one mutation. It is a phrase that Muin -- I don't who coined it now, but we all use it: tell people what you know; tell them what you don't know.

You have to have some clinical utility to offer a test at all, but that clinical utility and the clinical validity -- and we have had this discussion many times here, and we have had them on the previous task force -- changes on a very regular basis. And what a lot of us have been worried about is the ability to take a flow like that and match it with a review process that is much more batch oriented, which is, you send in something, it gets reviewed, and then you wait a while, and then you send in something else, and it gets reviewed.
And I think what I would like to see, and I think it is going to be crucial if we are going to get the full value out of genetics in medicine, is that we have an initial hurdle that says you have to have some utility for some group of patients, you have to then keep upgrading the knowledge base that you are generating by doing those tests, and by other research that is happening.

It is not just by doing the tests you do, but it is by researchers understanding the disease better, and that somehow you then keep upgrading the what-you-know and what-you-don't-know.

With CF, it is now 10 years into that test, or 11 years into that test, and we are still doing that every month, every six months, whatever. The same with Huntington's, the same with other tests that people thought, originally, we knew the answer and it was clear we didn't.

So I think this is the process that we have been trying to propose for a long time, and defining that is going to take a bit of work, but I think that is what we are trying to do.

DR. BOUGHMAN: I have a question from the FDA panel perspective here. At this point in time, if a 510(k), for example, comes under review and it is approved, then there is the generic release, the approval of that test.

And in this situation, it seems to me that what some people may be referring to as this conditional phase, may actually be tied in somehow to the augmented CLIA regulations. I am not sure whether I am over-interpreting here, but that, in fact, we may be talking about a premarket release to a set of labs that meet certain qualifications rather than any community hospital lab that has one medical technologist. Or, are we really talking about the traditional premarket approval, that once it is released by the FDA, that is it.

MR. HILLBACK: Well, remember that the fundamental principle that we have talked about is that each lab in a home-brew situation develops its own test. That doesn't make it available to any other lab.

If we, at Genzyme, develop a CF test, and we want to sell that test to another laboratory, we have immediately gone and made ourselves a device manufacturer and are breaking the law if we do that. So we don't do that.

So you are talking about, and this is one of the problems that I think Pat alluded to, is that it is 700 test, but there are also a lot of different labs. Some tests, there are 70, 80 labs doing. It is a one-lab

situation. So part of the review process is, is this lab -- does it meet the analytical validity capabilities that it has to; and, does it have some clinical utility, can it show that there is utility, before you get that approval.

I hate to use the words "conditional" or all these things because that gets you back to the issue of getting paid and the problems of access for patients if insurers aren't paying by calling something conditional. I think what you have to say is, this is what this test does, and this is what it doesn't do.

If you can show that it does something that has some utility, then you have to be honest with that. You can't go advertise and say this cures warts on every little kid when that is not what it does.

DR. CHARACHE: I would like to be sure that our recommendations include the fact that, for genetic tests, some limitation on off-label use. So that I think that the requirement should be that the test is used for the purpose for which the sensitivity, specificity, and predictive values have been determined, and if you want to extend the BRCA1 to colon cancer, you have to do that under an IRB, not as a patient-care task.

DR. KHOURY: It seems to me, we keep going around the same issues. I have been listening to this now for the last few months, and I think every time I learn a little bit more. The three fundamental issues are the following: (1) oversight; (2) test classification; and (3) data collection, and they all feed into and are interdependent.

Clearly, if we want to provide oversight to all genetic tests, than you don't need a classification system, and you probably won't be able to collect data on all of them because it becomes impractical.

So you need a system of classification or categorization that feeds into high versus low scrutiny, for which more or less oversight is needed, or premarket approval. And for those, particularly, you need to have a system that ensures the data collection in a uniform way, using a template that some group agrees upon, perhaps a disease consortium model where the experts come in and define what that template --. It could be disease-specific or a genetic template that can be adapted to all kinds of diseases.

So it is really a step-wise process. Until you fix one of these three parameters, then the other two will still be up in the air. So basically, you have to fix the parameters of categorizing the tests to begin with, and making sure that there is a flow of information about these tests. A simple introduction to the market that is not very complicated, that is premarket approved by somebody, FDA or otherwise, and then the data could be collected and looked at on a regular basis to reevaluate where we are.

So I think these are the basic principles that I think we all agree upon. It is a question of implementation. And maybe SACGT can make these overarching principles, and then either get more in depth, get down to the 300-feet level, as Elliott was saying yesterday, or somebody else was saying, or leave the implementation to somebody else, but I think the more specificity this group can add to the equation, the better off the implementation of these recommendations will be.

DR. COLLINS: I appreciate Muin's characterization of the three issues. I think that is exactly right.

Those are the things we are struggling with. I have been a little puzzled by the conversation in the last little bit here, because it does seem to me like we are in a deja vu of enormous magnitude here of going back over several years to the Task Force on Genetic Testing.

I guess I would like to advocate strongly that we don't punt this particular set of decisions about who is going to have responsibility for what, because there has been enough punting already in other circumstances, and if we are not the ones to figure this out with the liaison members of the appropriate federal agencies sitting right here at the table, I don't know who will.

To give the Secretary the responsibility of trying to sort all that out rather than doing it ourselves, I think, really does fail to live up to the mandate that we were given, and potentially would expose us to ridicule, in fact. So I would hope we don't go down that particular pathway.

Now, having said that, I don't know quite what the answer is. I must say I think we have more work to do here, particularly in terms of understanding what FDA oversight would look like. We had a very useful presentation yesterday from David Feigal, but it sure didn't get me far enough down the pathway of being able to visualize what would actually happen once they did a categorization and picked a test as needing scrutiny. Well, what would that look like, and how would it be involved, and how much would it slow the process down of getting tests out there that the public is interested in.

I think we have got to iterate that discussion, and I hope we can do it quickly, before we have a very good chance of knowing whether we are recommending something that is a good fit, or actually is just going to gum up the works in a way that everyone will end up concluding was a bad idea.

DR. McCABE: Let me remind people of our previous discussions, then we will have Steve comment. The public feels there is a need for additional oversight, and we have agreed with that. In addition, we became realistic that the regulatory authority sits in the FDA at this point in time. So if there is additional oversight to be had, that is the mechanism for it to be had.

But we also made it fairly clear in our discussions, and I think in the writing, but perhaps not clear enough, that the FDA should not become a bottleneck, and that there would have to be creative approaches to prevent that from happening.

We had talked about the use of deemed status to bring in the expertise, as well as the person power, to deal with this, but I was a bit disheartened yesterday to learn that the way that is done in other federal organizations is not really amenable to the FDA model. So that, while we were recommending that, I think we were told yesterday that that recommendation would not do well within the FDA.

I think if that is what we feel, we should still make the recommendation because perhaps the models that are functioning in the bureaucracy right now are not the optimal models. But having said that, the purpose of that is to try and recall for us, communally, where we got to where we are. Now let's have FDA comment and see if it is doable within the FDA.

DR. GUTMAN: Joann actually alluded to the fact that the FDA actually has been doing a lot of brainstorming and thinking about models since the last meeting. The fact that Dr. Feigal was

somewhat nondirective represented, probably, a deliberate decision to be nondirective.

And frankly, what I would suggest you do, whether you recommend the agency or someone else do this, is in fact, right before you decide whether it is FDA or CDC or someone else's, is, you might make it as specific -- I think Muin is right -- as specific and as clear as possible, exactly what you want done.

Let me remind you, you can't have your cake and eat it too. I will be more explicit. I will probably get fired, but I will be more explicit about the kinds of models that you could put on the table. There is a model that is on the table about attempting to expand the investigational oversight of the products and allowing them to languish for long periods of time, maybe forever, hopefully not, but for long periods of time as data is collected by playing around with the IDE regs, either literally or figuratively, and assuring that it at least has better labeling.

Maybe there is registration and listing, maybe there is reporting of adverse events, and maybe for all, or for a subset, or for a broad subset, or for a narrow subset, there is some kind of either intensive or token premarket review. That is a possibility.

At the other extreme, there is a possibility that FDA could do what it always loves to do. We could make these all PMAs. It would be job security beyond any reasonable belief, and it would probably have a remarkable, chilling effect on the genetics market.
There is a name for unsubstantiated tests in the FDA rubric, of course. It is investigational tests. In fact, investigational tests are not only legal, they can be marketed, and they can be marketed for reimbursement. They are not supposed to, theoretically, be marketed for profit. We don't have any accountants checking on what people charge for investigational tests, not an accountant on the staff.

And then there are other options. I tried to indicate, and I think Dr. Feigal tried to indicate it, but it was a meeting ago, that with the banes of modernization came some blessings. There really are new products that you could apply to this product line. We have special 510(k)s and abbreviated 510(k)s for, frankly, some fairly high-risk products. We allow people to conform to standards. We, of course, need standards in order to conform to standards.

You can conform to design controls, and you can get by with fairly non-labor intense labeling reviews. You get what you pay for. That is not the same as the intense PMA that was described yesterday. It is a different kind of review.

So, it would help, frankly, whatever agency gets this lucky job, or whatever agencies get this lucky job, for you to sort through and decide what is more important, because it is a balance. I hate to be repetitive, you can't have your cake and eat it too.

DR. McCABE: What is the time limit now that something can languish? Is there a formal time limit?

DR. COLLINS: Actually, under the IDE, no. It has been liberalized. There are very long periods of time to languish.

DR. McCABE: So that mechanism already exists.

DR. COLLINS: Yes. Again, if you were to advise us to try to attack this through better control of the investigational stage. I can understand the reluctance to call it conditional, but, frankly, the investigational-stage products do get reimbursed. I think even HCFA will reimburse them in some cases.

It might be, again, to whomever you recommend and however you recommend, maybe there will be an opportunity for more concrete evaluation of what kinds of programmatic response there is.

Pat is right about the off-label use, by the way. She is not entirely right, in that, if we see a really awful thing, if we did see BRCA1, and we thought it was going to be used for brain cancer by a lot of people. Obviously, you can't control, perhaps, an eccentric chiropractor in North Carolina, but if we thought it was going to be widely misused, we would go the office director and we would ask for big, black, bold letters right at the top, "Not to be used for brain cancer," but we do that on a case-by-case basis.

Her concern is not ill founded, that our ability to deal with off-label issues are more clearly defined in a more linear way. If this is a concern of the Committee, you probably should tell the Secretary that.

DR. McCABE: One of the things that we could do, then, because the rubber has met the road. We are going to have a recommendation when we leave here tomorrow, and they are going to be specific, and they are not going to be to recommend another group to recommend.

So but one of the things that we could think about is saying that our understanding is that the FDA has the regulatory authority. We are concerned, however, that by standard operating procedures, they would become a bottleneck, and I think many of us have that concern, and recommend that there are models that are being developed, and these need to be considered, especially for the genetic testing.

DR. TUCKSON: I am not as concerned about us running in circles. I think it is getting clearer and clearer, at least for me. I am not all the way there yet, but I am beginning to understand it a lot better.

I agree that the first clear thing we need to do is develop the system of classification to define the stringency of premarket approval. I think we have done that. That work is there.

Secondly, then, to do the premarket approval, I completely agree that a test should not come to market without review, and that there ought to be this mechanism of temporary, conditional approval, with the requirement that ongoing data collection can lead to a more final approval. The first step there is the CLIA role for, does the lab meet the analytical validity before the approval can occur. I think that, to me, makes sense. It is easy and straightforward.

Second, no test approved for patient can if the result is not interpretable. The initial hurdle must be that it shows some utility. Who defines that? I will come to that in a second. The next issue we said is, keep upgrading what we know and what we don't know, based on experience and data. Additional oversight, I believe, is also a continuous review of the standards of care and practice by the clinical community.

So what I think, at the end of the day, you wind up with, is a consortium with the FDA and with the private sector. You have the industry and you have the clinicians, the professional organizations of clinicians, who are able together to take a very hard look at the data and at the standards of practice, the standards of care.

You then involve FDA formally in this process. You have a consortium of people that are able to provide other inputs. There are a number of models for that, whether it is in the transplant community in terms of UNOS and how they work, whether it is the new National Quality Forum which brings together, formally, HCFA and AHRQ, and other federal agencies, with the private sectors who have to do performance measurement. Together, they work it out, with each organization bringing to bear what they have to bear.

And then finally, the continuous updating of data that is transparent and that is uninhibited by proprietary considerations is a built in feature that allows you to have the mechanism to go forward.

To me, that is not punting. I think that we can get that specific, but what I would hope is that we wouldn't get boxed into a corner, in conclusion, that says that unless we designate FDA alone, that we are then punting. I don't want to get boxed into that either or. So what I think we get at, is a consortium that clearly indicates this, with the designated role of CLIA in terms of its approval of the analytical validity.

DR. McCABE: Yes, I was going to say that you really already had a consortium because you had the FDA, you had the private sector, you had HCFA and CDC because you had mentioned CLIA. And I would argue that through some of the mechanisms that we have learned about in which the other agencies -- or, all of the agencies are beginning to talk to each other and collaborate more effectively, that there may be opportunities for the other agencies to be involved as well.

DR. BURKE: I would agree with Reed that I think the deja vu is encouraging because it means we are getting warmer. What I think keeps happening is that we get clearer about what we want, and as we get clearer about what we want, we get more reality checking about the fact that there isn't a system already in place to give us exactly what we want.

So I think, as we clarify what we want, we simply need, as I think Reed outlined, to acknowledge that. I think we already did that in our initial report by acknowledging that FDA had legislative authority but that FDA had to be flexible, and also that we acknowledge the consortium collaboration for data collection.

So, let me just add a couple of other points to that. I think, in our discussion in the last couple of days, we can also add increasing clarity to the concept that we expect many existing genetic tests, and many genetic tests that will come for premarket approval in the future, to be able to pass through an approval process relatively straightforwardly.

The classic example would be a diagnostic test for a high-penetrance genetic condition, the kind of test that we definitely do not want to impede. That is the example of the test that must have a flexible

process under FDA.

And we need to look again, I think, at the deemed-reviewers, deemed standards-setting process. I don't think it is sufficient to say, no, that isn't how FDA operates. We need to look at that.

And then there is another set of tests that are high scrutiny, hopefully smaller in number, do require a much more careful process, and it will be a slower process. As FDA has told us, that is a reasonable trade-off.

Here is where I want to talk, though, to the point about conditional approval. I agree completely that a test should not come to market if it doesn't have good analytic validity, and if it doesn't have reliability under certain defined clinical situations. What we know is reality -- and I think the BRCA1-2 testing would be a good example of it -- is that there are tests, and likely to be a continuing stream of them that offer a well defined benefit to a very small subset, but a potential to be marketed to a much larger population with much more unknown benefit.

And I think one of the things we are saying is, yes, we really do want this system to include some fairly automated system of data collection. It is not saying that the test wasn't good to begin with. What it is saying is the test was good to begin with for a very limited indication and has potential benefit for a broader indication, but we can't know that until we get data collection.

I would ask, could you perhaps take what -- you were reading off your screen, Reed, so you must have it in there. Perhaps, you could take from your notes, make that a subfile and dump it to a disk that we could have, please.

MR. HILLBACK: I think Reed and Wylie helped move things forward, but I really wanted to go back and do a thing I have done several times this week -- I am not sure why -- which is agree with Francis. We have fun kidding each other.

Actually, I think it is very important that we do go back and forth. I agree very much, but I think what I don't really want to do is punt to anybody. We can punt to the Secretary. We can punt to FDA. And I think that is how it felt to a lot of people.

Either this committee has to decide that we want to go to 200 feet and make a lot of the recommendations clear enough that the wiggle room for anyone, whether it is the Secretary, or FDA, or CLIA, or industry, or the American College, or anybody, is somewhat defined by us rather than by them, or we can decide to stay at 10,000 feet and punt to the Secretary or punt to FDA, or whatever.

So I do think that if we want to take a hard run at it, we need to say, very clearly, some of the things that Reed, and then Wylie expanded on, some of the things that Francis has said before, and other people, and say, this is a much more detailed vision of what we are trying to achieve. And then I don't feel so much that we are punting to anyone, as people then have to try to figure out the gory details of how to make that work in a real world.

DR. McCABE: Pat, I heard you click off your mute, so I will call on you in just a minute.

But to follow up on that, what we could include also, if the committee felt this was appropriate, a statement that we are basically sending this recommendation to the Secretary. If the Secretary feels that this recommendation, as we have outlined it, is appropriate, then we are prepared to get into the trenches and work on the details with the agencies, so that we are not punting to anyone, but basically saying, does the idea make sense, and if it does, then we will pursue it.

MS. BARR: Well, I think that makes sense. What I was going to ask of those there is, I know that there is a panel system. We have discussed it within FDA. They don't like the deemed model, but they could in fact make multiple panels for review with some agreed upon standards and they would kick back to a later panel review. They do this for only those that are high scrutiny.

And then, if you had some kind of CDC-created data set, those high-scrutiny tests, in order to get out, would have to comply with that data set and some reporting mechanism. And that is somehow using both agencies.

Is that totally unfeasible?

DR. McCABE: Elliott, I am going to pick on you because you are representing industry, and one of the things we talked about yesterday was the proprietariness of some information.

But, would you go along with that, that if it was deemed that this -- inappropriate term. If it was determined that this was a test that required data collection for more thorough evaluation because of sensitive nature, because of unproven efficacy, again, to be determined by a panel subsequently, either this group or another group, do you think that that would be too much of a burden to place on industry that the data had to be collected through a central repository such as CDC in order to evaluate its efficacy?

MR. HILLBACK: Well, it is really hard to tell until you start thinking about individual tests, but the proprietariness of a test isn't about the data that comes back about patients, I don't think, because you are going to have to be able to explain, as you launch a test, what the clinical validity is. You are going to have to explain data about the performance of the test in order to use the test.

DR. McCABE: But there may have to be –.

MR. HILLBACK: So the proprietariness may be the fact that -- and I am sure we will get into this subject tomorrow -- that a laboratory says, this is a gene that we have rights to and nobody else does, but that is something that is known. The design of the test in terms of exactly how the laboratory procedures are done is not something that may be proprietary. We have a technology at Genzyme we call MASDA [ph] that we use internally, but you are not asking us to divulge all the details of how we do that.

So I am not sure where the battles come. I think it is something I would want to get something feedback from some other labs, but I don't understand why, if you are basically trying to develop a data set that shows greater utility, greater validity, why people are going to be negative about that.

Muin, you have been trying to do it. Maybe you have --

DR. CHARACHE: First of all, I think that the summary that has just been put on the table in terms of who should do the oversight, we are talking about two things. One is what the oversight should include, and the other is who should do it.

But in looking at who should do it, I see absolutely every disadvantage in punting and saying establish a new group to do it. We put a lot of thought into it. I think it is a very great group to come up with a final recommendation. And the concept of recommending that the three agencies work together along with appropriate other groups, I think, is very strong. And then, how to fit this together would be great.

I would hope that we could include, though, the concept that the FDA, which is our major resource here, be relieved of some of the restrictions that now make it difficult for them to operate, because otherwise I think we will end up with less oversight rather than more for genetic tests. There would be some real problems.

I think, in terms of what we want to encompass, I would urge that we not release, for example, a test for a gene that has been shown to be effective in one population and say now that since it has been shown to be effective in this small population, you can use it for anything you want and call it investigational for three to five years, or whatever.

I think if it is investigational after it is marketed, it should have the same oversight that it had before it was marketed, which is to say if it is experimental, it should be under an IRB and not out there for everybody to try for every type of tumor.

DR. KHOURY: I think we are heading in the right direction. At least things are coalescing.

I would like to address a little bit, potentially, some of the misconceptions around what a data set looks like. And then, coming back to the three pillars of what I think we are agreeing upon, some system of classification of tests, some premarket review, and then additional data collection analysis and dissemination.

I would like to challenge industry there. You can't have your cake and eat it too. If you are going to have an easy way for premarket without actually collecting or helping with the process of further data evaluation, and displaying this in a transparent way, then the whole triangle would fall through.

So I think what we can offer as multiple agencies, and I am not speaking for CDC -- and the other agencies, forgive me if I overstep my bounds -- is that there is a lot of work that can be coordinated across the agencies, especially NIH, HRSA, and AHRQ, that would help further develop both the primary data collection, especially around clinical validity and utility, and that leads to further pooling of these data in an aggregate way, using some common framework for analysis, and then dissemination, so that we have a box that says, this is what we know, and this is what we don't know.

That kind of information, I hope, industry will be willing to live with, because it will have, probably, no proprietary nature to it. We are not delving too much into the analytic processes of the test, but more of the clinical implication.

So in response to Pat Barr's concern about a CDC data set, I wouldn't think of it as a CDC data set, but perhaps a CDC-coordinated effort with the other agencies to develop a common framework to look at the way data are collected by multiple groups. Some of these groups could be private studies, or even international studies, or NIH-funded studies, with a template for analysis pooling and dissemination in the public domain.

That is what we can offer to be part of that triangle that we are talking about.

MR. HILLBACK: Can I just respond directly?

DR. McCABE: Okay, go ahead.

MR. HILLBACK: Sorry, Wylie.

Muin, I think you are right, and I guess I wouldn't think of it as a CDC data set either. I think if a laboratory has a test and we can get help from the public sector to encourage more physicians to help us collect better data on outcomes, that is going to make our test, over time, have improved validity and utility, or more accurately reflect exactly what the tests will do.
I don't understand why a lab would be against doing that.

DR. KHOURY: That is what I thought.

MR. HILLBACK: So I really do think that we get our cake and eat it too, in that sense, and that we get better data, and it should help, in the long run, create a more accurate -- I hate to use that word because it has other connotations -- but a more accurate, more useful test. Thank you.

DR. McCABE: I am going to hear from Wylie, Michele, Kate, and Ann, and then maybe we could put up on the screen what Reed had outlined, and see if people agree to that when they see it up there.

DR. BURKE: I actually think my comments follow, pretty naturally, from what Muin and Elliott have just said. I want to speak to the experimental versus non-experimental status of a test and ongoing data collection.

I agree completely that when there is tremendous uncertainty about the applicability of a test, it is experimental, and what we hope is that there is appropriate interest and funding from research centers to make sure that the research goes forward.

What I think is a reality with genetic testing, particularly the high-scrutiny ones that we are going to be particularly concerned about, is that these are tests that, as I have already indicated, come to market because they have a fairly well defined value for a very small subset, typically high-risk families, but what they also have is presumptive benefit for a larger group.

In other words, it is not just irresponsible, sort of, economic growth that leads to further use. It is rather that if BRCA1-2 testing has value for women who meet the same kind of criteria as the linkage families, four or more affected family members with breast cancer under age 60, et cetera.

It is also that there is presumptive benefit to women who are of Ashkenazi Jewish descent because of a higher prevalence of mutations, or to women who have much more limited family history, but some indicators in their family history that suggest genetic risk, early onset, bilaterality, et cetera. But we cannot state what the sensitivity and specificity and predictive value of the tests are in that group because we don't have the data.

Yet, I am not sure it is fair to say that they are strictly experimental. So I guess what I am saying is, I do think we need to encompass the idea that there are going to be genetic tests for which we can all agree ongoing data collection should occur, even though it is appropriate that the testing be offered in a commercial setting.

Here, I want to point out that this is not a discussion between federal agencies and the lab. It really is that we have to create some sort of data collection method that captures data from physicians and patients. And labs may play a key role in agreeing, perhaps, to be conduits. That is, to pass on information about registration and studies to referring docs for the referring docs to pass on to patients. I think there could be an agreed kind of cover letter type of thing that says, we need to know more. In order for this test to continue to be available, we need to know more.

There is a standard data collection mechanism that perhaps CDC surveillance experts have helped to design, and it is voluntary, but it is done in such a way that there is strong encouragement for physicians and patients to participate, and then you get the data that five years later enables you to say, for this group with presumptive benefit, no, it really didn't add anything. For this other group with presumptive benefit, yes, it did. The answer will be no sometimes, and will be yes other times.

DR. McCABE: Pat Barr, I apologize. I meant to call on you, and I couldn't see your arms waving around, trying to get my attention. You had something to say a few minutes ago.

MS. BARR: I think Wylie just said it, that what we need is an incentive system that encourages physicians who are going to order these tests, and labs and patients to say, I will participate in long-term data collection when I have this test.

How do you put those incentives in place. Well, the labs want it because there is a good data set that they are going to get some information back from. The doctors are willing to do it because they want to use this test for their patients. And the patients are demanding the tests.

So I think that is just a little bit of an elaboration on what Wylie said.

DR. PURYEAR: Actually, I wanted to expand on what Muin said. I agree that there actually are several models that are in the works now, actual relationships between CDC, HRSA, and the Bureau of Primary Health Care. To collect, I mean, it is not data on tests, but it is data on health outcomes, looking at some specific, chronic illnesses, specifically, actually, cancer, diabetes, and HIV. But it is a whole series over a regional area of physicians actually cooperating with both federal agencies in the collection of that data.

So I agree with, also, the model that Reed was proposing that it cannot just be a lab that is collecting

the data. You also can't expect the physicians to do this voluntarily. You have to engage –. There is going to be a lot of buy-in from both geneticists and primary care organizations, and primary care providers, to engage in that network.

I think you have to approach it slowly and set up some models. I mean, that was my caution yesterday, that before we go down the pike and actually propose something very strict, I really would like to see how the models work and what is really possible here, because I think you are asking for relationships that don't necessarily exist but that probably should exist.

Oh, and I am supposed to ask, where does the money come from. It is usually my job to ask, where is the money coming from. We need to talk about it. As somebody else said, where are the resources?

I mean, if you approach it as a model and then come back to the Secretary and say, this is a model; this is how much it is going to cost, that may be more realistic, because I don't think we know what the model precisely looks like, and I certainly don't think we know what is costs.

Pat also said there is a whole question of IRBs, too, that needs to be thought about.

DR. McCABE: One of the things that we are supposed to be doing this afternoon. I hope we get to it, but if not, then we will get to it tomorrow, and that is prioritization, which basically says, all of these things are going to cost money. They probably all can't be done, and so, we need to pick what is the most important or the top group for the Secretary.

MS. BEARDSLEY: I just wanted to make explicit something that I think is implicit in what everyone has been saying. That is, that if we have some sort of a preliminary review or approval, or whatever you call it, investigational or whatever, one really important piece of that is making sure that during that period the labeling or what is said about these tests is truthful, and there needs to be some strong system built into this preliminary review concept to make sure that that is the case.

DR. McCABE: Thank you.

MS. BOLDT: Kind of going along with that as well, when I look at this, I assume most of these genetic tests are going to be applying for IDE. I mean, if they did go through the FDA system, I am just assuming that they would want investigational device exemption.

No? You are shaking your head.

But if they did, I guess one of the things is, I think there has to be an enforcement of the regulations that these labs can't charge more to make a profit off of those. If that was enforced, then there would be more incentive for these laboratories to actually collect the data and be able to then get full market approval so that they could then be charging.

So I think part of it comes down to enforcement of the regulations that are already in place, and we are not doing that now.
DR. McCABE: Joann, do you want to read what --

MR. HILLBACK: Can I just respond to that?

DR. McCABE: Sure, Elliott.

MR. HILLBACK: Be careful what you wish for there. If you say, well, you can't make money for a couple of years, a lot of labs are going to say, why the hell would I do this test at all?

I wouldn't overlay an existing system. I think one of the big problems that a lot of us have is with conceptualizing, we are going to overlay all of the existing system onto genetic tests. One of the big problems, when you have a test that you are only going to do 100 tests in two or three years, there is no way to justify it financially. Every extra dollar you spend developing that test is another reason not to do the test.

And Genzyme does a lot of them, and our genetic testing business, the DNA part of that, doesn't make money.

Ann will probably fire me, except she doesn't outrank me, so I might get away with it, if she was still here.

But we are not there yet because the volumes are still low. So I don't think you want to use money as a penalty, because money is a significant blockade to people even bothering to develop these darn things. I think there are other ways to make sure people do things right, but I don't think using the reimbursement system to get at this is the right way to do it. I really don't think so.

DR. McCABE: Are we close to ready to come up on PowerPoint?

So, Joann wrote something, also.

DR. BOUGHMAN: I can't read it that far away. I am not sure I can read this either.

If you turn to page 23, we are talking about the former bullet at the top, under Issue 4. I believe page 23 of our report --

DR. McCABE: Of the Oversight document.

DR. BOUGHMAN: Of the Oversight document. You saw that Dr. Gutman had exactly three and a half seconds to determine whether this was doable or not. He said at the end of the three and a half seconds, it was clearly a tall order.

One of the points that I would like to make before I read what I am suggesting should be the changes, or incorporating discussions of today, is that, in fact, one of the mechanisms that FDA does have is postmarket data collection, postmarket evaluation, that has not been used and imposed as fully as it might have been. And I think that may be one of the ways that we can incorporate what it is we are talking about here.

So you can look at what is there already, but let me read to you what I might suggest are some of the changes:

> Because of their regulatory authority, the FDA should be the lead federal agency in the review, approval, and labeling of all new genetic tests. Using criteria and standards informed by practice standard in place in professional organizations and regulations of other agencies, including CLIA, the FDA must delineate review processes for premarket and postmarket evaluation.
> These processes should focus on the claims of analytical and clinical validity made by the developer of the test and must minimize both the time and cost of review without compromising the quality of the assessment of test validity.
> To facilitate test availability, requirements for postmarket data collection may be imposed in the approval process. Data formats for pre- and postmarket evaluations should be developed in conjunction with the CDC. The SACGT is willing to serve as a resource for the Secretary in facilitating the review and implementation of these review processes.

Now, I think that the way those phrases are put, we now have the two steps, at least in the current generic terminology of premarket and postmarket.

That doesn't mean new models can't be expanded within these, but I think the way I have worded this falls within the broad brush strokes of current FDA and CLIA regs but, in fact, explicitly includes all of those organizations, and the professional organizations, and standards, and, in fact, requests the FDA to include the professional organizations and others in the development of the premarket kinds of strategies.

Now, that could be through ad hoc membership on the panel, and/or an ad hoc panel that would help develop those. The laboratory forum. I think that there would be a lot of ways that other groups could be incorporated, but I think those words make more explicit the intent but doesn't change the main intent from our previous statements.

DR. McCABE: But it does include a little bit more of our thinking in there, too.

DR. BURKE: I agree. I think you have done a beautiful job of capturing the additional nuances. The one change I would like to see is the addition of clinical utility. I would like to see it say analytic validity, clinical validity, and clinical utility.

This is in the middle:

> These processes should focus on the claims of analytic and clinical validity and clinical utility made by the developer.

DR. BOUGHMAN: I actually had that, but it was written on the back.

DR. BURKE: I think it is great.

DR. KHOURY: I think this is a step in the right direction. I think what is missing is a couple of things here that I can see, off the top of my head. One is the issue around the data collection, pre and post should be developed in not only the formats, but there is no real requirement to put together some kind of a knowledge base of what we know and what we don't know that is transparent to the general public, and not embroiled in the bureaucratic processes of FDA or any other agency, that it has to be sort of an ongoing process of trying to tell the world that this is the data we know and we don't know at any given point in time.
And also, it does not lay out the collaborative relationships among the federal agencies that will participate in that data collection effort. So it makes it like a two-way street between CDC and FDA, that we provide FDA a little bit of help, and then they do their postmarket surveillance.

Now, there are different ways of doing surveillance. The FDA model is a little bit different from the CDC model. They both compliment each other. I mean, I don't want to put words in their mouth, but they do compliment each other from an epidemiologic and statistical perspective.

I think you have to build on the collective wisdom of doing the postmarket assessment from different points of views rather than keeping it completely under the regulatory paradigm, which I think may be not the way to go.

DR. MCABE: Is there a wording change you would recommend here, Muin?

DR. KHOURY: Not yet, but I have the concepts. I think --

DR. McCABE: You are going to have to come up with it very shortly.

DR. KHOURY: I need a piece of paper, at least.

DR. TUCKSON: I also think it is a great addition. I will try to think of the words, but can you scroll up on the -- the points that we come back and capture --

DR. McCABE: We were going to come back to this

DR. TUCKSON: She has done such a good job. The thing that I just wanted to see is the first point about the system of classification to define the stringency of the premarket approval. I think we want to get that classification into this narrative somewhere right at the beginning. That is why we did all that, and that is what it works.

The other thing that I think we need is to just find a way to get in there, I think the initial hurdle about showing some utility, I think, is important, again.

Finally, in terms of the actual consortium activity, I am concerned about saying the FDA is the lead agency for the project. Yes, FDA is the lead agency on the premarket side. The data collection, which we consider to be equally important, that is somebody else, not FDA. It is a lot of other people involved. It is CDC, it is HRSA, it is AHRQ.

So I guess what I am still looking to sort of not have as a lead agency, but to see the consortium of

consumers, the consortium of clinical people all together, and that we don't make it just a predominantly one-legged stool with a bunch of additions on top of the one leg.

DR. McCABE: But what if we change that to: The FDA should be the federal agency responsible for premarket review, including -- well, if you took out "lead agency," just said premarket review, responsible for premarket review approval and labeling of all new genetic tests.

So it specifies their responsibilities. It takes out "lead agency," implying that they --
DR. PURYEAR: Except that I don't think that is a problem. They actually do --

DR. McCABE: You need to use your mike, please.

DR. PURYEAR: Well, FDA should speak for itself. I mean, I know with vaccines, they are very actively involved in premarket approval. I think what is different about genetic tests is that you still need the postmarket approval, and there needs to be an agency coordinating that. But I think Reed is right, that what we could propose for that postmarket approval is a consortium, and I think that is what the Secretary has to approve.

All of this has already been done. That is already there. FDA has the authority to do all of that.

But that consortium, I think, is what is unique. The kind of data collection that needs to happen, FDA by itself cannot do. You do need relationships that do not presently exist, and I think that is what we could propose. If the Secretary likes it, then you could work out the detail.

DR. McCABE: Reed, you'll have some wording.

DR. TUCKSON: No, I like that. I mean, that that makes sense to me. The only other issue -- I just want to make sure we get them all on the table, is that again –.

DR. McCABE: Before we leave the wording on this, what if we started off this bullet saying, for review, or for regulation of genetic testing, a consortium approach, or more than one agency will need to be involved, some way to get the idea across.

Because we start the bullet with "The FDA," you lose the fact that we are recommending others down there. So if we state that for regulation of genetic tests, multiple agencies, in collaboration with the private sector, may be required. And we can put that into english. Then we can proceed with the bullet

DR. TUCKSON: I could live with that. I think, again, what we are saying is that because the activities that what we are here to recommend involve a number of activities, from the assessment of laboratory clinical validity to data collection and so forth, it requires, it demands a variety of federal agencies to be working in partnership with the private sector and consumers, therefore these people need to come forward.

The only other point I wanted to make sure, Ed, that we got in there, was this notion of the transparency of the data collection, and that there would be this sense that we would be calling

specifically for -- and I don't want to have Elliott get me -- but I think we do really need to make sure that we are stating that we are expecting to have a complete and uniform data set that is not going to be inhibited, because otherwise, what will this committee, this consortium, mull over and use to upgrade the certification.

DR. McCABE: Well, what I would propose, is that we take the outline that you made, Reed, and build that into a paragraph preceding this bullet. And we'll need to look -- I was trying to see where it will fit. There are a couple of places where it could fit, but I think this makes a nice rationalization for why you need the bullet that we have there. Is that reasonable?

DR. BOUGHMAN: We could take –.

DR. McCABE: But I think the logic –. We need the entire -- we need to take your outline, convert it into paragraph form, or perhaps it might be better the leave it as some sort of an outline.

DR. BOUGHMAN: I don't disagree with that, Ed. In fact, we may have a lead-in from the previous bullet on page 22. Yesterday, I had actually added, in my own copy here, where we say, "Based on the rapidly evolving nature of genetic tests," and so on. Where we said, "Additional oversight is warranted for all genetic tests," I had added the phrase, "both in the premarket phase of test development and follow-up on test implementation," which would be a kind of lead-in for this pre/post.

Then, with more of Reed's wording in the text in between, and, I believe, some minor modification here. And when we move to the "postmarket," we need to separate a sentence there, move the "postmarket," and then shift the emphasis on "the uniform" or "aggregate data collection," or something. We will have to work on that.

MR. HILLBACK: There are two suggestions I would like to make, one up in the early part of this. I think there are some factors that we can list that are part of the rationale of why we are thinking this way. The number of quote, unquote, orphan tests that are going to be there. There may be orphan tests for major diseases because they are only looking at the mutation that causes a subset of a major disease. So it is not that there has got to be an orphan disease, but an orphan test.

So things like orphan tests, the rapid generation of new information that requires some method that is not in the history, et cetera. So I think if we can get that richness of what causes some of the heartburn for some of us in that opening piece that you described, that would be useful.

But the other thing I wanted to come back to --

DR. McCABE: Could you prepare something on that?

MR. HILLBACK: Yes. I will. I will. That will be fine.

DR. McCABE: Okay. Before, like overnight tonight.

MR. HILLBACK: Yes.

DR. McCABE: Thank you.

MR. HILLBACK: Then, the other thing I would like to come back to and see the sense of -- is the very last sentence. I am not sure "willing to serve" conveyed the feeling I got around the table. I thought we were saying that we wanted to serve.

DR. McCABE: We desire to serve.

MR. HILLBACK: We desire to serve. Then I would change that to say, "to facilitating," not the review, but "the development and implementation of this review process." The very last line.

DR. BOUGHMAN: The development and --

DR. McCABE: Desires to serve.

MR. HILLBACK: And "development and implementation of this review process," not "review and implementation." See that on the very last line? Yes, right there.

DR. McCABE: Sarah doesn't like "desires." We need another word.

MR. HILLBACK: Yes. Wishes, or strongly wants to participate. Huh?

PARTICIPANT: Proposes.

DR. McCABE: Proposes to serve.

MR. HILLBACK: Proposes we should serve. Proposes we should actively participate. A lot of phrases.

DR. McCABE: Okay. Pat Charache -- well Pat Charache, I think, was on the same point, too.

DR. CHARACHE: I think this is very helpful and very clear. I wondered if there is a way, perhaps before this summary paragraph of indicating concern with some of the restrictions that the FDA now has on them that prevents them from doing the kind of review that they may want to.

I think the most egregious issue is this off-label use of something that is good for one thing, for tumors for which it is unrelated. And I really would love to see the Secretary know that they have to get Congress to rethink some of these things.

DR. McCABE: We have to recognize, though, that that involves legislative change, which is much more difficult than regulatory change.

DR. CHARACHE: Yes. I just wanted to flag the fact that this is important.

DR. McCABE: If you wanted, again, to write something up overnight, we could take a look at it.

DR. COLLINS: I also want to strongly endorse our chairman's suggestion here as now appears in the last sentence about our continued involvement, and maybe suggest adding some additional specificity to what that means.

It seems to me, we are particularly interested, if we are going down this pathway, to have some more specificity from the parties involved in this process about exactly what would they do with tests of various types, and what would be the outcome of that in terms of possible delays in test availability, cost, and so on.

I would be willing to propose a sentence to that effect, if you want to listen to it.

DR. McCABE: Sure.

DR. COLLINS: Which would be right before the final sentence, to offer the following:
Before actual implementation of this review process, detailed modeling of the proposed plan for a variety of tests --
DR. McCABE: Wait a minute. You have got to go slow.

DR. COLLINS: Listen to it first, and then you can decide whether you want to put it in there. I am not asking you to type it up.

Before actual implementation of this review process, detailed modeling of the proposed plan for a variety of tests of different scrutiny levels should be undertaken, including analysis of cost and potential delay in test availability.

That could then be followed by our volunteering to assist in evaluating that kind of modeling, which is what the last sentence says.

DR. McCABE: The one thing that I would consider putting in there is, also, some sort of a timeline, because otherwise they could just postpone implementation forever. So we might want to, we could put that --

DR. COLLINS: At our next meeting.

DR. McCABE: But we can put that in the verbiage, not necessarily in the bullet, but we could specify that this should be done in a timely fashion because of the concern about the need for oversight.

DR. COLLINS: Okay. Add in a timely fashion.

DR. BURKE: No, Francis' comment covered what I wanted to say.

DR. McCABE: Steve, we have just created a lot of headache for you, but since you may not have a job after your previous comments, you are probably safe.

MS. BEARDSLEY: I think Reed has a bullet about the conditional marketing in his section, which I

am not sure we have captured in there.

DR. McCABE: Can we find it, please.

MR. HILLBACK: I thought we were going to put Reed's insert in.

MS. BEARDSLEY: Oh, we are going to put Reed's in?

DR. McCABE: But not in the bullet. It was going to be in the paragraph. But is there something you feel needs --

MS. BEARDSLEY: No, I just want to make sure that line gets in.

DR. McCABE: All of Reed's stuff will be incorporated. I think it was a very logically thought through, but I think that it serves more as background to our logic than for the bullet, per se. But if there is something that is in Reed's outline that should be in the bullet, we should pick up on that.

MS. BEARDSLEY: Well, I was going to propose that possibly --
DR. McCABE: Can you get closer to the mike. It is not picking up.

MS. BEARDSLEY: The notion of temporary or conditional approval should belong in the bullet.

DR. BOUGHMAN: Can I just reiterate that in fact what I have suggested here would mean that the test is approved but would hang with it requirements for postmarket data collection that are not usually imposed or imposable.

That really is different, and, I think, strongly worded, that we are addressing our issue that we don't want to hold up access to this tests, but in fact, the developers and users of the test are going to have to be willing to collect data on the formats that CDC puts forward, and get that data aggregated in some way that is not currently the standard imposed on 510(k)s.

MS. BEARDSLEY: Can I just say I agree with you, and I think we have captured the notion that postmarket data collection.

I am not sure we have captured the idea that tests will be allowed to be marketed in some way on a fairly limited base of information, as long as there is some notion of clinical utility and validity.

DR. BURKE: As one of the proponents of the conditional idea, if I am understanding Joann correctly, I am very comfortable with this idea. I think if we combine, in essence, required postmarket data collection, and presumably that requirement would be applied to certain tests and not others. So these would be the high-scrutiny tests, the very ones that we were talking about conditional approval for.

As long as there is a requirement that that data collection go forward, and we have an ongoing process to make publicly available what we know and what we don't know, I am comfortable that market forces, particularly what insurers will pay for, will take care of what I was trying to take care

of with conditional approval.

In other words, what will happen is that as data collection goes forward, it will become evident that some presumptive benefits aren't panning out and others are. And as long as we have got a method for organizing and disseminating that information, health care payers will pay note. So I am comfortable with that.

MR. HILLBACK: I would second that because, Kate, I think "conditional" has all sorts of ramifications. I think what we are saying, what Joann is saying, and Wylie is saying, is, we approve this test as it stands to do what it says it does. That is not conditional. That is as it is.

If you want to get something more approved, you have got to do something more, but you don't get in this weird situation of having to tell a physician, well, we've got this conditional test that you can offer the patient but you have got to tell them it's a conditional test. And now you get into this, well, what does "conditional" mean. Does that mean we don't know if it means anything?

I think if there is no utility, then we should never be in the market. If there is some utility, then it should be focused on that utility. To put in these modifiers that are charged words, I think, is very dangerous.

MS. BEARDSLEY: I am less concerned about the words that get used than the idea that the test will be allowed to be there and that people will be allowed to take advantage of them, and that we won't end up in a situation where the test won't be allowed to be on the market, at all, until a lot more is known about them than is known already.

I am not sure we have captured the idea that we are looking here for a system in which we are not going to need full clinical validity and utility before a test gets to market.

DR. BURKE: If I can just respond to that. If we required full clinical utility, the vast majority of genetic tests would never get to market. It just wouldn't happen, and I don't think it will happen. I don't think that is even in people's minds, I mean, if you go by where we are now. The reality is that very good evidence on analytic validity and reasonable evidence on clinical validity is the bar that most tests usually have to pass.

What I think you are speaking to, though, has -- I mean, I am just talking about what genetic tests are out there. What I think your comments speak to is labeling. It seems to me that part of our improved attention to data collection, and to what we know and what we don't know, is labeling. So I could imagine much better labeling than we now have about tests, making it clear, in fact, what the limitations are in our clinical utility data.

DR. McCABE: Steve, do you wish to comment?

DR. GUTMAN: Yes, I do. I think what you are doing is absolutely right, because you should put down what you want as a committee. It is the responsibility of the Secretary of the agencies to address this. As I told Joann, this is a tall order, from my perspective. This is a daunting workload, even if you resort to a very pragmatic model with a limited basis of data, and the concept of intense

labeling fits that very well.

God knows, I work with 55 scientists who do this every day, many with an incredible passion. It is a lot of work. There is a lot of tension. There are colorful interactions between sponsors and the agency in a classification which would dichotomize and allow us to, frankly, concentrate on the most worrisome subset of tests as small as anybody could make it, and/or that would, frankly, throw out all the low-volume tests, whether they are worrisome or not, because they publicly have less impact, at least on the first round.

Anything that we can think of, or you can think of, that makes this more constrained, would be appreciated.

I have a couple of specific clarifications. In terms of postmarket, the agency does have the authority. We don't call them conditional approvals, but we have lots of products -- or, I shouldn't say lots of products. We certainly have a handful of products in which we have cleared the product with a narrow claim. That is something we actually advise sponsors, to help them minimize their data sets, is allow them to start with narrow claims.

We find, in fact, that particularly when there are marketing advantages to broadening or adding claims, that they inevitably do the postmarket studies and come back knocking on our door months or years later, or in fact they put them out in the literature and don't bother to knock on our door. Look at the triple screening for Down's syndrome. Nobody has knocked on our door, and there is not a shortage of testing for that.

What we find is that, if there aren't marketing incentives, it is a little bit harder under our authority to, frankly, get them to complete the postmarket studies. I haven't retired yet, but I am certain that I will see a well-completed postmarket study before I retire, and I hope I see one from genetics before I die.

But the issue is that in the consortium, that you need, probably, either more incentives, and voluntary incentives, or financing, or something, whether it is regulatory, that, with all due respect, this is a different community. It is one I am less used to dealing with. There may be enough interest and real passion among the academic part of this community to, frankly, push the limits and do the postmarket studies.

I, frankly, don't expect that of sponsors of commercial labs, because they are not social organizations. They are business organizations. Their business is to help support the public health. I don't expect them to necessarily, maybe, to donate to the symphony. I don't expect them to do great academic work. And so, some thought needs to be factored into what kind of strength you give this postmarket study.

In terms of clinical utility, I thought Dr. Feigal did a pretty good job, but I will reiterate in case you guys didn't get it, we don't do clinical utility. I don't know, there may even have been a test or two where we have looked at outcomes, but in the eight years that I have been there, ever remember us clearing anything as actually having clinical utility.

We always look at analytical validity, and we frequently look at a surrogate end point so that you can make clinical sense of the test, what its sensitivity and specificity in a defined population would be, but even when we cleared triponin [ph] we assumed that was going to help in dealing with patients with heart attacks. But we never went out and said, well, gee, that could produce improved triage and save 20 lives in this intensive care. We never did that. We cleared the test because of its behavior and the fact that there was biologically plausible benefits.

So if your idea of clinical utility from our standpoint is biologically plausible, we are very comfortable. Otherwise, I would suggest you give this to Muin and let him work on the clinical utility part, and it would be a great enterprise.

DR. McCABE: Well, that is partly why I think that we are arguing for a consortium, because we recognize that this isn't something that your agency is comfortable with.

DR. KHOURY: I appreciate Steve's comments. We come from different worlds and different cultures, but I am learning the FDA model by the hour now, I guess by the minute.

Let me reiterate the various ways and incentives to do this postmarketing piece and the three levels of complexities there that I mentioned yesterday. The first one, which could be the less intense type of analysis and review whereby you scan the appropriate published literature according to a pre-specified template or criteria, and then you put them back into this database of knowledge, or the knowledge base of what we know and what we don't know, which will include clinical utility.

The second would be the consortium model whereby you gather the groups together, including industry. I think there would be some incentive there for participation, if not financial, but at least otherwise to be part of this consortium, using a similarly predetermined framework for data collection. Then you go do this a bit more intensively, which will have a higher price tag for that.

Then the final step would be do the more labor-intensive technology assessment, which would take even further complexity coming back up with standards of practice and what is an appropriate use of tests using the U.S. Preventive Services Task Force model or the Cochran collaboration, or any of the above.

So for various tests, you can do any number of these, depending on public health needs, depending on the pressures, depending on the systems of classification, obviously. That would feed into this knowledge base of what we know and what we don't know.

But I wouldn't be too much easy on industry, getting them off the hook, saying, okay, we pre-approve. I think there could be some strong language and monitoring for that is obviously difficult to enforce from an FDA perspective, but when it is all said and done, if there is a knowledge base that is publicly available and there is a consortium out there that says, okay, here is what we know and what we don't know, and then you put up on the Web a bunch of empty boxes that the health care providers wouldn't know how to interpret, or the reimbursement mechanism wouldn't know what to do with that data, to me, that is a strong disincentive for industry not to participate.

That is two double negatives. If there is an agreement on a framework or a model for how we do this,

and then you go slowly build that database or the knowledge base, initially with a bunch of empty boxes, year after year with more knowledge, eventually leading to technology assessments in some fractions of these cases.

So we can build that knowledge base together. And it is a little bit different from the pure regulatory framework that Steve has in mind, but I think these two models hopefully can work together, side by side.

DR. McCABE: Okay, let me tell you what I want to do now, because we still have some public comment at the end and I want to be sure we have time for that. I would like to spend the next 10, 15 minutes going through the bullets in our document, recognizing that some of them have been modified, and discuss with you what I would write in the letter.

Now, it will be organized differently than it is organized here, but I want to hit the high-priority points. As I look through them, there are some that don't require a lot of resources, some that are more philosophical. But I would like to talk with you, and then be sure that all of you agree with the letter that I am going to write after this meeting.

But basically, if we go to page 13, which is where we first see bullets, we talk about no tests being introduced before it is established. Some of these were modified by yesterday, and Sarah has those modifications. We will get them up tomorrow, but I just want to have a good feel for the prioritization before we end tonight.

Basically, that first bullet is really subsumed into the large one that we have just been working on. That one does require resources. It will be a high-priority but it is stated more philosophically, at this point. Definitely, the public should be involved. Again, there are some issues in terms of travel there, but they are relatively minor and it is important that the public continue to be involved.

We will talk about genetic education and counseling, and speak to the education piece as what we will be doing as one of our next proposed activities.

And then, we have already advocated for the genetic anti-discrimination, and we will reiterate that in this letter, that we feel that this is a cornerstone to the continued development of this.

Any disagreement so far on that?

[No response.]

DR. McCABE: Under Issue 1, on page 13, again, that bullet will be brought into -- it is part of the logic for the subsequent bullets.

And then we jump ahead by quite a few pages before we get to other specific recommendations. On page 19 there are some bullets, but again, they are criteria. They are more logic than recommendations, per se. If you go to page 21, I don't think we have changed, that first bullet was what we have said today, that the responsibility for collecting initial data on the analytic validity of

tests lies with the test developer. Initial knowledge of clinical validity is essential to assess safety and efficacy. We have talked about that.

Since data sharing and analysis are critical -- and again, some of these have been modified, but we will get back to those modifications. But again, this is big piece of all of this is what we have been working on for the last hour.

DR. BURKE: I just want to comment, in both bullets 2 and 3 need to come into consistency with what we say later in the document about data collection. I don't think we need to work on the words now.

DR. McCABE: They are not exactly the same as what we came up with yesterday either.

DR. BURKE: Right.

DR. McCABE: So we can look at those tomorrow.

Obviously, protecting confidentiality and privacy are important. Laboratories should be encouraged or required to make pre- and postmarket data on genetic tests available in a timely, accurate, and understandable manner. And we talk about the coordination of that. So again, I think what is going to come down as the top priority and the most resource-intensive is the bullet that we have worked on for the last hour.

Postmarket data collection, again it is subsumed, really, within that bigger thing. On page 22, additional oversight is warranted. Again, that is not where the resources are. It is the implementation of that.

Then on page 23, we have changed this bullet substantially, and what Joann is working on now is breaking it down into three sub-bullets that have pre-market, postmarket, and the role of the SACGT. It was getting a bit long and things were getting lost in the middle, she felt. And I think that is wise, since it is so important to have it so it is understandable and easily visualized.

CLIA. Again, I think we may have modified that one. Okay, we didn't modify that one, but that is fine. The DHHS agency should be provided with resources, sufficient resources, to carry out this expanded oversight. Again, that is why we are going to say that is the top priority and will require the most resources.

IRB review. I don't think anything has changed there. And that will require some resources, and we will talk to that, that there needs to be education of IRBs about these genetic issues. Some are developing boilerplate that may be helpful, and some of that should be coming out fairly soon. On page 26, "FDA should give particular attention to the review of genetic tests that are used to predict diseases." So we are basically beginning to say what are high-scrutiny diseases. Again, I think that becomes subsumed in that major summary bullet. We talked about social and ethical concerns.

There is a typo, Sarah. No. 4 here needs to come out.

MS. CARR: Whoops.

DR. McCABE: We changed the next bullet to a multi-disciplinary group. There should be something about given deemed status. I am sure Sarah has this in her usual clairvoyance. She takes all of our thinking and puts it to paper.

Then that "individual and family members considering a genetic test should have access to appropriate genetic education and counseling." I think that is very important. Again, that may fall out of the federal agency, and therefore no resources for the agency, for the department.

Written informed consent. Again, that is important. "Current regulations under FDA and Federal Trade Commission should be enforced." Those will require resources, but we are saying that current regs should be enforced.

So in my read of this, what I will highlight in our letter is the bullet, the big bullet that we spent the last hour, hour and a half, working on, because I think that lays out the structure. It does require an investment of resources, but I think that we can argue that the American people, through the outreach activities that we were charged to carry out by Dr. Satcher, have really requested that there be this increased oversight. So that, the investment that is being requested by the American people.

DR. GUTMAN: I have a very important clarification, just to make sure that I am understanding this. Of course, I guess there is still a chance for editing and for interpretation when it goes to the Secretary.

You really are talking about new genetics tests, and you are talking about a freeze in the status quo. So that if we were to register and list those tests on the market -- you are defaulting them to a consortium, so that our liability is limited to things that are not now on the market.

Am I interpreting --

DR. McCABE: My interpretation of what we have said in that large bullet is that, first of all, that there not be a freeze until we get this system in place. The way I have read this committee and the input from the public, that is not what we want. We do not want things to stop, that a system should be developed and once it is developed and reviewed, then that would shift into place. Until that time, then things will continue as they are now.

DR. GUTMAN: No, I understand that perfectly.

DR. McCABE: Now, that is for new tests. There was a bullet that, again, we worked on yesterday. I don't remember which. It is on page 26. Is that right?

Where is it, Sarah? Okay, so it is on page 26. It is the one that used to have about the USPSTF. It now reads: A multi-disciplinary group given deemed status for this purpose should review genetic tests that are already on the market for evaluation of clinical efficacy and developmental guidelines about their appropriate use.

That, we worked on yesterday. There is a whole series of these that Sarah took what we had discussed and wrote out last night. I don't know that we will get to those until tomorrow, look at the specific language, until tomorrow afternoon.

DR. COLLINS: I am not sure I quite understood the consequences, but I am a little worried about setting up a situation where there might be sort of an avalanche of tests put on the market quickly, before this new system comes into place, tests which may be of very limited clinical validity.

Are we setting up a circumstance where people will try to be grandfathered, and we will have a lot of grandfathers that we later on regret?

DR. McCABE: Well, what we are saying is that there will be a group that reviews those. So, in fact, if that happens, that they will be subject to review. And I would certainly think that that group would look at the timing of that submission, along with the claims that have been made on them.

On the other hand, I understand your concern. This has been discussed before. I think that it has also been fairly clear to me -- but this is to me, so the committee should discuss this -- that we also do not want to enter a situation where there is an important disease for which a gene is identified next week, and we say, oh, that can't move into the marketplace because of the SACGT recommendations.

I personally would feel that that would be one of the worst things that could be an outcome of our deliberations, but that is probably worth discussion if others -- please, I am speaking now as a member of the committee, and not as a chair of the committee, so if you disagree with me, please say so.

MS. DAVIDSON: I agree. And I just want to also elaborate that we really heard at least two voices from the public. One was certainly caution and concern about the quality of tests, but there was also a very strong voice, particularly from the lay advocacy groups about the need to not set up structures that in any way is really going to slow down or inhibit research.

DR. CHARACHE: I agree. It would be a very serious mistake to say that we couldn't introduce new tests because this is going to take a while to work out, but I wonder if perhaps the wording could be changed slightly to -- or, perhaps add, using the principles employed for new tests, will review. So it makes it clear they are not going to get a free ride.

DR. McCABE: Okay, good. I think that is a very important addition to that bullet, and we can add that when we review the language tomorrow.

MS. BOLDT: I guess I have a question. Do we want to add language to this bullet point that you just read that we also, as the SACGT, would like to be involved in forming the specifics for reviewing tests already on the market?

DR. McCABE: Again, maybe we can put that in the letter because I think that we are saying that overall, that we want to continue to have involvement in this, that the group that works out the details. So basically, we are floating this to the Secretary. If she agrees that we are headed in the right

direction, then we would work on the details.

MS. BOLDT: But that is not explicit now.

DR. McCABE: See, what I was thinking was putting it in the letter to say that for all of this, we want to continue to be involved in the implementation.

Is that sufficient, do people feel, or do we need to include it in the bullet? I think we would include it in almost every bullet is the concern. We have put it in the big, sort of the big bullet. If you feel that this is important enough, perhaps it is, since this is all the old tests. The other was the new tests. We could add language.

Kate, you could add language saying that we wanted to be involved here, because that is then the two major action bullets for the thing. That's fine. But we will put it as an overarching thing in the letter.

DR. COLLINS: This is a different point, but I recall yesterday when we talked about the definition of a genetic test and got more explicit about what is under that umbrella then we had been before. We agreed we need to come back and look at some of the bullets, because in fact we have now extended the definition to include tests that are being used solely in research, as well as tests for somatic mutations.

I think some of the language that is in here, particularly about, say, FDA involvement in all genetic tests. If we are now deciding that this includes tests which are solely being used in research arenas, those go through IRBs, and it may be that the bullet that we have in that regard needs to be modified. We talked about we are going to have to come back and fix this, but we never did.

DR. McCABE: Okay, I think Francis' point is that you can have tests that are clinical research, but the test is a clinical test, in essence, being used in a research setting.

Is that right? So we had said that research should be done under IRBs.

DR. COLLINS: Which absolutely is right. I am just worried about some of the bullets that are talking about genetic tests that FDA should be involved in reviewing as though they were actually being used in clinical settings. I am more concerned about tests which are being done where the results are not given back as part of a research protocol, which still needs IRB approval, but it would not involve the FDA, per se.

DR. McCABE: We are going to go one quick pass over this tomorrow and look at some specific language. If you could identify for us which ones. If you can get that to Sarah at the beginning of the morning tomorrow, we can then get it up in PowerPoint so everybody can see it.

DR. BURKE: Just following up on that same point. It is possible that we can capture this in the principles in that paragraph based on Reed's points that is going to come before the FDA paragraph. It is also possible that we can capture this by making it clear the pre- and postmarket approval processes have to do with when a test is ready for commercial.

The other piece, the one that really does come under the test classification concept, we may want to explicitly capture that test classification will look at level of scrutiny based on characteristics of the test, but also taking into account characteristics such as somatic versus inherited mutation testing and orphan disease issues.

It may be that we want a little bit of that specificity in that test classification bullet.

DR. McCABE: Could you perhaps look at that tonight to help Sarah with the language? Is that Issue 2, Wylie?

MS. CARR: In Issue 2, you are going to add?

DR. BURKE: Well, it could either be added in Issue 2 or in the paragraph that is going to precede the FDA, that sort of final summary thing. I think Reed had an introductory concept about the importance of test classification.

MS. CARR: I think that would address the problem some people identified of lack of consistency between Issue 2 and what we decided, or you decided, in 5; right?

DR. BURKE: Yes. I will look over the language, the characteristics listed in Issue 2, and see if those need to be modified. Then we can look at what this rewritten paragraph looks like tomorrow and address the consistency issue.

DR. McCABE: Barbara, Pat Charache, and then we are going to have public comment.

DR. KOENIG: I just have one point that I don't have clarity on, which is, in terms of the process that we are recommending, will the entire initial review of all new genetic tests proposed be done within FDA itself, or will that be done as part of the consortium?
The sort of entry point at which the assessment of different levels of need for oversight, different levels of scrutiny, I am not clear as to how that is going to be accomplished. Maybe I have just not been paying attention.

DR. McCABE: At this point we have still said that they will be responsible for it, but I think the way it reads, we have implied that they may need to seek help with this. Somebody has to be responsible. We have still left them responsible for it, is the way I read that.

DR. KOENIG: I have two other points. Are we going to come back to the additional recommendations that we also didn't get to? In particular, I am concerned about whether we finished the discussion about genetic education and counseling, and the direct-to-consumer market issues.

DR. McCABE: The bullet is in there, in terms of the direct-to-consumer market, that HHS should enforce the current regulations. So I think that is still in there. That is the way we had left it the last time, was saying, the regulations are there, they are just not being enforced.

Regarding your other point, your first point.

DR. KOENIG: The genetic education and counseling.

DR. McCABE: Yes. I think that what we are going to do is, after our discussion this morning, say that we need to visit that and develop another position on that. We have talked about whether we call a strategic plan or a white paper. I don't think we have decided. We will probably decide that at the next meeting or tomorrow afternoon.

DR. KOENIG: Okay, so we will be able to discuss that further, or we will table it for later discussion.

DR. McCABE: Right. That will be one of our next -- my take on this morning's discussion was, that will be one of our next products, will be to try to develop some strategic plan for improved education.

DR. KOENIG: Well, my only concern is the issue of the suggestion that I made yesterday about whether -- and I am not sure if this is relevant in terms of resource allocation and involvement of HCFA, for example -- but since the public comments about the need for genetic education and counseling and tying that into tests were so strong, do we want to somehow tie together the notion that if tests are going to be offered and paid for, it should be done in concert with genetic education and counseling?

DR. McCABE: Let me read what we wrote yesterday. I can't remember if we wrote it, or if Sarah, again, deduced:

> Genetic education and counseling is required for any test of high scrutiny. There is an insufficient supply of health professionals trained in genetics, and greater efforts are needed to train health professionals in genetics.
>
> Because genetic education and counseling are essential features of genetic tests, organizations that pay for genetic tests should also pay for the education and counseling services.

Is that the sense that you wanted included? Okay.

DR. CHARACHE: One of the concerns that we have had expressed is the thought that all genetic tests will require the same level of scrutiny. I am not sure whether we have added the comment, which I have got here as:

> The level of oversight scrutiny required for a given genetic test will vary with the category of the test and the complexity of its technology.

DR. McCABE: We certainly discussed it. We will capture that. I think that was part of what Wylie was talking about, too. We will make sure that that is clear in the document.

DR. CHARACHE: I think there are two purposes to that. One is the category of the test. The other is the complexity of the technology required to perform it accurately.

DR. BURKE: And I will make sure that I look at that, vis-a-vis what was written in Issue 2, but I think when we look at that rewritten paragraph that includes the FDA stuff, and Reed's stuff ahead of it, we need to make sure that the idea is consistently captured there as well.

DR. McCABE: Pat Barr, do you have anything to add?

MS. BARR: I am here. No.

DR. McCABE: Okay, thank you. Are you going to be with us tomorrow?

MS. BARR: I could be, yes.

DR. McCABE: It is up to you.

MS. BARR: Well, no, I can be. If we can set it up again, it would be great.

DR. McCABE: Okay. Sarah is reminding me we start at 8:00 tomorrow.

MS. BARR: That might be hard, so maybe I can call in the number and then you can call me.

DR. McCABE: That will be fine. We will be happy to do that.

Before we break for the evening, we have a time for public comment. Is there anyone in the audience, any members of the public who have any comments or questions for us? Other than Mike Watson.

DR. McCABE: Go ahead, Mike.

DR. WATSON: Only, actually, a couple of comments based on where we have ended up rather than why we are there.

I would not forget that not just rare diseases but there are rare mutations within extremely common diseases, and I wouldn't want those to get constrained in the ability to go looking for them. They tend to be the most highly complex analytical methods of genetics, probably. There will be many families out there who won't be able to access the high level of complexity of what may be their rare mutation or their private mutation in that individual or family.

So I would capture both the rarity of the mutations within common diseases, as well as the rarity of the diseases themselves.

DR. McCABE: Yes, Elliott, Elliott captured that concept earlier today by talking about the orphan test, as well as the orphan disease. We will try and figure out where to incorporate it into the document because I think that is an important point.

DR. WATSON: And on that point, I would think that there is probably also room for CLIA to be looking at those very high-complexity levels, because certainly within the laboratory community we have been developing methods whereby within the CAP programs. We are going to begin tiering the inspection process so that we have board-certified laboratory directors inspecting those laboratories, performing those most highly complex methods of genome scanning and interpreting some of these rare variations.

DR. McCABE: Thank you. Judy, do you want to comment on that?

MS. YOST: I just wanted to say we recognize our shortcomings and appreciate your comment, and we will be talking to you about helping us resolve that because we are also thinking that the majority of the laboratories, actually, are going to be conducting these tests are probably going to be accredited anyway.

So I mean, it may not be worth the added value for HCFA to do all those inspections. We have to look at various models ourselves, how to oversee those.

DR. WATSON: I think we can target a lot of the pieces by the consortium approach a lot better than we can by any individual group.

MS. YOST: Exactly. I see another role for the consortium there, personally.

DR. WATSON: Although I probably shouldn't, I think the one concern that I have with FDA, we have talked about home-brew and we have talked about off-label use, but one of the things that comes with FDA's increasing authority is also increasing control by the legislative process. Genetics will and still does have a significant reproductive decision-making component to it. And I would want to make sure that we didn't compromise that by where we place various levels of oversight.

DR. McCABE: Point well taken. Unfortunately, I think you are right, that as we increase federal authority, we also increase federal control. So I think that it is something to keep in mind and to observe as we move forward.

Any other comments from the audience?

[No response.]

DR. McCABE: Just for the panel, the staff has made reservations for six at Asia-Nora at 7:15, so if there are five others, then I am sure we can probably expand. It is an American cooking with Asian influences on M Street. So if anybody wishes to join me at the restaurant, please just let me know. We will be leaving here about 7:00.

Thank you very much. We will recess until tomorrow at 8:00.

[Whereupon, at 5:55 p.m., the meeting was adjourned, to reconvene at 8:00 a.m., Wednesday, June 7, 2000.]