P R O C E E D I N G S (8:15 a.m.)

The Oversight of Genetic Tests

DR. MC CABE: Good morning, everyone. Welcome to the sixth meeting of the Secretary's Advisory Committee on Genetic Testing. The public has been notified about this meeting through an announcement in the Federal Register on July 12, and a posting on the SACGT's website. We appreciate the public's interest in our work, and we would welcome hearing from members of the public in attendance during the comment period this afternoon.

We have three main goals for today's meeting. First, I would like to welcome Dr. Beverly Malone, Deputy Assistant Secretary for Health. Dr. Malone will brief us on the steps the Department will be taking to review SACGT recommendations on oversight of genetic testing in preparation for transmitting them to the Secretary.

As you know in our meeting in June, we reached unanimous agreement on our final conclusions and recommendations regarding the oversight of genetic tests. We submitted our final report, Enhancing the Oversight of Genetic Tests, to Dr. Satcher in mid-July for transmittal to the Secretary. Dr. Malone will explain the process that has been put in place to review the report and gather relevant agency perspectives on the advisability and feasibility of implementing our recommendations, as well as the timetable for completion of this assessment and the target date for transmittal of the report to the Secretary.

Although we have submitted our final report, there is a key element of the recommendations that we are still working on, the development of a classification methodology to determine the degree of scrutiny required for a given genetic test. The methodology can be a useful tool to help the Department focus attention and resources on these tests that require the most scrutiny.

We have put a working group together chaired by Dr. Wylie Burke to help develop the methodology. The working group met yesterday, and Dr. Burke will report on the outcome of the meeting, and lead our discussion of the issues and the categorization of genetic tests.

I want to thank the members of the working group, and Wylie for your leadership. As everyone will hear today, important progress was made. It was a great meeting, and thank you, especially to Wylie.

Our goal today in the second task is to work toward an approach that we will recommend to the Secretary.

Our third and final agenda item for today is to engage in an extended discussion of current and emerging issues in genetic testing. The goal for this discussion is to identify future study topics, set priorities and outline our next steps.

I have just a couple of updates that I would like to tell you about also. In your packet, the green packet, you will see a letter from Secretary Shalala thanking us for the letter of April 24 2000, requesting that high priority be given to support and for enforcement of legislation prohibiting genetic discrimination. Secretary Shalala stated her strong support for this legislation.

Also, yesterday I was invited to brief Dr. Ruth Kirschstein, Principal Deputy Director of the NIH and her Institute and Center Directors on the SACGT. We had an insightful and vigorous discussion, and it certainly helped focus some of the issues for me, and I think it will be very helpful to all of us.

For those of you who represent your agencies, this is something that we would like to do with each of the agency directors. So you might talk with Sarah about setting these briefings up.

Also yesterday, as Chair of the SACGT, I was asked to brief Phil Barnett and Kristin Amberling, staff to Henry Waxman, the ranking member of the Committee on Government Reform and Oversight, who wanted to hear what we had learned about patents and licensure at our last meeting.

Before we get started, Sarah will review the conflict of interest rules with us.

MS. CARR: Thank you, Dr. McCabe. As you all know, you are considered special government employees when you are here for SACGT meetings, and thus you are subject to the rules of conduct that apply to government employees.

The rules and regulations are written down in a document called Standards of Ethical Conduct for Employees of the Executive Branch, which you were provided at the beginning of your service.

I'm just going to remind you about two of those rules today. One rule relates to conflict of interest. Before each meeting of the Committee, you are asked to provide us with information about your personal, professional and financial interests. This information is used as the basis for assessing real or potential conflicts of interest or even the appearance of such conflicts that could compromise your ability to be objective in giving advice during our meetings.

If you are found to have conflicts, waivers can be granted, because the need for your advice outweighs the potential for a conflict of interest created by your interests.

Most of you have been granted waivers for general matters. If a specific issue comes up during the meeting that could affect your interests specifically, you will have to excuse yourself from the deliberation or participating in the discussion, and leave the room.

The other rule I wanted to mention was confidentiality of the information. Sometimes you are privy to confidential information, and this is the case right now. We have completed the oversight report, submitted it to Dr. Satcher, and until it goes to the Secretary it is considered confidential. So you are in possession right now of confidential material, and you have to maintain the confidentiality of that.

We are going to be hearing from Dr. Malone about the timetable for the submission of the report to the Secretary, so we will have a better sense of when we might be able to release it to the public. But please maintain confidentiality with the information you receive as confidential.

Thank you.

DR. MC CABE: Thank you, Sarah. We are very pleased that Dr. Malone could join us this morning to tell us about the steps that the Department will be taking to review SACGT's recommendations on oversight of genetic testing in preparation for submitting them to the Secretary.

As Deputy Assistant Secretary for Health, Dr. Malone is one of Dr. Satcher's key advisors in substantive program and political matters, policy and program development and legislative priorities. She also serves as an advisor to the Secretary on public health and science issues.

Prior to joining HHS, Dr. Malone was Dean, Interim Vice Chancellor of Academic Affairs, and professor at North Carolina A&T State University School of Nursing. In the 1980s, Dr. Malone was the Assistant Administrator for Nursing at the University of Cincinnati Hospital. Her clinical experience includes practice, both as a registered and medical surgical nurse in private practice and personal therapy and professional consultation.

Dr. Malone was president of the American Nurses Association from 1996 until this January. She has served in important advisory roles as a member of the U.S. delegation to the Royal Health Assembly and the Advisory Commission on Consumer Protection and Quality in the Health Care Industry, as a participant in the President's Roundtable Discussion on the Patient's Bill of Rights, and as a board member of the National Patient Safety Partnership. Dr. Malone holds a bachelor's degree in nursing from the University of Cincinnati, a master's degree in adult psychiatric nursing from Rutgers University, and a doctorate degree in clinical psychology from the University of Cincinnati.

Thank you very much for being with us today, Dr. Malone.

Report on HHS Review of the SACGT's Final Report on Enhancing Oversight of Genetic Tests - Beverly Malone

DR. MALONE: Thank you. I am delighted to be here. I think I have been with you before in Baltimore, at the School of Nursing, and so this is my second opportunity to join you.

I bring you greetings on behalf of Dr. Satcher, who also sends his strong appreciation to the Committee for the laudable job you have done in your report. We anxiously awaited it, Enhancing the Oversight of Genetic Testing recommendations of SACGT, and he has received that report.

In receiving the report, he delegated our group to get together -- when I say our group, I mean our Department -- in terms of developing a response and recommendations to the proposed recommendations that you had made, so that we would be in a supportive stance when the report went to the Secretary. That group that came together involved the CDC, the FDA and involved our colleagues in HCFA.

Then we also had Dr. Bill Raub and Lily Engstrom, who is with us today, in terms of ASPE, which is basically our -- who is the Assistant Secretary for Planning and Evaluation; that is Dr. Raub's position. So we had a group, and then we had OPHS. This is a very small group, but we

wanted to make sure that we were focused on the issues that we needed to be. We don't have the larger group. There is a larger group that meets on a regular basis about genetic testing. Dr. Raub is the chair of that group.

The group that is meeting is the group that has the majority of the responsibility for the oversight of genetic testing within HHS. We wanted a coordinated response, not just individual responses from each group. We thought the best way to do that was to pull ourselves together and make that happen.

Just to give you the background about the larger group, the larger group is the HHS Genetic Testing Group, chaired by Dr. Raub, as I pointed out, with representatives from AHRQ, which is the Agency for Healthcare Research and Quality. It used to be ACHPR. From HRSA, our Health Resources and Services Administration, from NIH, from CDC, from FDA, from HCFA, and from ASPE. So you can tell that we have narrowed it a little bit.

They will continue to meet and Dr. Raub will serve as the liaison between the two groups.

The goal is for our SACGT small working group to complete its work in the next several weeks. We will make recommendations to Dr. Satcher. He will then accept, reject, whatever he would like to do with our recommendations, and forward the report to the Secretary. At that point it will be a public document when it is received by the Secretary, and it will go into clearance. It will be cleared within the whole entire agency.

So that is the process that we are using. The time line is not as specific, I'm sure, as you would like it. The next several weeks is a little bit vague, but that is the best I can give you at this time. I am open for questions and any discussion that you would like to have about what we are trying to accomplish in I believe a very complementary and supportive way of the work that you have already done.

DR. MC CABE: Thank you very much. Do any of the members of the Committee have questions for Dr. Malone? Any questions about the process now? Could you perhaps explain the kind of recommendations? We talked a little bit about this yesterday, and to me it seemed like this was kind of an implementation report that you would be doing out of Dr. Satcher's office that would then go to the Secretary, is that correct?

DR. MALONE: I think that is a very appropriate way to describe it. It would be what it would take to make it happen. We have the right players talking about that.

So I believe that it will be a more complete package when it goes to the Secretary.

DR. LEWIS: My question is, you were talking about the various agencies that were involved. Many of those agencies if not all of them have had ex officio members on this Committee. I'm just curious in terms of the coordination between the reviewers that you are using and the people -- are we able to get the expertise of the people in terms of the agency coordination?

DR. MALONE: I'm happy to say that the people that

are representative in your work here are the people that are meeting with us around the table. They have got too much invested not to be around that small working group table.

MR. HILLBACK: I guess I would just ask, are there any things that you think will get in the way of this moving along over the next four or five weeks, giving time for Dr. Satcher to write a cover letter, et cetera?

DR. MALONE: My understanding is that the recommendations that you made are very representative of things that we have dealt with along the way. There is not a lot of surprise in those, although there is more clarity.

It is almost as if there has been a getting ready phase -- timing is everything. I think if I were talking astrologically, the signs are lined up for us to get this work done.

DR. MC CABE: I think also, as I mentioned to you in our conversation in the middle of yesterday afternoon, I was very optimistic that we would have the addendum to you according to our schedule of September 30 from the working group that met yesterday. By the end of the afternoon, they had in fact achieved a very important progress. There was discussion that this was something that had been attempted for five years unsuccessfully until yesterday.

So I think people are coming together and that we will have that part of the plan to you and the recommendation to you as anticipated, after our deliberations today.

DR. TUCKSON: Remind me, what happens if something that we push strongly in terms of our recommendation, but it poses a concern when it is finally reviewed by the Secretary, is there a mechanism or an opportunity for further conversation about that before this is over?

I know our meetings are set at some periodicity, but could there be a scenario where we could recommend something, let's say the addendum that Ed just talked about, which we worked pretty hard on and will discuss a lot today, let's say you all don't like that. Is that like, we don't like that, throw it out and that's the end of it? How does that work?

DR. MALONE: I would turn to the staff or to Dr. McCabe to answer what your options are. I just know that I work for the Secretary, so maybe they could be clearer on those options.

DR. MC CABE: The other thing that I should mention is that I have been invited to brief Dr. Satcher on August 22. So we will have some time to discuss both the progress that we make today as well as perhaps the progress that has been made at that time.

DR. TUCKSON: So it is a face to face that will occur, a chance for clarity or clarification if there are areas of concern, and if necessary you could bring that back to us?

DR. MC CABE: Yes, certainly.

DR. TUCKSON: Thank you.

DR. MC CABE: Is there anything else? If there isn't, thank you again, Dr. Malone, for taking time from your very busy schedule to be with us this morning.

DR. MALONE: I have to tell you, colleagues that Dr. Satcher is not in the office this week. My boss, Dr. Lurie, is also not in the office, so I am in charge. So I appreciate the fact that you kept this brief for me.

DR. MC CABE: Thank you very much. One of the key recommendations we made in enhancing the oversight of genetic tests is that the FDA should be involved in the review of all new genetic tests and that the agency should develop new review processes for this purpose, in collaboration with other agencies, private sector organizations and public representatives.

We recommended that the FDA should correlate the level of review applied to a test with the level of scrutiny warranted by the test. We also said that the level of scrutiny required for a particular genetic test would vary, depending on a number of factors, including the unique characteristics of the test itself, and the targeted disease or condition.

To assist FDA in determining which tests warrant more thorough scrutiny, we concluded that a classification methodology was needed for this purpose. Although we outlined a number of possible criteria for and approaches to test classifications in our final report, we realize that the task of actually developing the methodology required the additional time, effort and expertise of an ad hoc working group.

I asked Dr. Burke who made extensive contributions to the development of our recommendations regarding the criteria that should be used to assess the risks and benefits of genetic tests, which will be the basis for the categorization scheme, to chair the Working Group, and many of you agreed to be on it. We also invited a number of other experts to serve on the group. A roster of the entire Working Group is in your meeting folder.

As Dr. Burke will explain, the goals of yesterday's Working Group meeting was to work toward the development of a proposed test classification methodology. As you will recall, we indicated in our final oversight report that we would complete the methodology by September 30, 2000, and submit it to the Secretary as an addendum to our final oversight report.

Dr. Burke, we are all eager to hear about your progress yesterday and begin our own discussion of the methodology. Again, I want to thank you and all the members of your Working Group for coming together yesterday and putting together what seems to be a very workable draft of the methodology.

Report on the SACGT Working Group on Classification of Genetic Tests - Dr. Wylie Burke

DR. BURKE: Thanks, Ed. I think we had a very active and productive conversation yesterday. I have a few overheads to go through the basics. I am going to end with a list of issues that we think still require a fair amount of discussion. I will try as I go through the outline of what we are proposing to identify those issues that will then come up later.

But I want to start with a diagram that Joann did

for us that really helped us to focus where we needed to focus. This diagram acknowledges that when you think about test classification, there are two categories of issues. One is lab issues and the other is in generic terms medical and social issues.

Under lab issues, you might ask whether or not the test is complex, and if the answer to that is yes, there would be issues around ensuring that the test is done accurately and that procedures are in place for appropriate quality assurance.

Early in our conversation with Joann's help, we identified that there actually are procedures in place at the FDA for this kind of determination. Above and beyond that, we have the ongoing work of the lab forum which is working together collaboratively to put particular attention on issues raised by genetic tests, particularly home brews that have not traditionally come through FDA review. So we felt that this was first of all technical work, and second of all technical work that was either in place or in process, and that that was not the troubling or difficult issues that we needed to focus on. Rather, what we needed to focus on was the issue of how do you take a test and sort out the medical and social issues and try and determine whether a test falls into what we had been calling going into the meeting low scrutiny or high scrutiny.

As you will see in a moment, we are now talking about scrutiny levels one and two.

So I just want to introduce this by saying, this is where we focused our attention.

Then we had another table that helped to clarify gains that Francis has provided for us. That was one which helped us to envision the different stages at which a DNA test might occur or a genetic test might occur, recognizing that our definition of genetic tests is broader than DNA.

We call these steps A, B1, B2 and C. A is a circumstance where testing may be done, but this is done within a research setting and no data is returned to an individual patient. So this might be in the very early stages of genetic test development, where there may be some population data being accumulated. There may be some basic association questions being addressed, but patients are not receiving information back.

At this step, IRB review pertains to the research. Neither CLIA nor FDA is involved.

At step B1, there is a transition, because we now have testing still being done under the research umbrella, but testing results are being given back to individuals, either back to the patient, the person who was tested, to the person's family or to the person's physician.

IRB review still pertains, but because results are being given back to an individual patient, CLIA oversight is also a factor.

Then we get to level B2. B2 is the point where tests are given to patients -- actually, let me say we then transition to B2 or C, and let me clarify that in just a moment. But the fundamental transition is that tests are now being undertaken and results are being given back to

patients outside of research settings, and the people who are being tested are no longer human subjects.

So IRB review is no longer the oversight mechanism, and it is at this point that we envision the FDA oversight can occur. CLIA oversight is an ongoing issue obviously in terms of oversight of laboratories, but when we have talked about FDA having a pre-market review, this is the point at which you have to have the pre-market review. In other words, this is market as we go to B2 or C, and it is before B2 or C that we need the pre-market review that FDA is involved in.

Now a word about B2 and C. We had struggled for quite a while, and I think this table helped us get to the point of recognizing that in a general way there are two kinds of genetic tests. There are genetic tests that have enough clinical validity that at least under certain circumstances it is reasonable to use them in a clinical setting outside of the research protocol. Yet there still are many questions about them, and a great concern to have ongoing data collection and study.

That would be B2. C represents those genetic tests where we have a fair amount of certainty about what we are doing, but we may still have interests in ongoing data collection, but we feel like the major questions are answered.

So the point is that a test jumps from the A-B1 range to the B2-C range, and that is the point at which FDA review is important, but there may be different pathways. There may be the occasional test that goes from A to C. That is going to be rare. There may be tests that go from B1 to C. A lot of genetic tests though probably go through the B2 phase.

So we found weighing this grid out helped us to see where the FDA reviewed occurred, and helped us then to think about test classification for that pre-market review. It also underscores a point that I will get back to, which is the tremendous importance of coordinating IRB oversight and FDA pre-market review.

The next issue that we worked through was the concept of different levels of review. In thinking through the different levels of review, we were thinking about that B2 and C classification, that is, the concept that some tests come to clinical use for good reasons, because they have clinical uses, yet have lots of questions associated with them. In general, we will see those as requiring greater scrutiny. Other tests are relatively straightforward, major questions appear largely answered, and those seem to require less scrutiny.

We thought it was useful to be a little bit neutral in our terminology, so we adapted scrutiny level one and scrutiny level two to capture those.

I just want to go through the bullets here. You will see that many of the bullets are similar, so I am going to emphasize as I go through the differences in character for these two reviews.

Scrutiny level one, first of all, is a streamlined review. We see the genetic tests that are pretty

straightforward and don't raise a lot of questions and don't have a lot of uncertainties attached to them, as deserving an efficient mechanism of review.

The scrutiny in level one and level two would be reviewed by standards that are agreed to collaboratively. So I think that is a really important point. This had come up in previous discussions. This was folding in a point that we had discussed before, that we would see standards set in consultation with professional organizations, consumer representatives and others, potentially a collaborative group of agencies.

So you have this streamlined review, a test offerer who knows ahead of time what the standards are. There are straightforward standards, a test needs to meet those standards, and so there is a packet of information that is pulled together that includes the test offerer showing how those standards are met.

It includes assurance of pre-test and post-test information per a standard template. Let me spend a little bit of time on that, because that was another major concept for us, and I think one that really helped us to get through our work yesterday.

That is, the concept that one of the most important things for any genetic test is that people have appropriate information before and after the test. Before the test, that appropriate information includes indications for testing and test limitations. There should be clear, readily accessible information for people who are tested, for docs who order tests, that explains what the test does and doesn't do, what the limitations are going into the test.

Then afterwards, there should be a mechanism for reporting test results that also is clear and enables the average clinician to interpret what happened as a result of the test, what the test means, what the limitations in the information coming from the test are.

Again, we would see this as a process that will include collaborative work from professional organizations and other interested parties, and we would see the development of these kinds of standardized and complete information materials to be a critical aspect of appropriate delivery of genetic tests.

After that, we have some questions, and these will come up in both lists. We think that there may be a need to think about methods at least voluntarily for reporting adverse consequences, as for example adverse consequences are reported for drugs. We would like to capture adverse social consequences and we are not sure how to do that. But we want to acknowledge that that is an important issue that should be discussed.

We have for all genetic tests the question of how do we ensure informed consent, so we capture that question there. We do anticipate that even at scrutiny level one, there will be some ongoing data collection. When we note that that is likely to involve existing resources, what we are saying is that it may well be that for tests that fall into scrutiny level one, the concern with ongoing data

collection will be perhaps largely in the level of routine surveillance or other kinds of data collection methods that use existing strategies and resources.

There are different options. Once a test goes into scrutiny level one review, different potential outcomes. The test could be released for use. That is one result is pre-market review, in that the test will be ready for market or not released. A third possibility would be that something happens during the review in scrutiny level one that triggers a scrutiny level two.

So let me talk about scrutiny level two. Some of the same concepts are still there, so I am just going to emphasize the differences. First of all, we would anticipate with scrutiny level two that there is a detailed review of the pre-test and post-test information that is to be offered with this test, because there is particular concern that the information provided for a scrutiny level two test captures adequately the uncertainties and limitations of the test.

Again, it would be standards set in consultation with professional organizations, consumer reps and others, and the standards will take into account the greater potential complexity of the test. Other issues are as described for scrutiny one, the same concern with informed consent, the same concern to talk about methods for reporting adverse consequences. Then we would anticipate in scrutiny level two that data collection is really critical and may include new initiatives.

This might be very specific to different tests, that as tests come through the kinds of data collection that one might want to ensure might be different, and some tests might generate greater concern for outgoing data collection than others. We would anticipate that this could involve the need for new resources, depending upon the nature of the data.

The options or outcomes from scrutiny level two could include that the test is released, that it is not released, or that it is released with well-defined conditions.

So that was the background that got us to our scheme. Let me show you the scheme and talk about some of the issues that came up. Basically, we envisioned that the test would go through a procedure of questions that would enable it to be very readily determined as needing either level one or level two scrutiny.

I will talk about the first test that would come up for the first question, and I'll get back to it later because it is clearly an issue for discussion. But the idea was basically using a public health model, it makes sense to start with test volume.

We are not sure what the number is, and we are not sure how you would determine that number. Those are important questions. But the concept here is that the tests that are used relatively infrequently may a priori be the tests that we should not be focusing our greatest attention on. So the default for a test used infrequently would be that it will go to level one scrutiny. I will come back to

some of the issues that are raised with that concept.

That is the first branch point, tests not used very much, tests used relatively frequently.

Once we have determined that the answer to this is yes, the volume is above the level that would automatically put it into scrutiny level two, we then ask the question, is this test being proposed for population-based screening. This is not necessarily universal screening, but this is testing on the basis of a population designation rather than on the basis of a clinical condition. So this is testing of all persons of Ashkenazi Jewish descent, for example, for a given condition, or all pregnant women for a given condition, or any kind of other defined population-based screening.

We would say if the tests are proposed for population-based screening, it goes into scrutiny level two. If the answer to that is no, then the next question is, is the test predictive or diagnostic. That is, is the test being done on a person who has a medical condition for the purpose of identifying and determining that medical condition. If the answer is no, it is not predictive, it is not to predict future, but is it being done for diagnostic reasons, then it goes to scrutiny level one.

So here we have two automatics, population-based screening, scrutiny level two, predictive, not predictive, scrutiny level one. If it is predictive, if it is not diagnostic, then we ask some additional questions. Those questions get at three different criteria that would put a predictive test into the scrutiny level two category.

The first is, interventions are unproven or non-existent. The second is low predictive value. When we are saying low predictive value, we are taking into account the whole testing pathway. That is an important concept. That is, if you start with a genetic test and the test has in and of itself low predictive value but has additional confirmatory tests that can be done -- an example would be an HFE mutation test. If for some reason a person has an HFE mutation test and we have some possibility based on the positive result that that person may have hemochromatosis, we do have additional serum higher measures, for example, that we could do to determine the person's iron status.

So we look at the predictive value of the whole testing pathway that started with the genetic test. If there is low predictive value, that would be of concern.

Then finally, is there a significant potential for harm, either medical or social. Medical, what we are talking about is, does the test result potentially lead to a very risky treatment and particularly a risky treatment, the efficacy of which is not certain, or is there a potential for social harm.

I will acknowledge here and later that we need to work on the definition of that, but that would certainly include tests that might have significant stigmatization potential. An example for example would be a test related to increased risk for mental illness, for example. Any of those parameters would then put the predictive test into the high scrutiny level two.

So in summary, we would see scrutiny level two as appropriate to population screening tests and predictive tests that have certain characteristics that raise concern.

I'll give you an example of a predictive test that we think would not go into scrutiny level two. That would be a carrier test for an autosomal recessive disease with relatively high penetrance that is being done within a family. So that would be an example of a test that is predictive. It increases the likelihood that someone might face a question around an affected child, but that is a test that has good predictive value for identifying the carrier state for what it is intended to identify, and it is being done within a clinical setting under defined parameters, not a population screen.

By contrast, CF carrier testing done for all pregnant women would be a population-based test and would not fall into scrutiny level one.

So I think what I would like to do is talk about the issues. Or let me give you the choice. Should we stop and have any questions about this before we go into more detail about the issues?

MS. BARR: As you do predictive no or you go down to yes, you just gave an example when it is being used within families. Was there a sensibility that one is used for families and authorized in terms of low scrutiny that you are going to be able to prevent off-label use in a high scrutiny situation?

DR. BURKE: Yes. Actually, I think you are raising a very interesting question, and one that we think probably falls under the potential for harm social, or potential for harm whether it is medical or social, one could argue.

When you are considering the potential for harm of a test -- or let me start by saying, when you are considering a test in this algorithm, you are not considering a genetic test. You are considering a test used under defined circumstances. So it would be a carrier test under the circumstances used in family testing, but not in population testing.

One of the potentials that needs to be considered in a test under those defined circumstances is its potential for off-label use. So we thought it was likely that when you considered the potentials for harm in a test, one of them would be what kinds of off-label use might be possible and what harm might come from that off-label use. Some off-label uses we may not generate greater harms than indicated use, but others might generate quite significant harms. So that would be an appropriate question to come up under potential for harm.

DR. MC CABE: To press that further, perhaps this is directed to David, if it is felt that there are significant harms in certain uses that would be off-label uses, are there ways of prohibiting that off-label use?

DR. FEIGAL: This is actually one of the more contentious issues when the Food and Drug Modernization Act was passed, because industry had complained that we frequently did ask them to provide information relevant to

off-label uses. Actually, there is language in the law that -- and the law is still relatively new, but there is language in the law that actually tells us if the manufacturer is not making claims for an off-label use, we don't have any jurisdiction over that and can't require that.

That said, the trump card of this is safety. If it was an issue of a lower developing about a use for a test that was an off-label use that didn't present a safety issue, we would probably have difficulty calling for that information and pulling that in under FDMA. But when it is a safety issue, usually the safety trumps many of the other concerns.

DR. MC CABE: If I can follow up, part of the reason for pressing that was, I think that one of the issues that will be very important is the data collection. The data collection may drive some of these safety considerations, or lack of evidence regarding safety. That would then move into a liability situation for the companies that were using certain off-label uses, where safety was suspect or not demonstrated.

I wonder if there is experience that you can inform us about in that way. I'm sure that has come up in other areas as well.

DR. FEIGAL: The issue of whether there is an interest for the manufacturer or the laboratory not to look for certain kinds of data, because they may find things that then could create liability. I think most manufacturers don't explicitly start out that way. I think most of them want to provide a high quality product. I think with testing, the immediate risk is having inaccurate information and decisions based on the inaccurate information. The feedback on that I think is relatively good for high risk kinds of events.

There are times I think where economic concerns about how difficult it would be to, for example, prove that a cancer marker really predicted something useful, that those studies are so vague and so huge that part of the approach for many manufacturers is, if we make a high quality accurate marker test, it is somebody else's responsibility to figure out if that information is useful, in the meantime if you want that information, here it is.

That is one of the more difficult situations for us. If we are working with a genetic disease that is already well characterized, it is not a problem to get high quality information. But the predictive tests I think are much more difficult.

I think that there have been tests that have been proposed. One of the more controversial areas has been an area of whether or not there is such a thing as silicone allergies. So there have been a series of tests that have been proposed to detect silicone antibodies that have not been clinically correlated.

There we are taking the stance that there is no reason to market those tests unless you know what they predict, what the results are. Until someone can show us that those tests can predict something, we have not approved

them.

There probably would be a genetic marker equivalence to that, where long-term followup would be needed to know whether or not the marker could really deliver something clinically useful, even if there was some basic science. There is usually some plausible reason why someone says, this should be of interest.

So it is one of those areas that we frequently get into the longest discussions about, what is the claim that you want to make that this test is going to do, and what kind of evidence would be reasonable. Sometimes there is a solid scientific basis, and other times it is very exploratory. What exactly should be the information provided to the clinician and the public, that is I think one of the more difficult judgment calls. I think it is what we all have been grappling with.

DR. MC CABE: One last followup question if I could. I am pushing this because I am particularly sensitive to this as a pediatrician. Until very recently, there were dis-incentives to test drugs in children. Therefore, most of the medicines that we use in kids are off-label. This was very clear, that there was dis-incentive to do the test until the Modernization Act.

So it took legislation to give an advantage to the companies to overcome this dis-incentive. We may find that there are similar situations, and as we or whoever is monitoring this process, I think it is something we need to be sensitive to.

DR. KHOURY: I'd like to comment further on this. I think the progress that was made yesterday is tremendous, but the success of any classification scheme, as you can see here, depends on the data that is collected to get some feedback and input on this classification.

I think off-label use is a potential one that can mess it up basically, because you come up with a whole scheme and use it in family situations, but then it creeps up into the general population.

Also, the idea about the X number, that first box, what determines rare versus common. We have talked about a couple of these mechanisms for collection of data. Bob Martin is here from the CDC. There are ongoing surveys that CDC conducts with labs that provide testing in general, and this has nothing to do with genetics. These could be adapted or enhanced to provide the surveillance data that will allow us to provide head counts of how many types of tests are provided per year, so this initial box can be filled.

Also, the circumstances under which each test is being given, and therefore evaluating the appropriateness of that test. Obviously, the development of such an existing resource will have to be coordinated very closely with the FDA.

But this is one of those mechanisms that the CDC has to keep tabs on lab surveillance. This is what I have called earlier under surveillance of genetic testing as a process. As we move into the level two scrutiny, which is the enhanced data collection, and try to get a handle on the

parameters of genetics, i.e., the clinical utility and validity, that is where we kick up in a higher gear and work closely even with all the agencies, even including NIH and HRSA and AHRQ, to actually derive the parameters of the tests in terms of clinical validity and utility.

So there are these two mechanisms of data collection that are population-based. One is a mechanism of collecting data on genetic testing as a process through the labs, which would be a lab-based system, as well as developing the more higher scrutiny model to consortia and working groups that could be disease or test specific.

So this is the ideas we have in mind. I don't know if Bob wants to say anything more about this.

DR. BOUGHMAN: Let me add a couple of things from the perspective of this end of the table. I was much closer to the slides yesterday; you gain perspective by moving back some.

In a line that Wylie put up on the previous chart that was labeled FDA Review, in fact has a broader meaning, if you will. This is the collection point or the review process -- that middle line is the review process that we have as a Committee vaguely referred to over time, and is FDA coordinated, but in laying out the level one and level two processes addresses the issue that this Committee has had about a coordinated effort, or creating a whole new review process.

In what we have put forward, we are asking and expecting some real change out there in the world. We are asking the regulatory agencies to implement the scrutiny level one in a streamlined but slightly redefined process that is data intensive in certain kinds of ways in conjunction with professional organizations and consumer input and so on, one of the issues that this Committee has had.

Level two asks that this coordinated review in fact expand to include appropriate expert discussion on these very complex issues that don't come up routinely in some of the other processes that the regulatory agencies have had. That is why we are here.

We are asking for change in the regulatory mechanisms. On the other hand, we are expecting change in the scientific, professional, and even consumer communities. We have not been in the mode where as professionals or as consumers we have the concept of FDA or some sort of stamp of approval on the tests that we are having done under the situation that we are having it done.

When you talk about off-label use in this situation, we I don't think can ever stop certain kinds of off-label use without creating a new profession called the genetic police or something, to check out the labs. But the professionals who are ordering these tests can now have a different level of clarity about what the test is about, because of the way that it has been described either in the labeling process or in these data that are coming out.

So the people ordering the tests, the people having the tests done on them will have an understanding of what it means that they are trying this relatively new test.

I think that that also addresses some of the issues in ways that we have been concerned in consumer protection, when the IRB is no longer involved and now these tests are released to an unscrutinized beyond the laboratory mechanisms of CLIA.

DR. COLLINS: I think I would want to echo that. Again, I think it is always the case that Pat Barr manages to put her finger on the precisely most important issue. It is wonderful that you are here today to do that, as you always have.

I think our choices here though are limited to basically decide that a test could not be made available for patient care unless all possible uses of that test were considered to be justifiable. We put an amazingly tight bottleneck on tests which probably are never going to be appropriate for population testing, but somebody might do it and therefore you would end up hanging up the works.

So we are essentially forced into this model of considering tests not as what they are, but also what the use is going to be, and then counting on some mechanism for trying to at least minimize the off-label uses that might be inappropriate.

I think the labeling will help with that. But as Joann was saying, we have several other mechanisms. One is this whole notion, which we talked about quite a bit yesterday, about having pre- and post-test information in a standardized format made available to people who are undergoing this procedure, which should make it very clear what this test is for and what it is not for.

The other two are the professional practice guidelines, which I think can be very useful, and to some degree, although Elliott doesn't like it very much, the laboratories serving some function to assess whether the sample they got for a particular test was in fact taken in an appropriate setting, a check box or something of that sort, to avoid the most glaring problems.

I think we will need to monitor this very carefully. There are some examples already where things have not gone as badly as some might have imagined. I think yesterday we mentioned APO-E4, where there was deep concern about using that in a population screening method, which numerous consensus conferences agreed would be a bad idea.

But there is a role for APO-E4 in a diagnostic setting, and I gather it is being used in that circumstance. I would not argue that we have achieved perfect outcome there, but I think there has been a reasonable level of understanding. That is even without these additional oversights that we are proposing to put in here.

So while I tend to be a little optimistic and have to be careful about that, I think there are enough steps here that this model of depending on defining the approved use in a certain clinical setting and not expecting that that then suddenly expands to all possible uses, ought to be a viable way to go, as long as we watch closely.

MS. BARR: I would just raise another issue in this context. I don't know whether you discussed it or we will have to discuss it later. But that is speed of process

and the effort of getting groups together in consortium and creating standards could be far longer than is necessary or needed. It may be necessary, but it may prove not very useful.

So thinking about the tradeoffs of time and quality, it would seem to me in this whole thing, is something we are going to have to do as well.

DR. BURKE: And I would note that we believe there needs to be a standards setting process and how that would have to be raised to be discussed. So that point might be an important point in considering the process.

MR. HILLBACK: I'd like to do two things, to answer Francis for a second. I hate to do it again, Francis, and ruin your day. I agree with you, though.

I do think that the crucial parts are as you said, one, we are going tell people what we know and what we don't know, which is one of the things that labs would always like to do and try to do, because it does create a clear picture of what is going on. I do believe lab directors, because they are signing out cases, do have a responsibility to look at and put in context why is this testing done. There are times where we turn back cases now.

I think that if that gets to be an onerous task, we have not done a good job in designing the overall system, but I think it is part of it.

Just to give you the flavor of yesterday, I think there was a lot of concern and a lot of discussion all day yesterday about making sure that level one was really a fast and cost-effective approach. Francis reminded us yesterday that we had recommended in our report that once the details of this are fleshed out, then a modeling exercise and some sort of parameters of what are the expectations of how long things would take and how much they would cost -- both how much they would cost the government, and how much they would cost the testing laboratory, whether that is an NIH lab or a university lab or a commercial lab, in order to go through this process.

Those are things that have to be looked at, and we have to re-test whether we have designed a system that isn't usable.

So there was a lot of discussion yesterday about that, a lot of good discussion that had a good outcome.

DR. KHOURY: To respond to Pat briefly, this consortia, they would probably come together after the test is released to collect further data. So hopefully they will not contribute to the bottleneck. But as some tests are kicked into level two, then these working groups and experts and professional organizations will come together to pull the data in the long run and design collaborative studies. So hopefully they won't delay the system, but they will contribute to further building of the knowledge base.

DR. CHARACHE: Also, I want to reassure Pat that I don't think that drawing up the criteria that are required prior to implementation of the test will be an onerous task. I think it will have to be done very thoughtfully, but I think it will be generic.

We actually looked into some of these criteria

through the CLIA Genetic Working Group earlier. I think you can define what they ought to be, concepts of how many kindreds you have to test for a high prevalence disease versus a low prevalence disease, what type of proficiency testing and that type of thing; there is that whole spectrum.

But I think it can be drawn up generically. I think it will take a multi-discipline group to draw it up. But I don't think it will be on a case by case or disease by disease basis.

My concern however is that for each of the diseases that we define, there may be thousands of tests. The question is how to ensure that the FDA can be so structured or designed, or the test review can be so structured and defined that we retain the reasons why we want the FDA to do it, because they are good at analyzing tests, without getting this bottleneck that we are all concerned about.

DR. MC CABE: I just wanted to encourage the people who weren't here yesterday to speak up. Pat has. It has been very stimulating to have that. But I also would like to have the others who were not here, because you may bring a different perspective to this.

DR. BURKE: This is my last transparency. I'm going to go ahead and summarize the issues, and some of them are going to come up in the comments.

As we went through, we tried to keep track of and discuss a little bit the issues that we think will require further work. I have already mentioned that the issue of IRB oversight is obviously an important one. What we are now looking at is what we would like to see as a seamless transition from the levels A and B1, where IRB oversight is the oversight mechanism to the FDA review, and stages B2 and C.

What will be required there is attention to coordinating IRB efforts with FDA review. We think for example that it may be very important for IRBs that have oversight over genetic testing protocols to be aware of the FDA criteria, so that they may want to take those into account as they think about appropriate informed consent procedures or other kinds of human subjects protections. That would lead to guidance as our procedures are developed and we see that pre-market review process is developed, that is information that should go back to IRBs.

Test low volume initial criterion obviously needs further work to determine. I think there are two pieces to that. One is, what is the number and how do we get that number. As Muin has commented upon, there may be methods to do that. But another has to do with how many tests fall into that low volume category and what kind of tests they are. Therefore, there is going to need to be an ongoing review about whether that really is the right criterion to develop a smooth process.

Clearly, another implication of that low volume criterion is that we are defining two categories or two different types of scrutiny level one. That is, there is scrutiny level one that occurs when a test gets there, just

because it is low volume, and there is scrutiny level one that gets there because a test meets the criteria for an expedited review.

If a test gets to scrutiny level one solely on the basis of low volume, there are additional issues that probably need to be incorporated in that review. One of them obviously is some sort of checklist or review process that makes sure that the test does not have significant harms attached to it, so at least a review that says, yes, it is reasonable at the risk-benefit level to think about using this test.

But what we think we may also be getting at is orphan tests. So I think that is a complex issue. On the one hand, as a low-volume test gets to a level one scrutiny, there may be some additional concerns to make sure there are no harms attached to that test that might bump into level two. But there also might be special attention to the fact that this is a low volume test because it is an orphan test. So the kinds of expectations you would have, for example, about how much data should be available before a test becomes used need to be considered.

That segue ways to some extent into an issue in and of itself that we want to mark for further discussion, that is, how do you define an orphan test, is volume the right way to define it, are there other ways to define an orphan test, and how do you weigh the delicate balance between making a test available that is concerned for access, with concerns for test safety, including appropriate quality assurance, including that enough data has been accumulated, perhaps in a rare disease situation where it is hard to accumulate data to make sure that you've got an adequate test.

This as in many other places is a place where collaboration is tremendously important, and there really should be a role for advocacy organizations, because they are the target audiences for those tests. But that is an important issue.

Then when we talk about process and review, there clearly are a number of issues that are going to require further discussion and further work. We have emphasized the importance of test information, that is, having appropriate information ahead of time about indications and limitations, appropriate reporting of results.

I don't think there is any way we could underestimate the importance of that as we went through our discussion yesterday. That is a crucial piece to ensuring test safety, and how do you make that happen, who is participating in that process, who is reviewing that test information for adequacy. How do you define social issues in order to identify potential social harms is another issue that needs further discussion.

How do you set the standards for counseling in informed consent. Are there going to be tests where we have an explicit recommendation as part of the pre-test information for counseling? Are there tests where documented informed consent procedure needs to be available before the test is run, and if so, who monitors that. These

are questions that need to be resolved.

Then we had a discussion about panel testing, where we made I think some useful progress, but didn't resolve all of the issues. Panel testing, also sometimes the word multiplex is used. We thought panel testing was a neutral term that we would better want to use, but we acknowledge that there were different kinds of panel tests.

One panel test is a test that might test for multiple different alleles, even for multiple different genes, all around the same phenotype. So an example might be a panel test that tests for mutations related to HNPPC. We felt that a test of that kind, where you are basically testing multiple entities but all to answer the same question, did not pose risks above and beyond a single test of that sort. Obviously, there would be different test characteristics in terms of the sensitivity, specificity and in some cases improvements. But that could be viewed in the same way.

On the other hand, when you have a panel test that tests for multiple different phenotypes, that is, different disease conditions at issue, then you do have additional concerns.

Some of those tests may also be quite reasonable and efficient approaches. For example, a panel test that tested for several different carrier states as part of a prenatal testing circumstance, where all of the tests in essence have the same purpose, and are occurring in the same clinical context, might be able to be delivered quite reasonably and not raise significant concerns above and beyond those raised by each individual test.

But we felt there were a number of the issues that came up around panel tests for multiple different phenotypes, that is, for alleles associated with multiple different phenotypes, that probably could only be resolved by current research.

An example would be a test for 30 different entities. A standard that we would propose is that the counseling provided a for multi-test panel ought to incorporate the same level of information for each test as you would expect if the individual test were provided. It might be that at a certain level, a certain number of tests, that no longer is possible to do.

Pat, do you want to make a comment?

MS. BARR: Yes. I don't quite understand, if someone has gone through the process of review for each test and when the test is out on the market, you pull them back in when someone offers them in a panel, even though we may not think that panel is appropriate for a particular population.

That seems to me not -- I don't know if part of it is off-label, but that seems difficult. Did you think about how you would pull that back in?

DR. BURKE: What you're saying is, is there even an opportunity for review. I will say, we discussed that briefly but not sufficiently to fully answer that question. There would sometimes be an opportunity for review, because the nature -- the technical nature of the test would make it

a kit that would come back for review. I think probably there are circumstances where it wouldn't.

I obviously would be happy if there were more comment on this point, but I want to say that our conversation was not directed at how do you get a panel in for review. It was rather directed at what would be the review issues, and the question of, are the review issues different because it is a panel test as opposed to what they would be for each individual test. So that was the discussion.

DR. MC CABE: One mechanism just to throw on the table. We have talked about scrutiny level one for existing tests or orphan tests. One might think that -- we are thinking historically, but there may be existing tests in the future. So you might have a very streamlined evaluation. If you're bundling, all you are really doing is bundling, would there be some very streamlined scrutiny to see is the bundling appropriate.

The reason why you might want to do that, we got into some of this yesterday, or you got into some of it, I was just listening, but there might be some social consequences to that bundling. If that bundling was around a group of diseases of a particular ethno-cultural group, there might be significant issues about the bundling that didn't have to do with technical consequences, but had to do with social consequences.

So we might think that there isn't going to be a bright line when now there are no existing tests. There may be in the future ways that you would need to deal with existing tests, but with how they are going to be applied in new ways.

DR. BURKE: I think probably the most important point of our discussion was that there are empiric questions that could be studied that might help to inform how much of a concern it is to consider the panel nature of the test in review. Those would include what kind of panel tests were feasible, which will change over time, but they also include what kind of counseling in informed consent is possible relative to the number of tests, and also perhaps considering the kind of test information.

For example, as I mentioned, panel tests that test for multiple different carrier states as part of prenatal counseling is different than a quote genetic test report card that has multiple different predictive tests perhaps of different predictive value and implications at different stages of life.

So I think our main concern was that this should be recognized as an area where empiric research should be done to help to inform us about what the oversight issues might be.

Any other comments from the group on that discussion?

DR. KHOURY: Maybe you said it, but I thought we talked about in the panel, that when you have 10 or 15 conditions, the level of scrutiny at least should be determined by the one -- if there is one of these tests that has a level two, then the whole panel is pushed to level

two. But in addition to that, if all of them are level one, the bundling might somehow because of social or other issues push it into level two. But at the very least, it is determined by the level of complexity of at least one of them.

DR. FEIGAL: I think part of what is being blended in the discussion is what is a new test, and how much does an existing test have to change before it is considered a new test. As you can imagine, there is quite a bit of FDA and CLIA precedent on these kinds of issues.

The real challenge gets to be -- I think one of the things you pointed out before, at least on the Web there are 78 places that offer Fragile X testing. There is about 30 that offer Tay-Sachs carrier state testing. If they are all trying to measure the same thing, you may have some sense about what that information will convey and how to do all the counseling about that. But that still -- the more fundamental question is, how do you know each of those tests is performing well, consistently. The real challenge is to get the appropriate levels of specimens to be able to run controls and establish that the test can do what it says. That will be the real test for the panel for us, is how do you get enough reference samples independently evaluated to get an array that may claim that it is testing simultaneously for a thousand different kinds of things.

But I think it also gets back to the discussion about leveraging and the partnerships with outside groups. I think that there is going to be a very important role for the professional groups and patient advocates to help understand what the information means, how to do informed consent, what the counseling is. I think it probably falls more to CLIA and the FDA to figure out which of the tests that purport to convey that information are doing the job.

MS. BARR: I guess I am understanding a little bit better. In the enormous expansion of proposed testing that we imagine, there will be people who come with a whole new panel. It is not necessarily tests that have already been approved that they want to put together as a panel, but rather, look what we have done, this is a great panel, and that situation went to review. So that clarifies that.

The other issue for me though is, when you are talking about process of review, counseling and informed consent, and you talk about IRB coordination and guidance, I think a huge service to the industry, to the researchers, and to the consumers and advocates, is to try and move in this area to something that is a template, and to convince IRBs that this template avoids legal liability, which is what their lawyers are going to come in and tell them they have to add 16 other pages, and that it will be recognized as sufficient for a period of time, and there will be people who will upgrade it.

That does fly in the face of notions of local control over informed consent. So there will be a dilemma there. But I don't know if you are going to talk about it in the process of review, how you cannot talk about it for the IRBs as well.

DR. BURKE: I think that is very consistent with

our conversation yesterday.

DR. MC CABE: I think that is a point that is very well taken. I would like to suggest as a concrete recommendation that we have staff bring together the literature that has been done on this. There are templates, there are recommendations regarding informed consent that would help us become a resource for IRBs. Your first bullet there, coordination and guidance, and I would like to with the Committee's approval, we could have staff begin to put this together and bring it back to us at a future meeting, so that we could look at it and just see what has already been done in the research arena and in the implementation arena.

Is there any objection to us moving ahead with that?

DR. KOENIG: I don't have any objections. I just think it might be useful to coordinate with what is going on with NBAC at the moment, in terms of --

DR. MC CABE: This is specifically for genetics, specifically for the genetic issues.

DR. KOENIG: Right, but there has been a lot of work on vulnerable populations which might be relevant.

DR. MC CABE: There already is communication with the Committee, so we could ask the staff to carry out that communication.

DR. BURKE: Did you have a comment on that?

DR. CHARACHE: I just wondered, while we were taking advantage of the literature that already exists for the IRB, if we could also be thinking about what our expectations are of the IRB, what additional things should we call to their attention that they may not now be attending to for genetic tests.

DR. MC CABE: What I was going to suggest was that we bring this back and then determine whether we need a working group to actually move it beyond what already exists. But we will make that determination after we see the literature.

DR. FEIGAL: I think actually a working group on IRBs would be very useful, because there are IRBs at both ends. There are IRBs at the end of the institution that offers the test and there are IRBs for the physician that actually has to deliver the informed consent and have that.

There have been some interesting models of national IRBs that I think could provide quite a service, and would actually give a way of bringing in some of the leveraging that has been discussed. The local IRB can always ignore the national IRB and insist on reviewing it itself, and large universities tend to do that. But for the practitioner in an office-based practice without access to a regular IRB, it may be the only one they have, and there may be many hospitals, including community and university hospitals, that would actually welcome a national IRB in this kind of an area.

MS. BARR: I just think that even as we do the literature review, someone should be in touch with PRIM&R, because I know they are first of all thinking about a regulatory branch and second of all, their board has devoted

a fair amount of time to the issue.

DR. MC CABE: Do I gather David was recommending that we develop a working group at this point in time rather than waiting until a future meeting? What does the Committee -- I saw a lot of body language suggesting that people agreed with that. I think it would probably be the next step, but I would be happy -- we would begin to develop a working group on this issue, if people felt it was appropriate.

DR. COLLINS: I would strongly endorse that. The other connection that we ought to be sure we make very quickly is with Dr. Koski, the new director of OHSR, because obviously this is going to be a hot item on his plate. Whatever we do, we ought to be sure we try to set it up so that it is of maximum utility and well coordinated.

DR. MC CABE: If people would like to volunteer for this, I think there are going to be a number of working groups that fall out of this report that has come back from the working group. The people who would like to volunteer to work on the IRB working group, you can let Sarah know at the break, but be cautious, because you don't want to be on too many of these working groups.

DR. BURKE: I just have a couple of additional remarks about issues, but one of them is the most important issue for discussion, although I'm not sure any one is the most important. Data collection is clearly a very important issue.

What we have said is that the data collection throughout this process and for both level one scrutiny and level two scrutiny tests is important. We need to figure out how to make use of its existing resources to get surveillance data or other data that would be useful to understand how tests were used and what the outcomes of testing are. We need to put attention and ultimately probably resources into additional methods of data collection or additional efforts in data collection that are appropriate to make sure that the questions about scrutiny level two tests get answered. That too needs to be coordinated. There clearly needs to be a lot of discussion about how to make that happen.

MS. BARR: One way is in a template for IRB review, which talks about within the protocol that is being reviewed, whether there are mechanisms for data collection. So there will be some overlap on these issues for sure.

DR. BURKE: And certainly we could imagine an outcome of scrutiny level two might be that there is an identification of the need for certain kinds of data to be collected as this test is made available. But I think we have had plenty of discussion before, saying it is not as simple as just telling the lab to do it. In fact, the data that we are most interested in probably isn't even going to be accessible to the lab.

It is also realistic to say that those kinds of data collection aren't likely to occur without a mechanism and resources. So this becomes a very important issue for discussion.

I think one could even say that if you don't

figure out that piece of the puzzle, a lot of where we want to be over time won't happen. Tests will come into being that have questions and the questions won't get answered. So that is important.

The two final bullets on my list. Clearly, what we are proposing now seems to make sense and seems to move us forward, but might not be the right thing. We did have some discussion at the end about not letting the perfect prevent us from achieving the good. The point there really is that whatever we put in place needs to be looked at and reviewed as we go on, and there needs to be an ongoing oversight of the oversight procedures we put in place, to tinker with them and adjust them to be what we want them to be.

Then just the final emphasis, which I think has been there throughout, that we see this as being able to be accomplished only if we use a collaborative model. I think we have identified all along the way the particular players in the collaboration.

So other comment?

DR. MC CABE: Thank you very much, Wylie. We still have a few minutes to pursue discussion on this, if people wish to. Michelle?

DR. LLOYD-PURYEAR: I have a question. Can you go over again how the work that was done yesterday is going to be coordinated with the lab forum, which CDC is doing, and then the separate PHS lab group that Dr. Malone spoke about this morning, how we are going to be coordinating all these different efforts?

DR. BURKE: I think what I can say vis-a-vis the lab forum is, to some extent that needs to be discussed, how things would be coordinated. But if I am understanding that correctly, and Pat and others may want to comment, the lab forum is working on a number of issues that are somewhat separate, although obviously coordinated with where we put our main energies yesterday. The whole system has to obviously coordinate.

I guess I find it easy to think about the lab forum work as fitting into what Ed just referred to in terms of working groups. It seems to me the lab forum is working on a lot of technical issues that ought to come back to this Committee, so that the Committee would be able to understand how they fit.

Do you want to comment on that?

DR. LLOYD-PURYEAR: Except that it was never officially set up as a working group, and I want to see that kind of coordination.

DR. MC CABE: Bob, would you like to comment on that? If you can come to the mike, you can be Francis Collins.

DR. MARTIN: Pat Charache may want to comment on this as well, but basically we do see the laboratory forum as working very closely with this group. The laboratory forum has actually been set up under the auspices of the CLIAC, the Clinical Laboratory Advisory Committee. Again, we have worked very closely with this group and we will continue to do that.

Clearly there are areas that are technical in nature that the laboratory forum can best address, but also from the description of the work that went on yesterday, there are clearly areas that are overlapping as well. That is why it is important to be working very closely with the group.

DR. LLOYD-PURYEAR: But is the laboratory forum different than what was spoken about this morning at the Secretary's level?

PARTICIPANT: Yes.

DR. LLOYD-PURYEAR: So what is the coordination between the laboratory -- because it seems like it is the same people meeting and talking about the same things.

DR. MC CABE: I think perhaps Sarah can give us some clarification on that.

MS. CARR: My understanding is that what Dr. Malone was describing was the group that has been put together to review the recommendations in the SACGT. The outcome of today's discussion in terms of the classification methodology that Wylie went through will be submitted to the Secretary through Dr. Satcher as an addendum to the final report that went forward before. Hopefully we will be able to do that in time for that group that she said has been put together to bring that along and to submit it together, perhaps when the oversight report goes to the Secretary.

In terms of what the laboratory forum at CDC does, they take the methodology that we put forward, and if the recommendations of this Committee are adopted by the Department in some form, then perhaps that forum may help in terms of implementation of that in collaboration with FDA and the other agencies to which their recommendations apply.

DR. MC CABE: One of the things that we had stated in our recommendations, our report, that we could reiterate specifically in this context in the addendum would be that there be such coordination, that it was important that there be such coordination of these different activities, which I think is happening. But we could specify that more explicitly.

DR. CHARACHE: One of the nice aspects of the work that had been done in the first two meetings of the laboratory forum was the overlap with this Committee and the group that was here as part of the Working Group yesterday. There were six members that had direct overlap, both from the FDA and the CDC, as well as representatives from the American College of Medical Genetics, the representative from the College of American Pathology, but the laboratory oriented aspects which are participating in the forum.

So this is intended to be a collaborative group. The work that was done yesterday, as pointed out with the original diagram that was drawn, the emphasis was on the medical and social aspects of genetic testing. There is the whole other side of that, which has to do with the level of scrutiny required, which is based not on the nature of the disease that we are talking about or the frequency with which testing occurs, but is based on the complexity of the test itself, and oversight which is associated with assuring test accuracy, and ensuring that there is program validity

and clinical validity.

That is an area in which the composition of the laboratory forum group can be very contributory and would then be tied in with a similar type of interaction that occurred with the other arm yesterday.

So I see it as an opportunity to take advantage of the expertise with the slightly broader laboratory group focused on the laboratory issues that then get tied into the other issues that are being addressed here. That is how I see it as a member of the group.

DR. MARTIN: Actually, Pat just covered that very well, and I don't have anything else to contribute.

DR. MC CABE: Thank you.

DR. KOENIG: My comment is off the lab issues.

DR. MC CABE: Maybe we'll just hold that. Victor, did you have a comment on the lab issues?

DR. LANIER: No, nothing on that issue.

DR. MC CABE: Then Barbara?

DR. KOENIG: I just want to go back to Wylie's presentation and to the template, and to the issue of how detailed our suggestions -- I think our intent yesterday was to create a flow diagram that would be flexible and would allow the agencies who had to actually develop regulations with a lot of latitude to do that.

But I'm just wondering, when we consider the issue of tests that might be released with special conditions, if there might be a couple of issues that we want to highlight. One of them that we did talk about was the possibility of documentation of informed consent.

But the other two things that we may talk about later this afternoon that I have some concerns about is -- one is the issue of the direct-to-consumer marketing piece of this, and whether that might be something that we would want to flag in that list of possible special conditions under some circumstances.

The second one is the issue of access and availability in terms of whether a particular test should be offered only with the order of some sort of health professional, as opposed to a direct purchase situation over the Internet or whatever.

DR. PENCHASZADEH: I just wanted to react in general to the outline that Wylie presented. I am very pleased to see that things are coming into place. I am very satisfied with the flow diagram.

I think that there are some issues that were already pointed out that are probably some of the most important issues in terms of dilemmas. One is the off-label use. I am still not clear as to whether the mechanisms for enforcing proper use, once the test is approved for one use, and who will be in charge of monitoring that, that it not be used for purposes for which it has not been approved for.

I also wanted to comment on the panel testing. I do think that the complexity of a panel test is probably much more than the sum of each of the tests, because of all of the issues and the medical and social consequences. So I think that I would be very surprised if a panel test doesn't require a high scrutiny, even if most or even all of the

individual testings are of low scrutiny. At the minimum, because of the medical or social consequences and the complexity of the decision making and the need for counseling, which leads to a third issue, which I think is already addressed to, which is the informed consent and counseling issues. Again, my concern is how are these things going to be enforced and taken by the medical and the genetic profession in general in order to ensure safety in addition to access.

DR. MC CABE: David, do you want to respond to the off-label?

DR. FEIGAL: One thing to remember is that off-label use by practitioners is explicitly legal. No one is asked to enforce that. The only real practical enforcement in the marketplace is what third parties will reimburse that has some controls.

But I think it makes sense that off-label things be legal, and that it not be regulated. So I think there are some things that you are going to get from regulations, but off-label isn't one of them. Off-label refers to what the manufacturer is allowed to promote. There is a higher standard for advertising in the practice of medicine, which is hard to believe, but that is the logic of the law.

DR. BURKE: My remarks are very much in keeping. In our discussion, we acknowledge that it is not possible nor appropriate for this regulatory process to regulate medical practice. But we thought that in what could be accomplished in the procedures we were talking about, the greatest benefit would come from the attention paid to information about the indications for tests, limitations of tests, and reporting of test results. In this kind of oversight of genetic tests, that is the best way that you can help practitioners to make appropriate use of the genetic tests.

DR. PENCHASZADEH: Just to follow up, people also put an -- on professional organizations and policy makers in general to determine what are the appropriate uses for a particular test.

DR. BURKE: Yes. I think it is important not to confuse what could be accomplished in this kind of oversight mechanism with clinical practice guidelines. That is where we get bogged down in the way that Pat indicated.

I think the information that is provided, the pre- and post-test information includes what the test is being offered for. So what the manufacturer has gone through and proposed the test be used, how it has been reviewed, but also what we know and what we don't know.

MS. BARR: I think that much of the answer should be in education rather than trying to convert regulation. It will overlap this direct marketing issue to some extent. You do want the public to know what is out there and what it is good for, and what it is not good for. That may be done by creating sets of questions that become very popular in the public; when you are getting a test, please ask your doctor, is this the off-label use or another use. If it is off-label, why is it off-label.

So it is trying to educate the public about the

kinds of questions they should ask of their doctors, which can have when it gets picked up a profound impact on the practice of medicine.

I think the other question I have, which is directed at Barbara, is that social concerns are contextual and cultural all the time. So who is on the committee or why they are on the committee or who the experts are that you listen to, sets that contextual tone. I wondered if you had addressed any of that at the working group level.

DR. MC CABE: I think the answer is no, though Barbara was referred to as the social conscience.

DR. BURKE: Clearly, I think it is fair to say that we understood that it is a significant task that requires further discussion.

DR. MC CABE: I'm going to move on to just wrap this up and come to some agreement about how we will proceed with the report of the Working Group.

MR. HILLBACK: I think both Wylie and Pat said some of what I wanted to say. I think the key here is back to the old bugaboo phrase we have used for a long time, which is what do we know, what don't we know, making sure that there is a clear template of how data can be presented, what data needs to be presented, making sure it is presented clearly so that the practitioners and eventually the patients can understand it.

I guess my next point would be, since the rest of our day is going to be spent talking about what we work on next, to put in my advertorial for going back to one of our key topics we talked about a year ago, and that is how do we get the user to be able to read what we have now said we are going to make available.

So I want to segue way through the next section into my bugaboo, that I don't think we have done enough, I don't think the system has figured out how to do enough. I know Kathy Hudson and the NIH is doing a lot, but I think this is a major problem. We may create a great document and if nobody can read it, we haven't solved the problem. So that is my advertorial. Thank you.

DR. MC CABE: Thank you very much, and thanks again to Wylie and the Working Group.

Having heard the discussion both yesterday from the working group and then today with the full Committee, to me I am very impressed with how far things moved yesterday. I think that we have a very good outline for an addendum with the materials that were presented and the overheads by Wylie and the discussion that was had yesterday as well as today.

I would seek approval from the Committee then that we go ahead and flesh this out into a document that we can submit to the Secretary by way of Dr. Satcher. Is that acceptable?

DR. PENCHASZADEH: Yes. I understand you fleshed out some examples. Probably the document should expand on showing with particular examples how this will go.

PARTICIPANT: So moved.

DR. MC CABE: There is a motion on the floor.

PARTICIPANT: Second.

DR. MC CABE: Second. Any further discussion of this motion? In terms of practicality, Sarah, can we then e-mail around for comment? Do we have to bring it back, since we have really discussed it all in the public, as long as we don't go beyond what we have discussed in public? Then we can move it forward after e-mailing it around. Once we have it, we will put it on our website so that it is fully available to the public.

Further discussion on the motion?

MR. HILLBACK: I would just like to make sure that we capture some of the richness of yesterday's discussion. I think there was a great consensus that Francis led about how do we make sure that as the details get evolved, that we review what those mean and what the implications might be. So some of that that got captured which is on tape from yesterday needs to make sure that it is in the report, because I think what Wylie put together is fabulous, in terms of a template. But it needs a bit of a flower bed to grow in, I think.

DR. MC CABE: If there are other points that people would like to see that would be enriched in the document, we should bring them here and discuss them around this table, since this is the public forum. Yesterday no one was excluded, but it wasn't a full meeting of the Committee, so it wasn't quite as visible as today is.

So other points that people feel should be emphasized?

DR. BURKE: I'll just say that I don't think there was any major topic of discussion that hasn't been raised as a point here. The detail that Elliott is referring to is just detailed discussion, as for example when Pat raised her question about panel tests. We obviously had spent a lot of time about that. We had spent a fair amount of discussion on off-label use.

I think every topic that we discussed hasn't been mentioned here, but if I am forgetting one, please, other members of the working group bring them up.

DR. CHARACHE: There was one that may be covered by the listing of the ongoing review. We raised the question of what happens when a test is first introduced as low volume and then becomes high volume - does it then get a re-review. Then the whole question of tests that are already on the market. I think that was a point that was on our list of things to think about in the future.

DR. BURKE: Yes. I can elaborate on that a little bit. We had a comment from Steve Gutman that there are procedures in place that can accommodate minor technical revisions and tests, and we definitely would not want to create a situation where something had to come back to review because there was a minor technical change, even a change that might change the sensitivity or other test properties.

On the other hand, we could envision that a test that now is used for universal screening and wasn't previously, something that would change its level of scrutiny, that that might well be an indication for it to come back for review. So how to accomplish that would

certainly need discussion.

DR. LEWIS: I just have a process question. If this becomes part of the report which is now a confidential document, when we develop our addendum, does that also become a confidential document? When you said putting it on the website, I was just concerned in terms of whether that became a public document or whether it was part of our report.

DR. MC CABE: Point well taken. It will be public when it can be public. Hopefully from the timetable that we heard this morning, by the time we put this together, the other document might no longer be confidential, and therefore -- I'm learning this process as well, but yes, we will certainly put it on when it is available to be put on.

DR. KOENIG: I have a question referring back to the initial point in the flow diagram about the volume. This is just a point of clarity. Are we going to continue that discussion today or is that going to be something that we basically are delegating for later consideration to the agencies involved?

DR. MC CABE: This is a point that we needed to take up. Why don't we take Reed's question, then we'll come back to this point, because it is a more general one, about which issues are issues that we should advise the agencies on and which issues are within their purview in terms of implementation, and there is a series of these.

DR. TUCKSON: Actually, I may be in danger also of muddying the water. Elliott's comment about how we deal with subtlety and nuance of communicating for the addendum. For example, you take the issue of volume that Pat just talked about. There was very elegant language yesterday that described the need not to bottleneck and to be able to move forward. Yet there was conversation to also respect that the language of scrutiny for low volume people is not lower, and we are not just trying to run roughshod over people who, to them, it is very important. There may be eight of them, but to those eight that is pretty damn important, so there are issues there.

So that subtlety of nuance that communicates well, both in why we came out and also the notion of a specificity of intervention that suggests putting patient advocacy groups on the panel of discussion, therefore you get that advocacy for orphan and low volume tests and populations. Those are three very important points.

For each of the major issues that we discussed, that sort of subtlety and nuance is going to be key. So that is going to require a lot of sending stuff around, I guess, and probably a lot of collaboration.

But what I worry about with Barbara's point is, some of these we still want to talk more about. What I'm still not sure about is where we got closure to something for the addendum and where we are going to have ongoing conversation that we don't have closure on. I'm not sure which ones are locked and which ones are going to have further exploration.

DR. BOUGHMAN: Point of order. Could I rephrase or make a friendly amendment to the notion to clarify this

situation? As we take the morning break, I believe the motion we may wish to approve to bring at least some sense of closure is that the Committee has accepted the report at least in spirit and at the end of the day, we will then know more clearly the content of what actually can go into the report regarding some of these points of discussion, rather than some of them have been discussed, and then ergo -- could already be in the addendum.

We might bring up some of these issues this afternoon again in the public forum, so that they could be addressed more clearly in what we are actually putting in the addendum.

DR. MC CABE: We can recommend where we would like to have more input and more discussion. We can also -- if we find that this is more contentious than I guess I had anticipated that it would be, we can hold it as a draft and bring it back to the discussion.

DR. BOUGHMAN: I'm not suggesting that the issues themselves are any more or less contentious than they were yesterday. I think the issue is what can actually be a part of that report because it has been discussed around this table and the full Committee versus what was actually discussed in a full day of discussion yesterday.

MS. BARR: I have two procedural questions. One is, although it was closed, can we as a group request that the transcript of that meeting be public?

The second is, my understanding was as the day proceeded, we were going to be identifying the issues that we wanted to pursue. So my judgment was that since we raised all the issues, the nuance will come out of the Working Group's ongoing discussion.

DR. MC CABE: We can put that transcript and make that public.

MS. BARR: I would move that we do.

DR. MC CABE: We already have motion on the floor, so we need to get this one clarified.

DR. KHOURY: I just wanted to echo what was said earlier, which was let's not throw in something good by -- whatever words you want to use. I think there was a sense of accomplishment, tremendous accomplishment yesterday, which almost took five years to get to that point. In keeping with all the issues that Wylie mentioned at the end from informed consent to data collection to volume tests, this reminds me what Elliott said about the devil is in the details.

Actually, you are going to be handing these broad recommendations to HHS. There will be a lot of discussions within HHS and across the agencies and the beginning of some implementation of some of these. I think those individual issues, I would urge the Committee not to drop in the next year or two, but as you discuss further what issues you want to take up in the future, at least be aware of the progress of implementation of your initial recommendations, and maybe take up one or more of these issues in more depth if you want to as a group.

MR. HILLBACK: I guess I viewed what we were trying to provide out of yesterday and today's meeting as

the beginning, not the end. I think that's what Muin is saying what we need to do, which took us a long time to get to, is to get this framework pinned down, knowing full well that not every detail will be right. Knowing full well that when we hand it to the agencies involved, that they will interpret what we gave them a little differently than what we interpreted it.

I think we talked yesterday about not allowing ourselves to be taken out of the process going forward. Therefore, with the agencies as they take our framework and do what they do best, which is turn it into a detailed action plan, a detailed law if that has to be done, that we have another chance to take another look.

To try and do that now and anticipate all those issues is impossible, and goes back to Wylie's eloquent point about throwing out the grade to get it perfect. I don't think we want to do that.

So I would propose that we move forward to get this done, get a recommendation and understanding, maybe with the caveat that it is a set of guidelines that we are proposing that we want to full well be involved in further down the line again, and get it moving.

DR. MC CABE: Judy, and then we're going to vote.

DR. LEWIS: I think my comments echo what has just been said. Basically what I thought we did and what I think we're doing is developing a policy document that has broad policy implications, and that what we are looking for is those people who need to implement it to come up with implementation guidelines that we will have a chance to review, and if they don't meet the intent of what our policy is, then we'll have another go at them. But I think for us to micro manage and do the job of the agencies is beyond the scope of our work, and I also think that it is a needless duplication of what there is a good infrastructure in place to do. What we have basically done is come up with some guidelines. For us to develop every last detail is not necessarily the work that we should be doing.

PARTICIPANT: Point of order. There is a friendly amendment, so doesn't Reed have to accept it or reject it? And as the seconder, may I encourage you to reject it?

DR. TUCKSON: I can't handle that kind of pressure. Oh, reject it? I reject it.

DR. MC CABE: Any further discussion on this? So all in favor of this motion say Aye.

(Chorus of Ayes.)

DR. MC CABE: Any opposed? (none opposed) Any abstain? (none abstain) So it carries. There was another motion.

DR. BURKE: My motion was just to put our discussion of yesterday, the transcript of the discussion, in the public record.

PARTICIPANT: Second.

DR. MC CABE: All in favor?

(Chorus of Ayes.)

DR. MC CABE: Any opposed? (none opposed) Any abstained? (none abstained) So we will do that as well.

Let's take a 15-minute break. We will come back

at 10:25.

(Brief recess.)

Setting the SACGT Agenda: Topics of Future Study

Discussion of Issues

DR. MC CABE: We will now turn to a discussion of current and emerging issues. We have allotted several hours for an unstructured discussion, which I know many of you have been looking forward to having.

Our goal for this session is to do a great deal of brainstorming. Then by the end of the day to have made decisions about what issues we think warrant the Committee's attention and will benefit from our involvement.

We will also need to decide on a concrete outline of our future study priorities and plans. Although we will have a free-ranging discussion today, I want to point out that there are materials in Tab 3 of our briefing books that remind us of some of the issues we were considering at our last meeting, as well as high priority issues we identified in June 1999 at our first Committee meeting.

Tab 3 also contains a copy of the transcript of the June 26 White House ceremony celebrating the completion of the working draft assembly to the human genome.

I was honored to be invited to attend that historic event on behalf of the SACGT. In addition to celebrating this magnificent scientific achievement and the benefits and promises, President Clinton also took care to point out that some of the concerns that accompanied the advancement of genomic knowledge are very real concerns. The potential for genetic discrimination was a particular concern.

In fact, President Clinton and Prime Minister Blair discussed the need for a multi-national, multi-cultural consideration of the ethical, legal and social issues surrounding the use of genetic information.

Because of the significance of the event and the importance of being responsive to the concerns that were raised, I asked Dr. Collins, who has had such a leading role in the progress of the Genome Project and was one of the key speakers at the White House ceremony, if he would be willing to give us his impressions of the issues that were raised that day and the weight given to them by the participants.

Francis, you may also want to give us a sense of where Congress is on the issue of genetic discrimination. As all of you know, Francis testified to the Department at last month's hearing on genetic discrimination in the workplace held by the Senate Health Committee.

Francis, if you would lead off, please.

DR. COLLINS: Thanks, Ed. I appreciate the opportunity to do so. I will not speak in a lengthy way, but I do think the events of June 26 were a useful way of sampling public opinion and getting a sense of what the concerns are as people reading about this milestone begin to respond to it in various ways, in terms of what their concerns were, particular regarding the kinds of issues that this Committee has been wrestling with.

It was a very significant day, perhaps more so than those of us involved in it realized, until it happened.

This was after all a bit of an arbitrary milestone, in the sense that covering 90 percent of the sequence -- it could have been 81 percent or 95 percent -- and it is still not a finished work. We have a couple more years of effort before either the public or the private version of the human genome sequence could be said to be actually finished, because there are many gaps and ambiguities still to be worked on.

But it was an occasion to stop and say, you can now expect that if you ask a question of the human genome sequence, you are likely to get an answer, you are extremely likely to get an answer. You may not understand the answer. Of course, we don't understand the script except in a very rudimentary way; we will be working on that for decades. But I think the world did stop and pause for a moment to consider the consequences of essentially crossing a threshold from a time where we had only glimpsed bits and pieces of this script to a moment where we now had essentially the vast majority of it in front of us, and the enormity of the task of figuring out how to understand this and apply this to the benefit of medicine now looms quite large, but it is also quite exhilarating and exciting that we can tackle that.

Certainly the fact that this milestone did attract the attention of the leaders of both the United States and the United Kingdom and a number of other countries that were part of the international sequencing consortium, including France, Germany, Japan and China, made this the most visible moment for genomics, since the genome project had started 10 years ago.

I think there is much about that that is a very good thing. Ed has already referred to the fact that the transcript of the presentations at the White House is available to you under Tab 3, and mentioned the fact that in our spontaneous interchange between Clinton and Blair, the idea of some sort of international focus on some of the ethical, legal and social issues was suggested to President Clinton.

Wylie mentioned that if that was to go forward, it would be Tony Blair's job to do it, because he wouldn't be there, since his term is near its close. But I think that was an indication of just how significant these issues are now looming in many peoples' mind, and that is a good thing.

I think it is a particularly good thing because we have prepared in many ways for this moment by having an ELSI program, by having scholarship that has been carried out by a host of experts over the course of the last decade, and a wonderful set of recommendations and policy options that can now be put into place.

I think if there has been a challenge for the ELSI program, it is how to translate that scholarship into actual policy decisions, recognizing that the policy apparatus is not something which is so easily understood, much less controlled.

So the good news I would say about this particular announcement and what followed has been the significant raising of public potential and thoughtful commentary on what it means to have our instruction book largely read out.

There were many commentaries that I read in the press and Sarah sent many of these around to you all on the Committee to have a chance to look at them, that were targeted on the issues that people were most concerned about in a fairly thoughtful way. That clearly signals a chance in public interest about this, which has been up and down, to something that I perceive will now be much more sustained.

The issues that were raised, both in the White House events and subsequently, are for this sophisticated group familiar ones. Top of the list, genetic discrimination - are we going to solve this problem. This Committee I think very effectively put themselves on paper and sent the letter to the Secretary about this issue, and I think the time is now to see that attended to.

I'll come back in a minute to what has been happening in the Congress since June 26. Also, other issues that were raised in the commentaries, privacy - does your genetic information fall into other peoples' hands and how are we going to take care of that.

Certainly there were a number of pieces that focused specifically on our mandate of genetic testing and its oversight, and how is that whole explosion of information that is anticipated to come out of the genome project going to be managed in a way that benefits people and doesn't put them at risk.

There were comments about the need for better public education and health professional education. If genetics is going to be mainstreamed in medicine, are we ready for that. Again, that is a topic that this group has discussed in the past and a number of other efforts are under way to try to deal with that.

Perhaps the more long distance concerns are ones which there is less concrete to say, because most of them are at the moment scientifically rather uncertain. And of course, many of those fall into the category of enhancement and what are we going to do about setting any boundaries between the use of genetics for the treatment or prevention of disease and the enhancement of human characteristics, which are really traits and not diseases.

Those discussions I think to be honest are still at a fairly rudimentary stage in most of the formats that I have seen them in, although there are people working hard on these issues, many of them supported by the ELSI research program, that have begun to refine this I think in a very useful way. But those kinds of conversations have perhaps not spilled out in a public forum in quite as broad a way as the ones have say with discrimination.

So all of this, I would say, is a very good thing. As a concrete example of that, the actions in the Congress since June 26 have been notable. After several years of interest but not necessarily definitive action on the topic of discrimination in both health insurance and the workplace -- although it should be noted that there has been some very important action in the case of health insurance with regard to the Kennedy-Kassebaum bill, or HIPAA.

Certainly the Congress was energized by this announcement in late June to take a closer look at the

remaining loopholes that need to be addressed. I should certainly point out that the Administration has been pushing at this, and the President has been personally very interested in those issues, and that was manifested of course by the Executive Order back in February, which outlawed genetic discrimination in the federal workplace, seeking to lead by example with the hope that this would be echoed in the private workplace as well.

Following the White House announcement, only two days later Senator Daschle, the Minority Leader in the Senate, who is the major sponsor in the Senate of a broad bill on genetic discrimination in both health insurance and the workplace, introduced his bill as an amendment to one of the appropriations bills, and led what I thought was a very interesting and rather inspiring debate on the Senate floor about the merits of this particular piece of legislation. A number of other Senators rose to express their views on this, some of them in fact quite passionately. I have not seen that level of discussion, much of it quite well informed, Senator Daschle's remarks were extremely well informed by the nuances of what is trying to be accomplished here.

Ultimately when that came to a vote, it went down on a mostly party line vote. The majority party argued that this part related to workplace discrimination, had not been subjected to appropriate Congressional hearings, and might be covered by the Americans with Disabilities Act, and therefore this piece of legislation which is sponsored by Daschle in the Senate and Slaughter in the House, was not viewed by them to have been sufficiently vetted for their support. At least, that is my understanding of the arguments that were put forward.

But immediately after that, Senator Jeffords, who is the Chair of the Health Committee in the Senate, introduced basically the heart of the GOP Patients Bill of Rights, which relates to genetic discrimination, extricated that and introduced it as an amendment to the same appropriations bill, and that passed.

Now, that sounds great. The problem is, this appropriations bill still has to be conferenced with the House and is apparently headed for a veto at the moment anyway because it is dealing with educational spending. It places some difference between what the Senate and the House have been proposing and what the Administration wants. But it was as a statement of principle a fairly exciting moment to have this other piece of legislation about genetic information and health insurance attached on to the appropriations bill.

I hope I'm not confusing you, because this is a bit confusing. The Jeffords amendment, which is taken from the GOP Patients Bill of Rights, relates only to health insurance. It does not cover the workplace. It has in some peoples' view some things that are not as strong as the Daschle bill in terms of enforcement and disclosure. But nonetheless, as a statement of principle, it is welcome indeed to see this sort of thing happening.

Now, making good on the suggestion that the

workplace issues do need more attention, Senator Jeffords did call a hearing of his committee, and Ed has just mentioned that. Various folks came as witnesses, including Daschle himself to talk about his bill, including Paul Miller of the EEOC, who I think presented fairly compelling arguments on why the ADA, even though one would like to have it be effective in this circumstance of workplace discrimination based on predicted genetic information, that hasn't been tested in the courts, and there are strong reasons that if that protection is needed, it would be best to do so with new and effective legislation.

I also had a chance to be a witness on this particular hearing, as did a number of other folks from a patient organization and from a couple of organizations representing business views. I guess it would be fair to say there was not unanimity of opinion about the Daschle bill in particular or the principles in general. But certainly at the end of the hearing, Senator Jeffords did say to Senator Daschle that this was an important topic and he would like to work with Senator Daschle to try to get something done about this if possible this year.

So that kind of forward momentum is now happening. The followup to that has been continuing interest in the Senate and also now interest on the part of the House Commerce Committee that are also deeply engaged in looking at some of the details of various legislative options, and particularly the whole business of definitions, which always ends up being really critical in terms of whether this is a piece of legislation that is going to provide the kinds of protections that are necessary.

So I do think there is some reason to feel a bit more optimistic that action is going to be taken, but we still have many steps in between where we are now and where we would like to be, which would be the signing of effective federal legislation that outlaws the use of predictive genetic information in both the health insurance and the workplace with appropriate language and appropriate provisions for enforcement. That is an outcome we can hope for.

The other interesting thing was that this whole issue appeared, as several of us noted this week, in the GOP party platform that was issued as part of the convention, and specifically highlights the area of genetic discrimination as needing attention. That is welcome news indeed.

So I would I guess argue that out of this, the main consequence has been an elevation in attention to the issues, not necessarily brand-new issues coming forward, but that elevation is an opportunity to take advantage of. As we talk about amongst this Committee what our future tasks might be, I would hope that we can look very carefully at what our mandate is, where we are best positioned to get involved in areas of public concerns, where there are other groups that may be better positioned in some instances to take on that mantle, and try to be realistic about sticking as much of our effort as we can towards our core responsibility of making sure that oversight of genetic

testing is responsibly carried out to the benefit of the public.

DR. MC CABE: Thank you very much, Francis, and thank you for your leadership in all of these efforts.

I would also like to point out that the Committee encouraged me to write the letter to the Secretary, that that was then used during the debate, so that SACGT did take a public position on this topic, and it was used publicly during the Daschle-Slaughter debate.

DR. COLLINS: It was, indeed. It was quoted on the Senate floor with a poster that had been generated by Senator Daschle and was pointed to as a strong argument for why something needs to be done, and Senator Daschle referred to it again in his testimony in the hearing.

DR. PENCHASZADEH: I have a comment to Francis. When people in the Congress talk about genetic discrimination, are they actually talking about predictive genetic information in healthy individuals or people who have genetic conditions?

DR. COLLINS: It is primarily the predictive kind of genetic information that is the cause for concern. If you are talking about a symptomatic individual in the workplace, then the Americans with Disabilities Act kicks in as a kind of protection. So the concern in the workplace is the predictive information.

In health insurance, the argument has been that if you include information about symptomatic individuals and take that off the table in the individual health insurance market, you will essentially destroy the individual health insurance market, because it depends on underwriting for its viability.

The Kennedy-Kassebaum bill takes care of group plans in terms of both issues. So the focus on the individual market is also on predictive genetic information. You can imagine how complicated it is to make a definition of predictive genetic information. It certainly needs to include family history. We have argued strongly all along that that needs to be the case. I think that point is reasonably well received, although not universal.

DR. LEWIS: My question and comment would be around using the Americans with Disabilities Act to look at something that -- if you look at genetic information as variability rather than as disability, because we all have a certain amount of variability in our genomes, I worry about the fact that saying that any kind of genetic variability then becomes a disability.

DR. COLLINS: You're not alone in that. Chief Justice Rehnquist in his opinion in a Supreme Court case called Bragdon v. Abbott raised this as a side comment to the decision. In that case, it was related to a symptomatic individual who was HIV positive, but that certainly did reverberate with a lot of people, the idea that any genetic variant that predicts future illness would create a label of disability on that person. Essentially we would all then be disabled. The meaning of that would tend to be diminished, and there are consequences of that that we might all regret.

DR. LEWIS: And in terms of what that argument was

intended to do, which is to provide a combination as opposed to --

DR. COLLINS: The argument which the EEOC put forward when they issued a guidance about ways in which ADA might apply to predictive genetic information was a sophisticated one. It basically went to the so-called third prong of the language of the ADA, which is the "regarded as" clause. That says, if your employer regards you as disabled because of information they have obtained and uses that to deny you employment or a promotion or fires you on that basis, that is a violation of the ADA.

So you could see, if an employer finding out that you carry a risk of colon cancer decided you're not a good risk anymore, that is a specific example the EEOC used, then you in fact have been injured and the ADA ought to cover you under that regarded as clause, even though you are not actually disabled.

DR. MC CABE: We have certainly heard stories and public commentary where people have made claims that this has happened to them. Some of them were very touching.

One of the things that I learned about the ADA in discussions with Paul Miller is that the time frame with which to seek any kind of redress under the ADA is actually very short. I forget what -- it is like 60 days or 90 days. Do you know the number, Francis?

DR. COLLINS: I don't.

DR. MC CABE: It is a relatively short period of time that one has to do this. So in fact, those who are involved with advocacy groups and other groups, it is very important to educate individuals about what their rights are here, because it takes too long to become educated frequently; it is too late and the statute of limitations has passed.

MS. DAVIDSON: Two things. I just wanted to make sure everyone knows about the pilot study that the alliance together with the Coalition for Genetic Fairness is doing. This was our effort back in December when we to some extent foresaw this was going to happen. We couldn't believe it was going to happen in an election year, but here it is.

We realized just from our contact with the public through the help line that there weren't the solid cases that we would need for testifying as well as for the news media. So we disseminated probably about 3,000 questionnaires. This is not a scientifically based study. We are not looking to establish incidence. We are trying to identify and profile cases so that we can put some more concrete personal profile on this issue, and also so that it can't be dismissed as though it doesn't really happen.

But now we see after about six weeks about 250 completed questionnaires, 60 percent of which want to have a followup interview by a genetic counselor. So we are proceeding with the interviews. This is actually a much bigger turnout that we had expected, given the dissemination was fairly passive at that point. This is coming out of pocket somewhere.

So I'll be bringing that information back to people as it becomes relevant.

The other is, I just wanted to be sure that everyone is familiar with and follows the Coalition for Genetic Fairness. This is the coalition that has been meeting together for about a year's period of time, hosted by the National Partnership for Children and Families. The Alliance has been one of the founding members along with the ACLU, Hadassah, March of Dimes, Alpha One Foundation, and many others whose names escape me right now. It really is a coalition that could not have come together at a better time. The National Society of Genetic Counselors is also on the steering committee, and probably a couple of other health professional groups. But I think it would be good for this Committee to meet someone who is on that committee.

DR. COLLINS: I'm glad you mentioned that, because I think that has come along at a wonderful time. They have been quite effective in spreading the word about this. In fact, one of the witnesses was at the recent hearing.

MS. BARR: I have a question for Francis. My understanding is that the funding for this group now is coming out of the Secretary's budget rather than ELSI funds. Is that correct? The Task Force was an ELSI based organization.

I'm just wondering what are the other ELSI events or groups now doing and tackling that is the same or overlapping or how you structure that now.

DR. COLLINS: We have a couple of groups looking at the structure of the ELSI advisory process about three or four years ago, and they recommended that we needed a variety of different oversight groups at various levels within the scheme of things.

I think we now have quite an interesting collection of such groups. That is going to be important as we talk about possible topics today, to figure out some what their agendas are.

Of course, there is the National Bioethics Advisory Commission at a very high level in the scheme of things, and they have certainly paid a lot of attention to genetic issues with informed consent, with stored tissue and so on.

We have this group at the Cabinet level, with its main focus being genetic testing, but we had the charter passed out -- I guess we can remind ourselves of what it says about the range of topics that this group might take on.

There is at NIH a trans-NIH bioethics group which is coordinating ELSI activities which is bringing up in many institutes, not just the Genome Institute, to try to make sure that those are well coordinated and not duplicative, and to inspire a higher level of discussion amongst NIH staff about initiatives that might be particularly timely.

The Genome Institute's ELSI advice has come in the past couple of years from a group called ERPEG, the ELSI Research and Program Evaluation Group, whose charge was in part to prepare the new five-year plan for the ELSI program. That was prepared and published in Science in 1998, and more information about that is up on our website, but also, to give the ELSI program advice about the current status of the

research portfolio and identify any gaps.

They recently submitted to our advisory council an overall review of the ELSI program, and then by prior agreement basically went out of business. At that point, we have now endeavored to set up a new ELSI review group. We have lots of acronyms in the government, so this one is just ERG, which will be in an ongoing way giving the NHGRI advice about the ELSI program, in particular trying to identify areas of important opportunities to try to stimulate research. But this is very much focused on the ELSI research program.

Then of course we have within the Genome Institute in the Director's office a vigorous policy operation, which Kathy Hudson oversees, which has been interfacing with the legislative and administrative interest in things genetic, and drawing upon many of you to help us in that regard. I think that has been an extremely important part of this translation of research findings and the policy options and hopefully legislative or administrative branch action.

And we have partnered as you know, Pat, because you are going to be a part of this, with various consumer organizations, particularly in trying to distill recommendations and then publish them in visible places.

So there is a whole array of expert groups looking at the issues that range from very basic research questions to policy implementation, trying to take advantage of the strengths of each in the appropriate way.

DR. MC CABE: Thank you very much, Francis. I know you have a conference call. Is Kathy going to join us then?

DR. COLLINS: Yes. I might say, if there was any bad news about June 26, it certainly was that the public understanding about what is being done about ELSI issues would seem to be quite limited. We probably have not disseminated information about what is going on here.

That might be something SACGT needs to think about - so these things are being looked at, does anybody know they are being looked at. Op-eds were written to rather prominent newspapers, suggesting, hey, what is going on here, nobody is paying attention to the ELSI issues. We need a commission, without realizing there already are all these groups that are far along in debating some of these issues. So we do have a public information campaign of some sort here to get the word out, but this is not entirely something that we have paid attention to.

DR. MC CABE: Thank you. That is where we are going to go next. If you look at the charter that was passed out, just to remind us, if you go to the end of the second paragraph under purpose, it says, to assist in addressing these cross-cutting policy issues, the Secretary's Advisory Committee on Genetic Testing identifies policy issues raised by genetic testing and makes policy and procedural recommendations to the Secretary on how such issues should be addressed.

Then if one goes to the top of the second page regarding scope, the scope of the Committee's charge includes recommending policies and procedures for the safe

and effective incorporation of genetic technologies in health care, assessing the effectiveness of existing and future measures for oversight of genetic tests, and identifying research needs related to the Committee's purview.

So having looked back at what our charge is, I would also like to have you turn to Tab 3. If you look at the first part of Tab 3, possible issues for us to consider, and these are topics that have been raised before, certainly issues related to oversight report followup. That is what we did this morning, that is what we will do in developing a working group on IRBs, and there will be other working groups that fall out of that.

So that will be ongoing. We need to continue to help the agencies and help the Secretary develop the appropriate mechanisms for oversight, since that was one of our primary charges.

Issues emerging from progress in sequencing the human genome. That is open-ended, but Francis raised the issue of education. If one looks at both the meeting of June 5-7, 2000 and June 30 1999, the first point on both of those was education, enhancing genetic education in health professionals, or we actually said it more broadly at our first meeting, education including counseling and comprehensive education of professionals and the public. Francis pointed out the importance of education of the public as well as the professionals.

We have talked about informed consent in genetic testing involving family information, and we discussed that at the last meeting, and had some input there.

Human gene patenting and licensing practices and access to genetic tests. We were encouraged by the Institute and Center Directors for NIH yesterday that, should we proceed with this, we should be very, very focused on it, because it could be a major distraction for us, given the complexities of this and the implications of it. We spent quite a bit of time gathering information.

Access to testing was raised this morning again, diversity issues, particularly special concerns raised by the use of genetic tests in ethnic and minority populations. Stigmatization including concerns about insurance discrimination, privacy and confidentiality, we addressed that in our letter that was used very prominently.

Rare disorders came up again yesterday and today as something that we need to consider. I will remind everyone of some data that we heard earlier. If one looks at the number of diseases being tested for, half or more of those diseases are rare diseases. If you look at the GeneTests website that was printed out for our briefing book, there are an awful lot of those gene test entries where there are one or two laboratories testing for them. So those are clearly rare disorders, one would presume, because otherwise there would be more marketability for those tests.

The introduction of tests into clinical practice and how that proceeds, use of evidentiary-based models and outcomes assessment, economic issues in genetic testing and

oversight, and the impact of direct marketing of tests.

What I would like to do by the end of today is to have focused on two or at the very most three of these to move forward on. We are still going to be involved fairly deeply in issues related to the oversight report. I think we will need to be very, very selective if we are to be effective at all. So I would suggest that we limit to two or at the very most three issues, and that even among those we prioritize them.

DR. BURKE: I think the quick easy comment is that we are already committed to one item on the June 30, 1999 list that you have just alluded to, the rare disorders. In other words, I think we already know that we need some sort of working group looking at definition and how that interacts with the volume criteria we have proposed in our model.

MR. HILLBACK: I think I would just like to extend that, Wylie, and suggest that the concept of access is one that has a number of pieces which -- orphan diseases, orphan mutations was another phrase that we used a couple of times in the last meeting. I think there is a lot of topics there. But that could be extended to some of the other topics. We could take on a reasonably broad but not impossible to get arms around issue about various problems or potential problems with access.

So to me, that is an actual extension from what we have done in the last few days, but expanding the scope of it a little.

DR. BURKE: I would just say that I think it makes most sense -- it makes a lot of sense to include access as one of the pieces in an orphan/rare/low volume test kind of situation. I think it would probably be pretty good to recognize that we are focusing on certain access issues and not others.

MS. BARR: I am struck by the education issue, but it seems to me that there are a number of professional groups trying to deal with the education of professionals and that the need has been clearly identified. But there are no groups who have taken the broader issue of the appropriate strategies for educating the public.

I think that if we are going to take that on, while we need a presentation of the overview of what other groups are doing with regard to education professionals, then we can certainly write another letter in support, identifying the incredible need there. Our time might be spent better doing what nobody else is doing, which is looking at how to inform the public.

DR. LEWIS: I just wanted to comment on making sure that our umbrellas are broad enough and specific enough. To me, the issue of access is sufficiently important that it is access around reimbursement and other issues. If we try to do rare diseases under the umbrella of access, we might be trying to take on too much and the issue might end up becoming too broad.

I see access as a piece of rare disease, but I also see other pieces of access that go beyond the rare diseases. So I would -- even though I hear what you are

doing in terms of trying to get us to deal with as many issues as possible under the umbrella, I want to make sure that we do not end up taking important issues and not giving them their due.

So I would see access as a separate issue, although I certainly would see access as an important piece to the rare diseases. I think that is what you were saying.

DR. KHOURY: Just to add to the laundry list here, obviously all of these issues are worthy of attention. I'd like to point to you a couple of items in that last list, the introduction of tests into clinical practice and then use of evidentiary-based models and outcomes assessment. Let me just make a small case here for us to look at.

We have spent quite a bit of time as a group dealing with the issues of oversight and classification issues, and I think we have come to closure on some things and moving from A to B1, B2 and C. But when you come down and think about this as a process of oversight separate from a process of how we begin to think when and if genetic information is useful to prevent disease and improve health outcomes -- in other words, when is there any value added for using additional genetic information to the more traditional medical or public health things we use.

I think that whole area of evidence-based medicine and public health is worthy of attention. I don't know whether you want to bundle it under a followup to the oversight, because that has a regulatory overtone, but more of a stand-alone issue that would be a mixture of science and policy that would draw upon the work of different groups like the U.S. Preventive Services Task Force and the other things.

To me, that is a very crucial element for how do we actually move beyond gene sequences and gene discovery to actually begin to use that information. So to me, that is a natural next step after the regulatory or oversight paradigm, is how do we begin to establish the guidelines of when we move between B2 and C and B1 and B2, and these kinds of things that are a mixture of science policy and politics.

MS. BOLDT: I have two points. While we have looked in our last meeting in terms of the different issues that are going on with education in terms of medical professionals, I don't think we really know if it is comprehensive enough. So I think we do still need to look a little bit more if it is reaching everyone that we needed to reach.

The other thing too is, I really think we need to, as a mandate from our Committee, say we need a work force needs assessment of all the genetic specialists, and also any other health professionals that are specifically working in genetics. We don't know what that number is, and we can project and see if we are going to need more trained specific genetic professionals as well. So it is two-tiered.

MR. HILLBACK: A couple of things. Judy, I agree that we have got to be careful when we get into this idea of access that we try to do so much that we don't do anything. But it seems to me that we can accept that that is an

overall issue that we want to deal with, create a laundry list of things in that, and then prioritize those so that we make sure that we cover the right things, rather than just take it on as a big amorphous blob and maybe miss them.

I think there are several things. Orphan drug is in there, reimbursement is in there. I think even the awareness of the practicing physicians groups, how do we get them aware that certain tests exist is another issue of access, and not that there is a great differential between practices in one part of the country versus another, for example, in one community and another.

So I think there are a lot of potential issues around access. I don't mind having a big word like that, as long as we subdivide it and make sure we don't miss any of the other pieces.

I still come back -- if I had to pick two, access would be one. I still think the education issue is not being dealt with adequately by the various other pieces, whether it is public or user education. So I think we are talking about practical user education in their practice versus some of the other things that are going on. So those are still the two that make the most sense to me.

DR. LLOYD-PURYEAR: I would like to weigh in on education again. The presentation of one of the points in the presentation at the last Secretary's meeting was that things are going on that are very small efforts compared to what should be going on.

You're right, probably very little is going on in the area except for what little we have done within HRSA, and also NIH with the ELSI program. Probably the ELSI program is the most significant effort in public education, and there needs to be more. But just because there is stuff going on with health professions education again with ELSI and HRSA and AHRQ, I think a lot more needs to be going on, a lot more targeted, actually.

I think the duty of the Secretary's Advisory Committee on Genetic Testing, if it is put forth as a specific need, then you do start to see things filter out that are concrete. I also would weigh in for a broad look at issues around access, especially if they are reimbursement issues. I think that is very, very important and something the Committee could look at.

DR. LEWIS: I'd like to weigh in on the education issue too. I think there are three prongs to the education committee. We have talked about two, but to me the professional education piece has two parts to it. One is having a sense of what is in the current curricula for the people who are currently in educational programs, and all the medical specialties, nursing and genetic counseling, looking at current curriculum, but then the other pieces looking at clinicians who are in practice who have been out there long enough that their genetic information might not be current.

So it is basic education, it is continuing education for health care professionals, and it is also public education. When I talk about consent, I look at it more than signing a piece of paper. I think it is an

ongoing process, and I think a lot of what I see as part of consent issues are also educational issues, in terms of what will a test do, what will a test not do, what are your rights, what are your responsibilities. I see that as a part of public education as well as professional education.

So I would like to see us look at education in three areas: basic education, continuing education for health care professionals who are in practice, and also public education. I think that is a really important area. I don't think we can do enough in that area.

I also agree with Michele in terms of another issue as being the access issue. Even though some things are available doesn't necessarily mean it is available to everybody.

DR. HUDSON: I think most of the issues we have been talking about are important priorities. I am a little concerned about using as a criteria those issues where we can make the most effective contribution.

I think the education, while very important, is also very, very hard and very, very broad. I think there are a number of targeted education issues specifically that were brought up yesterday with respect to IRBs, and I think that is a big issue that we should have very high on the list. I'm not sure if that is included in these follow-on issues, but I think that is probably among the areas where we can make the most important contribution.

I also think that a criteria should be whether or not there is another group that is effectively taking on or can take on the issues. I wonder whether or not health professional education, if we don't already have enough groups out there tackling those issues, that maybe we could reinforce rather than reinvent.

On public education, I absolutely agree, there is not enough being done currently. But again, this is very costly and very hard work. I wonder whether or not we could narrow the focus there to specifically educating the public about what this Committee has done and decided, and widely disseminating in an accessible format what we have learned as a part of this process.

DR. BURKE: I think those comments are very useful in helping to focus on education. I think there is a very interesting relationship between some of the emphasis we found ourselves taking yesterday on the need for appropriate information about tests, both before tests are taken and after tests results are known, and where we might have a role of professional and public education.

So for example, there is a lot of work being done about what works in CME and developing methods and interactive strategies and so on. I don't think we should take that on. I think that kind of addressing of professional education in genetics should occur elsewhere.

But there may be a very important role for this Committee to define what kind of information ought to be included and then disseminated in effective education strategies about genetic tests, and what kind of information is important for physicians, what kind of information is important for patients.

I actually think if we put some careful attention to that, we might be able to create in essence the templates we need to do for our oversight, but also some guidance and even some concrete elements that then could get incorporated into a wide variety of educational strategies. Those templates would I imagine include ones that are appropriate for professional audiences, ones that are appropriate for lay audiences. I think they could pick up on some major issues of use of evidentiary models and outcomes assessment, introduction of tests into clinical practice. In other words, I think there is a piece there that is highly relevant to those.

The information should be provided in an evidentiary-based format, for example. I think I would say that focus on public education, that is, making sure that whatever we do in this area includes how to package information for the public and what information it needs is not only public education, it is also an important element of access.

DR. PENCHASZADEH: I think we are running around the two main issues, which are access and education. I would certainly support to take access as a major topic, and trying to determine within access some of the specifics that we should concentrate on.

I think one of them should be access for the rare orphan diseases, the questions of reimbursement, which I would broaden to how genetic testing is taken up over and over by the health care providers and insurance and so on.

Along that line, I would like to ask your followup on what you mentioned about the issue of patenting and licensing and the comments that you were referring to from yesterday. I recognize that the issue of patenting is a very complex issue, and may be out of our expertise or realm. But the use of the licensing of patents and its effect on access, I think one of those issues within access should be looking at how their licensing is affecting access. I would like to talk a little bit more about what advice you got from what you just mentioned in that meeting.

DR. MC CABE: It was Rick Klausner, who is the director of the NCI, who basically was questioning why we had taken on the issue of patent and licensure. I pointed out that it was because issues were raised during the public comment that related to concerns about this.

Our discussions focused on their impact on genetic health, and that so far, we had been very focused on this.

It is an area that seems to be something that is catching fire on the Hill a bit. There are already two Judiciary - Government Reform and Science was the one that I spoke to yesterday, but there are two other committees.

PARTICIPANT: Judiciary Committee.

DR. MC CABE: I thought there was one other in addition to Judiciary - the Science Committee. So there are two committees that have already had hearings on this. It sounds like government reform is beginning to do homework to determine whether they want to take this issue on.

We have already been a resource to the Government Reform Committee expressing the broad range of opinion that

was brought to us. That was my role yesterday, was to educate them with respect to the broad range that had been described to us by the various constituencies.

I think Rick then followed up with a concern, and I think we saw a bit of this when we had the discussions. Once you bring that topic out, there are a lot of individuals who are impacted by that. I think that was his concern, that there are so many other things that we could be working on, that it could distract us.

I think if we take that on, if we take patent and licensure on, that we would have to do it in a very, very focused way and be quite cautious.

MS. BARR: I actually have a question I think you could answer. We are a Cabinet level group, and our job is to make recommendations to the Secretary of a particular group of agencies. Therefore, should we not be only looking at issues where we can make recommendations that you could act on?

Therefore, in looking at professional education, to what extent can she (Secretary of Health and Human Services) take action that would impact professional education? If there are ways that that can be done, then we should look at that. But I assume that that is central to our mandate.

DR. MC CABE: Sure, yes, that is. We are advisory, so I think that is a very important point, that we are advisory to the Secretary, and we should do things where we can advise her, and there is some description of how that advice could be utilized by her in our charge.

DR. CHARACHE: I think Wylie has summarized a lot of what I was thinking of, but I would emphasize that I think the education is a cornerstone for the success of the work that was outlined yesterday. I don't think it will work unless the users and the public are informed. They will find ways of jumping over the fence if we try to put fences there unless they understand them.

I am wondering also whether we might be of greatest value in establishing what the content of what we want to impart, in defining essentially the curriculum that we would like communicated to the health care professional, different levels of professionals, the laboratory directors as well as the clinical users and the public. But if we define what the content should be of what is needed to be imparted, then we might also be able to play a role in determining whether this content is already being considered, or helping to coordinate other groups who are in that area and make recommendations of how this could be achieved.

I also think that in addition to access, the issue of orphan diseases and tests should be included, but that may be included in our other list, which is the leftovers from yesterday's work.

DR. TUCKSON: I find myself very much starting at the place that Pat Barr was. I find myself re-reading the charter again just a second ago.

I think the issue is that we need to focus on those things that the Secretary can do something about.

That is the key focus for us.

Out of that, I think things start to lump together. I think that I would advocate for two areas, the first being access. I think the way that Elliott tried to describe a focus for access, we are saying access is several things. It is the rare and orphan disease issue. It is the reimbursement issue. It is the disadvantaged communities issues, those who are left out, dealing with that constituency is there. And very much, it is the practice issues, the introduction of tests into clinical practice.

I think it takes the stuff we did yesterday and says, let's figure out how to help giving that body of information into the professional societies so that they can do what they need to do to cause that stuff to get introduced into clinical practice and evidence-based medicine.

Finally what access is, it is clearly counseling and informed consent. Without the counseling and informed consent, you go nowhere. It is the rate-limiting step. I would pull out of access the counseling and informed consent and I would put that as my second group, which is I think public education, which I think is clearly the second area.

The major target I think for public education is to prepare the public to participate in the patient-health professional relationship, dialogue and conversation around giving consent for a test, giving consent for a clinical study, and then being able to be involved in the counseling and understanding the meaning of that counseling pre- and post-test. So to me, that is the second area. That is the second area related very much to the access issue.

MS. DAVIDSON: In my own mind, I want to go back to the charter and what I saw my purpose as being sitting on the Committee. And certainly it is in terms of ensuring that the public has high-quality test experience. That takes having good tests, which we have made a substantial step forward on. That we ensure that they are knowledgeable users, which is the public, the health professionals, and then a whole subset of IRBs, laboratories, et cetera.

And then access. I have gone back and forth, and Reed, before you spoke I thought it was public education that was more important, and then as you were talking, I was still going back and forth. I will say that on the one hand, no one else is really looking at public education, and it is a huge topic and critically important. I have the same sense, that it would be easy to get lost in it.

But it is so important, because there are a lot of individual efforts that are going on out there. I think for all of this to have meaning and get translated into the access, we need to have a centralized view on what is happening.

At the same time, I like the way, Reed, you tied in all the access issues, because it becomes a much more discrete package. So what I would say is that the access certainly is a logical step, moving from what we accomplished yesterday, but public education needs to be kept on the agenda, because without knowledgeable users we are not going to really be able to ensure a quality test

experience.

DR. BURKE: I just wanted to say that I really liked, Reed, the way you formulated things, but I think it follows from that very nice laying out of how the major issues get grouped and prioritized that if we get counseling and informed consent leading us to public education, I think they lead us equally to provider education.

I actually like the focus on public education. I think we should keep that. I think we should say, what we want is the public to be informed and get the counseling and have the opportunity for informed consent that we want. I think that might be a way that this Committee then formulates some crucial material that gets incorporated into provider education.

DR. TUCKSON: Let me just say, I am not advocating for an agenda. I just want for clarity while I didn't express it well. I think what I see as important for professional education is the part that deals with the integration of tests and all the work yesterday, the evidence-based medicine stuff, getting that funneled through. Then that is the education that needs to occur.

What the Secretary can do is to facilitate through AHRQ and other mechanisms, providing a body of evidence, providing the stuff that gets translated into guidelines and so forth and so on for professional education.

So I think I am with you. I just wanted to clarify what I was thinking.

DR. MC CABE: Since informed consent and human subject protection falls within her office directly, this is something that certainly in terms of educating the IRBs, that is a facet of professional education, but a very important facet. Consents also should be educational to the individuals participating in them, so that is another way that we can help the Secretary.

DR. KHOURY: Reed and Wylie, you essentially summarized what I wanted to say. I just want to say it again, maybe in a slightly different format.

This group's major impact will be on what the Department can offer in terms of all the agencies represented around this table. So I think the two issues you have identified touch upon action items that can actually involve all of us and for which there are gaps out there.

With respect to the public education piece, I would like to echo some of that because we have struggled with it at CDC, and I'm sure NIH has the same way. If you had a 30-second slot on a Superbowl ad that you wanted to say to the public, what would you say to someone right now about genetics? Everybody thinks about GATTACA, about genetic engineering, about gene therapy, about the perfect babies, but what do you actually tell people today about genetics? There is a lot of confusion.

This issue is not easy to deal with. Would you tell them, know your family history? What would you tell people on the street, and how do you prepare them for this integration of genetic information into health care and medicine and public health? I think if we approach it from

that as the next logical step from what we have done over the last few months, we have prepared the way for this oversight of integrating genetics into medicine, and the mechanisms for that, so we reach a point where tests will be offered. Data will not be complete, and we have to be very careful in thinking about ways to transmit information.

So the focus on public education is something I like very much, and it will touch upon all the other areas.

The issue of access is related but somewhat different. If you have a chance to make a big difference on what you tell the public. But then the next step will be how to ensure that all segments of the public get that information. That becomes the underserved populations, the orphan disease issues and some of that. So these two things are related but somewhat separate, because access comes after the message that you develop first, and then everyone should have access to that message or the service or the information.

So whether you want to bundle them up or have two groups to deal with that, that would be up to you. But I like very much because emphasis. That would also take care of my evidence-based plea that I made earlier, because it is bundled up in that.

DR. LEWIS: I just don't want us to forget some of the other things that we talked about yesterday that we said needed to be ongoing discussions. I think they can fit under the umbrella of access and education.

One of them is some of the social issues that we talked about in terms of looking at some of that broader scope. The other is the issue that Francis raised as one of the ones that is high on the radar, which is genetic discrimination piece. I think those can both fit under access and education, but I would want to make sure that we at least pay some attention to both of them.

DR. MC CABE: Barbara, I remember you made a comment at the last meeting. We were feeling quite rushed and we didn't have a chance to pursue it, but you discussed the fact that frequently, people talk about education, but effective education is much more difficult, as I recall, something to that effect.

DR. KOENIG: I think at the end of the last meeting I was left after hearing all the presentations with the fairly strong conclusion, which I think supports what some other people have said here, that there is a lot already being done in the professional education arena. It may not be yet enough or complete, but I view it as almost like a boulder that is starting to roll down a hill; it is picking up steam, it is getting bigger and bigger, and it is not clear to me that we would get a lot of leverage from our work from getting behind that boulder that is already going down the hill. There may be some other areas that we could have more effect.

I think the point I was trying to make more was a little more -- not so much contentious, but I am sometimes concerned that education is seen as something that will solve all these problems where it really won't. So that was what I was trying to get on the table at that point,

particularly the kind of education.

I have had some concerns myself with how I see for example portions of the ELSI budget devoted to public education, or to high school aged education about basic genetics, which I think should not be our charge. I think making sure everybody knows what DNA is also not necessarily -- we need to be much more focused on some of the particular problematic issues and what the public needs to know.

I like the focus. I like what I am hearing. I think if we do engage in public education, then it should be very focused around these issues, and how to prepare people for the kinds of discussions that they will be having with health professionals, and to give them the language, the right questions to ask, as Pat Barr said earlier, those kinds of things.

So I think it shouldn't just be -- I want real education, not cheerleading.

MR. HILLBACK: I agree substantially. I think however if we were to just focus on public education, I think we would still feel like we only ate half of our lunch.

If our real objective is to make sure that when we present these much better documented tests that the users are ready to use, I think we would like to know that. I don't in any way want to comment on what is going on and what Kathy is doing or what other people are doing isn't going to do a lot of it, but I think we ought to look at that again in a little more detail and decide where in the professional education we might be able to make a difference, we might be able to change a tone, we might be able to add something.

It may be that we decide that 70 percent of our efforts should be public education and 30 percent the other. But I'd rather not make the decision ahead of time to narrow. I'd rather get into it a little ways and then decide that where we can make the difference is public education, and we can't do much but do some cheerleading or knocking down a door or wall or something for some of the other groups.

So I still like that, and I like the way Reed tidied up the access question.

DR. MC CABE: I looked at what the original list was, and the one thing that was still left on the original list that hadn't been brought into the topic was work force. But that also fits under access.

But the fact that we subsumed everything under two topics means that we will still have to prioritize. That is what we will do after the public comments, after lunch. We really do need to get that done before everybody starts leaving for their respective modes of transportation.

MS. BARR: I think I'm going to say something very radical, but medical professionals are part of the public and delivery of medicine is a partnership. No one part of that partnership is more important than the other.

So if we began to frame the language of partnership in medicine and then talked about the questions that need to be asked to create a quality genetic test

experience or quality test experience, I think we have a framework, not an answer of what we are supposed to do, but a framework about perhaps how we should do it.

DR. LANIER: This follows on what you said, Pat. It ties in with Barbara's comment. I think education particularly for professionals is certainly necessary, but it is not going to be sufficient. What I would love to see as one focus is to look at systems of care that would allow education to be integrated into practice, so it gets into some of the other elements we have had here.

We were talking about computerized decision making systems. I think that is where the rubber hits the road, in terms of not what the information is, because that is going to change almost on a daily basis, but also how you use that information in order to help clinicians and patients make decisions on a daily basis.

There are people who aren't having years of training in this. This is the way you get them up to snuff in terms of making the correct decisions and being sure that they are accurately done.

To get to Kathy's point of how this could come about, it seems to me we need a lot of research to be done in the area. So that would be one thing the Secretary could perhaps support for the research and how you do this. It is going to take some partnerships with the systems of care themselves, that is, the health maintenance organizations, the other systems of care, who will have to invest in this in a big way in order to have these systems available.

But I would love to see us figure out how we can do that and make some recommendations to the Secretary.

DR. KOENIG: I just want to respond to what David said and perhaps draw on some of my experience in other bioethics kinds of arenas in terms of the balance that one needs to strike between system changes and education of individuals, so that they ask the right questions.

It really is the case that it is bad practice to have a system in which people have to remember to make sure that they have informed consent. You have to at the same time set up a system so it is impossible for people to go through that system without it happening. Then it becomes -- it is not so much an onus on individuals.

So we need to be thinking -- for example, if you think about end of life care, you should have a system where at the right decision points those kinds of discussions become important and are brought up, even if no one remembers it at that point in time.

So I think if we could find some way of including in that educational piece the system change issues and those kinds of partnerships, I really think that is absolutely crucial.

DR. MC CABE: So let me recap what we have discussed and see if my notes make sense to the group.

First of all, I think the concept of the overriding principle is ensuring a quality genetic test experience. I think it is very important that we capture that, because then the others fall under that and it will help us with the prioritization.

Reed then gave us two broad designations, one being access. Under that, we included the rare diseases, reimbursement, disadvantaged communities. Then we talked also about small ethno-cultural communities as potentially disadvantaged by size and availability of information. Introduction of tests into clinical practice, and I added to your list the work force issues.

I think that the other thing that is out there is the discrimination. In fact, I think we have already advised the Secretary. We have advised the Secretary that we felt that this should be a high priority for the Administration, in terms of legislation, and she responded to us that it was.

So in terms of what we can do, asking what we can do, we need to see if we can do anymore than what we have already done. But I think we could put discrimination under that as a place to remember where it belongs.

Under public education -- well, under education, let's make it education and not public education, but under education you had counseling, informed consent, and you mentioned that those overlapped with access, which is fine, but we need to have places to discuss them.

Are there other topics under the education, and the other discussion should have led to their inclusion and I missed them?

DR. TUCKSON: Just the sense that the work of the integration of tests into clinical practice, the test interpretation and the data collection stuff from yesterday's discussion, all that leads to the professional education side of the house.

DR. BURKE: If I can elaborate on that, I think we are saying that there is a test information piece that we identified as being very important, that really is part of the content that gets captured when you address the counseling issues.

DR. LLOYD-PURYEAR: It is like there are two different kinds of education that we are talking about here. There is the education for what you need to know to have the quality genetic test experience, and that gets involved with informed consent and counseling. But there is the special kind of information that a health professional needs to know, and that includes from public health to genetic counselor to physician and nurse.

That is what Muin is talking about, the whole evidentiary-based modeling and the quality assurance that needs to go on. That is a huge body of knowledge. To me, it is a big topic that from what I understand came out of yesterday's talk. That is different than broad-based public education or broad-based provider education, I think. It is a very specialized kind of knowledge.

DR. KHOURY: I was wondering how to bundle this up somehow under the two topics of access and education. Even though at one point I suggested to be separate, I think this would be the bridge that we need before you can start educating, before you can start to have access. So when people say access, I say access to what?

The quality genetic testing experience includes

the fact that we should really weigh the pros and cons of actually using genetic information. That to me is the ultimate evidence-based requirement. In this day and age, given the negatives about genetics that are out there, we need to be very careful about that integration.

I think this group is in a unique situation to make broad sweeping policies and recommendations to the Department about that fact of integration. So we have recommended oversight, we have recommended data to be collected, but then the next step that begs the question, what do you do with all of this, and when do you actually use it for access purposes and education. So what do we educate people to do or not to do or systems to do or not to do?

So I think it could be viewed as a third entity, but if there are too many subgroups to deal with here, I am willing to bundle it up under one of the other two. But it is a very important aspect of what needs to happen next.

DR. CHARACHE: I think we do need a targeted approach to education of the IRBs. We need a list of what we want them to know, and then a strategy for ensuring that they have it.

Secondly, when we talk about access, I'm not sure we can without considering patents which limit access and limit the quality of the testing experience. So I don't think we can get into the whole issue of patents, but I don't think we should totally ignore it.

DR. MC CABE: That is an important discussion point, I think, so we should make sure that we don't lose that, and decide do we want to include patents and licensure under the access.

DR. TUCKSON: Given that you are trying to get us to summarize, I think I like your language of a bridge. I just want to keep focusing back, what can the Secretary do something about. The Secretary cannot through all the power and resources -- does not cause medical education or health professional education to occur. What she with her fabulous resources can do is to make available in efficient and streamlined ways the evidence, the new knowledge about test interpretation, all the data. She can provide these things in a way that others in the private sector do the education, have it available to them, can use it.

So I think the sense is that this bridge concept is exceedingly important as a way to view it, so what happens in the access and, all the other things we talked about earlier, bridge into the education of the professional sort of role.

Let me just lastly say, and I hate to complicate this, one of the things that I would urge us to put in this is under public education. Even though we keep focusing on what can the Secretary do, one thing the Secretary does have available to her is outside of her control, and that is, she connects with the Department of Education and she connects with some of those tools.

So when we get to the public education side, we might want to keep in the differential the opportunity for the Secretary to use her collaborative influence, which

allows us to talk a little bit about the larger issues.

I am particularly trying to lay a template for later discussion around the question of illiteracy in this country. Fifty percent of the American people cannot read at the level to participate effectively in the medical care system today. You add the molecular biological revolution on top of that, you've got a hell of a problem. The point being, the Secretary by herself ain't going to solve this, but the Secretary being encouraged to have a conversation with the Secretary of Department of Education for a collaborative effort allows us to have some new tools at our disposal.

It is much too early for us to talk any more about that at 10 minutes before lunch. I just wanted to put on the table that while we are focusing on what the Secretary can do, one of the things she can do is to work with other members of the Cabinet.

DR. MC CABE: Thank you, that is very important.

DR. BOUGHMAN: I was going to point out what I think is a cart and a horse issue. I believe one of the most important things that we can do for the Secretary of Health and Human Services as her Advisory Committee in this area is to help her define this as a problem, and allow her and try to re-emphasize the importance that in her daily kinds of interactions, whether it is with the Secretary of Education or whether it is in her speeches to the public or whatever it might be, how genetics now is pervasive.

Going back originally to what Francis said, we have been doing a lot of things, but people out there don't realize what this Committee or anybody else is doing. So I am really talking about, rather than education or even informed consent or information, I am talking about, it is time for genetic readiness out there, from every individual to the practicing physician to the laboratories that are doing these tests.

We outlined yesterday a new process that will demand that of certain kinds of laboratories. What we need to do is remind the Secretary that this is the time that her health care providers need to be addressing this, and in fact in order for the system to work, she, we and all appropriate groups need to be focusing on the other levels of education.

But I think if a work group is defined, their first job is going to have to be to crystallize that, so we can even give the Secretary, even if it is a three-minute overview. If we can't do it here, then we need to focus that down.

MS. BARR: I just want to remind us a little bit about politics. In choosing what we are going to do or how we are going to do it, we might think about an election in November and a reconstituting of government, regardless of which party wins in January.

So to the extent that we can look at some of these issues and make policy recommendations about resources and the kind of statement Joann has made, it would be wise of us to do. The kind of thing that we could do, like the discrimination letter, because that had impact, it is being

used by the public now, and that is what I think we should work to get out within the next two to five months.

DR. MC CABE: Thank you. In the last couple of minutes -- Susanne just checked and lunch is here, so just to give you motivation for this discussion, should we include patents and licensure under access? Is there anyone who feels that it shouldn't be on the list?

DR. BURKE: I will weigh in with at least some caution. I think there is probably -- as we work through the access issues, we may want to continue to be informed by experts from a variety of ranges of opinion about how patents and particularly licensing affect access.

My sense is that we need to recognize this as an issue related to what we are doing, but that this group is not constituted with the appropriate expertise to address that issue.

DR. KOENIG: I just want to second that, especially about the issue of expertise. Just the amount of time -- this is such an enormously complicated issue, I think it would be a black hole in terms of the time to try and get us up to speed to make a substantive contribution. There are other groups that are dealing with this.

DR. LLOYD-PURYEAR: I weigh in with saying the same thing, that the expertise isn't there, and it is a huge undertaking. I think it is being looked at by groups that have far more expertise than we do.

DR. CHARACHE: Two aspects of this. First, I do think that we should -- whether or not we elect to pursue the issue of patents and make recommendations on what should be done about them, I think we should note that this is a key aspect of access, and urge that other groups attend to it.

My second thought which I want to get on the table is that the patent issue is not just access, it is very specifically and directly the quality of the laboratory tests which are under patent. I think both those points should be very clearly stated.

MS. BARR: I would like to suggest that patenting is a very important issue, but that we make a recommendation that ELSI put some time and effort into it as an academic study.

One of the issues here is, is this kind of information an effort in terms of genetics different, are the motivations and the process of why we have patenting and why it has been so successful in the past, any different for this body of knowledge and for making this work within the kind of marketplace that this country has. It is not clear to me that anybody else is doing that kind of academic work.

DR. HUDSON: Can I respond to that?

DR. MC CABE: Sure.

DR. HUDSON: We do actually fund considerable academic research on the issue of intellectual property. Becky Eisenberg is a prime example of that kind of effort. I'd be happy to provide you with a breakdown. We might to able to expand that, but I'd be glad to provide with what we are doing.

DR. MC CABE: That might be good to inform us,

because that was different than what we heard at the last -- we didn't access that. It wasn't that we were misled or anything; we didn't ask to hear it at the last meeting.

MS. DAVIDSON: I just want to weigh in with others. I think this is a very important issue, and important for the patient advocacy community constituency. I see this Committee bringing its strengths in another way.

DR. PENCHASZADEH: I think that I would look at the issue but strictly from the point of view of access. I think at least there should be some principled look at eventual recommendations in terms of the interest of the public for the access. I would second that also about the quality of testing, from that point of view. That doesn't require that we get into all the political and economic intricacies of patenting issues.

DR. MC CABE: I'm going to give Elliott the last word before lunch.

MR. HILLBACK: I guess I would like to suggest that we can make the issue that we want to make sure that access is not significantly impacted by licensing practices and patenting. I don't know that we can do anything about licensing practices, even if we wanted to, and I'm not sure we can do anything about patenting if we wanted to.

I think we want to make people aware that there is a concern, but I think to go farther with that is a dilution of our effort, and I think we had much better spend it in other places. I do think it is okay to express the concern, but I don't think we should go further than that.

DR. MC CABE: Thank you. I think we have had a very productive morning. We will now take about a 10-minute break, and you will bring your lunch back here. It is going to be a working lunch. We will then have our public comment at 1 o'clock. But we will be doing some business between now and 1 o'clock over lunch.

(The meeting recessed for lunch at 12:02 p.m., to reconvene at 12:35 p.m.)

A F T E R N O O N S E S S I O N (12:35 p.m.)

DR. MC CABE: While you're finishing eating, let's just begin to talk about some of the points that were raised. I hope that we have captured everybody's thoughts in here. They are not in any order of priority.

That's what we are going to do between now and one o'clock, and between the public comments and our adjournment, which I estimate will be between three and four, aiming for 3:30 p.m. right now, but we'll see. If we

don't get done, then it will be five, or whatever. But we'll see if we can get done. I was pleased with the headway that we made this morning, so that's why I think we can try and get people out a little bit early.

So we had sort of consolidated in two main groups. One was access, and the other was education. Under access we have: rare diseases; reimbursement; disadvantaged/small communities, but disadvantaged or small -- you don't have to be both disadvantaged and small to be on this list -- introduction of tests into clinical practice; work force issues; discrimination.

And as we were putting the list together, we weren't sure whether we had decided that patents and licensure would not be on this list, or would be on the list, but we were sure that if it was on the list, it was toward the very bottom. So it's on here, and we can decide if that's appropriate.

So what I would like to do, before we go on to education, let's talk about prioritization. So that's the real goal of this exercise, because we still have to really focus on just a couple of things, two or three things. We can't say, okay, we narrowed it down to two, so we'll take on everything, because we grouped it under two.

Yes, Muin?

DR. KHOURY: I would like to make a case to move a couple of these to education -- the introduction of tests into clinical practice and work force issues. I think they can fit in either one of these two groups, but the specific one about introductions of tests into clinical practice, and the evidence-based medicine and public health in my mind, is more there than an access issue. I don't know how it ended up in the first tier. That way you might ease up the load on the first group.

DR. MC CABE: So the introduction of test into clinical practice and work force?

DR. KHOURY: Yes, move them to the second group.

DR. MC CABE: Move them to education. Anybody disagree with that? Yes, Pat?

DR. CHARACHE: I think I would leave the work force issues under access. And I think the other could go in either location.

DR. BURKE: I actually wanted to make a comment about a different issue.

DR. LEWIS: I think that there are work force with both, but I certainly think that part of what we need to do - access and work force - I think go hand-in-hand.

DR. MC CABE: Anyone who would object to moving introduction of tests into clinical practice under education? A lot of these could go either place, but does anybody object to that?

DR. BOUGHMAN: Let me just try something out that's a little bit different, because this is not really a list where all the elements are equal and/or parallel, I don't think. It seems to me that we might consider -- and just listen for a second -- we might think of access in like three different dimensions, not different topics, but different dimensions.

One is the introduction of tests into clinical practice, the access issues around that, beyond the oversight or regulatory process, are reimbursement and work force issues in order to get this into the mainstream, and other pieces of that, now necessarily solving those problems, but clarifying them.

Another kind of topic, if you will, is the numbers issue. One has to do with rare diseases. The other one has to do with special problems of disadvantaged or small communities as it relates to being a minority, and the definitions thereof.

The third category is simply issues that we need to keep alive and/or at one time or another make formal statements about. To clarify and put the issue on the table. And that includes the discrimination and patents and licensing issue. It may include something else. But those, I think, have different work implications for us.

DR. MC CABE: And you were agreeing with the move of introduction of tests into clinical practice to education?

DR. BOUGHMAN: I really see that under the heading for the reimbursement and work force issues. I don't think it's a separate issue. I think that's the question, how do we appropriately get all of these tests into general, mainstream clinical practice in this age of genetics? And the issues around that beyond making sure that we are suggesting that more high quality tests or tests that meet certain standards are who's going to do it and who is going to pay for it.

DR. BURKE: Actually, I now have two comments. The first is that I think this discussion may be telling us that our efforts to lump is perhaps -- we shouldn't push it too far, because it may be hard to lump.

The other point is really just a question. It seems to me we are in the process of prioritizing or generating a list for the purpose of prioritizing. But we also know that there is other work we have to do, that I think have committed to do, and some of it is overlapping. So it feels right to me to start by looking at this list and saying, what is on the list that we have already committed to do? And take that into account as we prioritize the remaining items as a list.

It seems to me that there is a rare diseases piece that includes access, but is more than access. And there is also a counseling and informed piece that may be covering a lot of what we want to cover in education. I see those as things we are already going to work on.

Also, we committed to IRB education, which isn't listed currently under education.

DR. MC CABE: I think it was under informed consent. So we are really already committed to all of these pieces.

Let's remember that we also still have the continuation of the oversight. And so that the IRB issue really came out of the continuation of the oversight. So it's really more of the IRB that we were already committed to, right? Not the counseling and the informed consent.

DR. BURKE: I don't think we have articulated what we might be committed in counseling and informed consent, but we did identify that as a question. That is that assurance of adequate informed consent is something that will need to occur as part of the review process, and how to do that is an uncertainty. I think we are committed to discuss it, at least at that level.

MR. HILLBACK: I think there are three things I would like to comment on. One is I think we ought to change the way this is written so that counseling and informed consent don't look like the only two parts of public education. So I would rather say including counseling and informed consent, so that it doesn't look like that's the list of the items that are there. I think it's really a much broader topic.

The second point, I think to go back up to some things that have been around the access side, to me, both the discrimination issue and the patents and licensing issue, and maybe this is exactly what Joann is saying, I think we want to keep a watching brief, but I don't think we should prioritize today.

I think we have said our first piece on discrimination. It's probably not our last. We have made some noise on patent and licensing. We have learned something. But when I look at this priority list, I don't put that as a high priority compared to some of the other things here.

But then when I come back to what would I do in access if it was up to me, I think rare diseases -- I agree with Wylie, we are committed. I think disadvantaged and small communities, we are the only voice or one of the only voices that is going to take that on. By design we have two representatives of the public on this group. We spent a lot of time on this topic in the snowstorm. And so I don't think we should back away from that. I think it needs to be there in the access.

And I think reimbursement -- the first three I guess is what I'm really saying. So I would push us to take on the first three and access, and all the pieces that we have outlined so far on education, and continue our effort on what we got started on the report we have already sent her.

DR. KHOURY: I would like to take us back into the unfinished business of oversight. The implementation of the recommendations came out from all the work over the last few months, plus this classification issue. It seems to me access, education, and then introduction of tests into clinical practice are three major headings that tie into the work that we have been doing over the last three months.

So the piece of follow-up, if there is such a piece of follow-up to work and overseeing the kind of issues that have been generated from the report, and will be discussed over the next few months, i.e., data collection, i.e., test classification issues, and then using different criteria to move on.

So I'm making sort of a three-way find of access, education, and introduction of tests into clinical practice,

which follow naturally from the work we have done. You can pick and choose which one you want to focus on. So I don't see much alternative in not really going after or keeping an eye on the implementation of the oversight recommendations, although we are giving it to the government and to all the groups, but there is a lot of unfinished work that needs to be done over the next few months. That way introduction of tests into clinical practice could be subsumed under that.

DR. LEWIS: In the area of I'm not sure who else is doing the work, just having the sense of adequacy of the work force, and some projections for what we will need in the work force may well be something that I don't know if we want to take it on, or if we want to suggest that some studies be commissioned.

I have some concerns that we are going to end up with both in terms of level of education and in terms of numbers, that that's going to be more of bottleneck maybe than the FDA stuff.

DR. MC CABE: Is NHGRI doing any of that, Alan?

DR. GUTTMACHER: NHGRI, along with CDC, actually several federal agencies are beginning to look at work force issues, certainly. They've been talking about it for some time, but they are gathering data, and looking at them in a more systematic fashion that some of them are just now sort of starting.

DR. MC CABE: So you are beginning to do that? So that if you are beginning to do that, it probably wouldn't make sense for us to commission that.

DR. BOUGHMAN: We may want to make sure it's being done.

DR. MC CABE: Is there any encouragement that is needed for that now?

DR. GUTTMACHER: Encouragement never hurts, but I don't know that it's necessary.

DR. BOUGHMAN: We may want to wait until Michele gets back. I think she may have more to add. She will be back in a minute. She got called out for the phone.

DR. MC CABE: We were just discussing the work force issues, and the agencies working together to develop some work force assessments in genetics. And we were told that the NIH, CDC, and you are part of this. Did I miss an agency, Alan?

DR. LLOYD-PURYEAR: AHRQ. But it's a work in progress. But I think it's the only effort that is out there.

DR. MC CABE: Well, I think it would be on our list. So do you have an idea of when you might be able to respond to us, and give us an idea of how things are going? Six months, a year?

DR. LLOYD-PURYEAR: Well, within six months.

DR. MC CABE: So maybe, Sarah, you could stay in touch with the agency representatives to see whether the next meeting or the meeting thereafter would be the appropriate place for a presentation.

Sarah and I talked over lunch. I don't remember if we talked about this publicly, but Kathy had volunteered to come back to us with a report, and we'll probably ask her

to do that the next time.

Yes, Wylie?

DR. BURKE: I have to think about this conversation we have just had about work force issues, and some prior comments about patents and licensing are very germane to what we need to accomplish today. And that is it seems to me if you just look for moment at this list as a list of things that we know, we have an interest and concern in, I think we need to be thinking very strategically about where to put our energies, what we can do best, and what is being done elsewhere obviously.

And it seems to me that it lays out into three different actions that we can take in areas of concern to us. In some areas of concern the appropriate action is simply to write a letter indicating our strong support or concern on a given issue. So what we have done on discrimination is a model for that. There probably isn't anything else we can do, and that is an appropriate thing for us to do. And I think we have been told that that may be true vis-a-vis patenting and licensing as well.

And to some extent once we figured out that that's the action, it becomes a lot easier to resolve what we should do, because we know we've got to have a full Committee discussion in order to be sure what the points are to be made. So it's an agenda item for a Committee meeting, and it's an appropriate letter.

And other issues, and I think the work force issue might be an example, that may involve sometimes a lengthier process than we just went through of discovery, which has to do with who is working on it. Once we know who is working on it, then the action item is for us to hear a report on that. Only after that report is it clear whether we should be writing a letter or doing something else.

Then I think there is a third category of activities -- I'm sorry, let me just say what I said for work force. It may well be that there are other issues that fall under that same category like the ELSI portfolio on research and patenting and licensure issues as an example.

Then I think there are some issues that really require us to do more substantive work. And I think the orphan disease issues that we have identified are an example. That is, there are issues where we have got to do the work of figuring out what is in that box, and figuring out what the regulatory implications of that box are. And that has to do with hearing from experts. It may have to do with some literature review, and it certainly has to do with work around the table. So I think it would be helpful if we start sorting out our list in terms of those different kinds of actions.

DR. MC CABE: Other thoughts, comments? Yes?

DR. KOENIG: One other issue on the initial list which hasn't come up yet in the discussion, and that was the possible follow-up based on the presentation of the family-based nature of genetic information and consent, and consent during research. But also perhaps during the testing phase. We should decide whether we do want to include that on our agenda, perhaps as the lower priority.

But it seems to me that if we do decide on some sort of an effort to educate IRBs, and to work on informed consent, that that would be a logical place to put that in. I think it is very important throughout the genetic process, both in the research phase, and then later in the more clinically-applied phase. I'm not sure if anyone else really is working on that, but perhaps NIH is, I'm not sure. But I would like to know what has happened with that, since we had such a long discussion of it in June.

DR. MC CABE: One of the things again, Sarah and I had talked about, since this had come up again, even in the context of professional education, including IRBs and education of the public through informed consent was that it would be very important for Dr. Koski(?) to know about what our interests are in this area. And I was planning to try and get together with him on one of my trips to Washington. When is he officially in place?

MS. CARR: Officially, after Labor Day.

DR. MC CABE: Okay, so that will work out probably well. So I will do that, and that will at least let him know what our interests are, and make sure that we aren't doing things in parallel, but more in conflux, and so forth.

It is almost one o'clock, and we do have time for public comment now. So I think what we will do, we have gone through some sorting of this. Will everybody sit with it, and we'll come back to it after the public comment. Then we'll really start saying how are we going to configure these specially, and what are we going to take on first.

Any just brief questions before we break?

Agenda Item: Public Comments

DR. MC CABE: Our first public comment is from Wendy Uhlmann. Wendy is current president of NSGC. She has been here for every meeting that we had while she was president of that organization. This will be her last meeting as president, and whether or not it will be her last meeting will be the decision of the future leadership. But we thank you for your input consistently in these meetings.

MS. UHLMANN: Thank you. It's been certainly a highlight of my presidential year, has been coming to these meetings.

The National Society of Genetic Counselors commends the SACGT for thoughtful, comprehensive deliberations it has had on developing oversight for genetic testing. We strongly concur with the overarching principles the SACGT has established regarding genetic testing oversight and recommend that the SACGT now look at what steps need to be taken for their enactment.

We completely agree with your overarching principle that genetic education and counseling are critical to the appropriate use, interpretation, and understanding of genetic test results. Lack of understanding about genetic testing can have adverse consequences for patient care. The 1997 Johns Hopkins University study on genetic testing for familial adenomatosis polyposis found that almost one-third of the physicians misinterpreted the test results, and close to 20 percent of the patients did not have valid indication

for testing.

This represents the experience with just one test, and a test that is relatively straightforward in terms of eligibility criteria and results interpretation. The potential negative impact on patient care due a physician's misinterpretation or misuse of a genetic test will only increase as a multitude of complex genetic tests become available.

We recommend that the SACGT take a multi-pronged approach which would include examining options for increasing the number of genetic professionals, in addition to educating primary care physicians, health care providers, and the public about genetic issues and testing. It is important to keep in mind that evaluation of a patient's family history, and performing a risk assessment can provide as much if not more information than ordering a genetic test.

Practitioners working at the front lines of patient care need to have a sufficient knowledge base to recognize when genetic services are indicated, and when referral to a genetic specialist is needed. To ensure quality patient care and informed consent, it is critical that steps be taken now to both increase the genetics work force, and educate providers about genetic issues.

This should include a concerted effort to integrate genetics into curriculum, training, and continuing education. Increasing patient access to genetic services requires that these services be affordable and covered by insurance. We applaud the SACGT for including in their overarching principles that organizations that pay for such tests, should also pay for the necessary education and counseling services.

All too often, patients have not had access to genetic services because it is not a covered benefit. We encourage the SACGT to communicate the need for coverage of pre-test counseling, post-test counseling, and the actual genetic test to the appropriate organizations.

We recognize that the development of criteria to determine level of oversight for genetic tests is just one part of a very complex process. Just as the SACGT has been working on oversight criteria, efforts need to be extended to centralize the long-term collection of data on genetic tests, with the privacy of individual data protected in order to evaluate and regularly review the level of genetic testing oversight.

In addition, computer resources need to be developed whereby a physician, while seeing a patient, can rapidly obtain needed information about the level of oversight for a specific genetic test. Similar to GenBank, this database would be continuously updated. This genetic testing oversight database could be linked to existing genetic resources so that the physician and health care provider could access comprehensive information and supportive resources.

Optimally, a long-term link should be established between primary care physicians and local genetic centers, and telemedicine links established for physicians who work

in locations without genetic services to make sure that patients are appropriately triaged, and receive needed genetic services.

We encourage the SACGT to continue its efforts to ensure that your overarching principles become a reality. The National Society of Genetic Counselors is very willing to work with the SACGT on these critical genetic testing oversight issues.

Thank you.

DR. MC CABE: Any questions for Wendy? Any comments?

DR. BOUGHMAN: I would just like to thank Wendy and the NSGC for their continued participation, and active participation response when we asked questions of that community. Even though it is not formally represented as an organization or whatever, that kind of partnership is extremely important.

DR. TUCKSON: I would like also just for the transcript and for the record also say that I agree with that. I think that the society ought to be very proud that they had you working here. That should be noted, and be given feedback.

DR. BURKE: And I'll add that I think the NSCG's effort to develop an algorithm for evaluating genetic tests was an important piece of the substrate of material we had to work with yesterday. That was extremely helpful to us. And I would hope that this organization continues to be one of the professional organizations helping us to work out some of the nuts and bolts.

DR. MC CABE: So I think one of the messages to take back is that your input has been very valuable to us, and we would urge your successors to continue to assure that there was input from NSCG to the SACGT.

Pat, did you have a comment?

DR. CHARACHE: I was just also going to thank Wendy for her input in all the discussion yesterday, which was extremely helpful.

DR. MC CABE: Okay, thank you very much, Wendy.

Our next individual for public comment is Mary Ann Wilson, who is consumer staff representative from the Genetic Alliance.

DR. WILSON: I want to thank you for giving us the opportunity to give some comment today.

Genome science is moving incredibly fast, and with the completion of the draft of the sequencing of the human genome last month, we are rapidly entering into an entirely new stage of genomic research and technology development. Tests are currently available for approximately 700 genes, most of which are associated with relatively rare conditions. That number will soon grow to thousands with the identification of genetic links to more common health problems, and soon we will have the technology to process multiple genetic tests on one assay chip alone.

With this explosion in the ability to diagnose, predict, and identify predisposition and susceptibility for a broad range of health problems, from common, complex to the rare, the Genetic Alliance welcomes the efforts of the

Secretary's Advisory Committee on Genetic Testing in developing appropriate levels of testing oversight for different categories of tests.

As an international coalition of 300 patient advocacy and health professional organizations, the Genetic Alliance is dedicated to supporting people who live with genetic conditions, educating the public and health professionals, and advocating for beneficial and consumer informed public policies.

The Genetic Alliance suggests the following core principles to guide deliberations as SACGT makes necessary and difficulty recommendations about oversight and test group need categories, and here are five of these. The first one is the issue of affordable access to quality services must remain central to policy decision-making.

The public deserves genetic tests and technologies of the highest quality possible, however, we must keep our eyes open to the fact that there is a delicate and dramatic, dynamic balance between quality improvement with increased oversight, and affordable access. We do acknowledge that there will be increased added costs, and perhaps industry disincentives.

The second: meaningful progress in research, policy, and health care requires the involvement of consumers. And that's individuals and families who are affected by genetic conditions. With respect to oversight and classification of rare disease tests, disease advocacy organizations can serve as the essential partners in deliberating options, making recommendations, monitoring impact on affordable access, and suggesting adjustments to the initial recommendations.

Third, to sharpen understand to the clinical validity and utility of each test, central data collection is an absolute imperative. The Alliance supports the establishment of central data repositories, and will work to raise public awareness of the benefits of these next research steps. As affected individuals and family members, we recognize that improved health outcomes require our 100 percent participation in this information gathering process.

Number four, to ensure the promise of genomics to improve individual and public health protections against the misuse of personal genetic information must be approved. And the Genetic Alliance stands solidly behind the SACGT's recommendations for increased quality assurances and central data collection.

However, until genetic nondiscrimination protections in health insurance and in employment are securely in place, our ability to participate in and contribute fully to the implementation of the recommendations can be compromised.

Because of the significance of this issue to the core mission of the Alliance, we are currently identifying and documenting cases of health insurance and employment discrimination. In preliminary findings, survey respondents indicate that they have experienced discrimination in relation to employment, health insurance, long-term disability insurance, life insurance, and admission to the

military.

We also report that fear of discrimination has affected a whole range of life decisions. Some choose to have the genetic testing which is essential for medical treatment, and some report paying for genetic testing out their pocket to ensure that the information would not go into their medical records. Others, fearing discrimination, have decided not to participate in the very research that could benefit their own health.

This pilot study will result in a better understanding about the impact of discrimination. It will enrich public dialogue about misuse of the public's genetic information, and bring accurate and relevant data to public policy decision-making. As our study progresses, results will be made available to this Committee to keep the public discussions informed and on target.

Number five, the Alliance also calls for swift action to safeguard personal genetic information through federal nondiscrimination protections. Federal protections will ensure our hopes for improving public health through new genetics knowledge and technologies. Federal protections will facilitate the collaboration of consumer organizations and the general public in the large scale data gathering essential to assuring quality genetic research and genetic tests.

We know the Committee has publicly gone on record to reinforce proposed protections, and the Genetic Alliance strongly encourages you to hold fast to your support of these protections. With these assurances that personal information cannot be used in health and enrollment decision-making, we can move swiftly to participate in the farsighted and thoughtful recommendations of the Secretary's Advisory Committee on Genetic Testing. And we thank you very much for considering our perspectives.

DR. MC CABE: Any questions or comments?

DR. COLLINS: I would like to complement you and Mary Ann here, and other folks at the Alliance for initiating this survey, because I think it could be quite useful to collect this kind of information. And I think all of us on this Committee will be very interested in learning more about what this teaches us about what is happening out there to real people, faced with real problems, that are not hypothetical.

DR. MC CABE: I know that you have received an overwhelming response, as we were told this morning, and are having to identify the resources to pursue this. Is there any idea when you will begin to have sufficient data that you might report it to this group?

DR. WILSON: The data is coming in all the time. We have over 250 completed surveys. Sixty percent of them have gone through a written informed consent process, and have requested a follow-up interview with a genetic counselor. At every step there is an ability to stay in the process all the way to being identified to talk with news media, to testify, to go on record.

The interviews are really taking a considerable amount of time, because we have a protocol and we really

want to ensure that they are only done by genetic counselors. So we are identifying resources, because this was not part of the budget. So if anybody has any thoughts about this, I would certainly love them.

DR. MC CABE: Well, could you keep Sarah informed, and let us know when you feel it would be appropriate to make a report?

DR. WILSON: Yes. We have information ongoing, so at any point, I may report at the next meeting, or if something comes up, we can at that point really draw on the data that we have at the time.

DR. MC CABE: Okay. Well, I'll leave that up to you when you feel it's appropriate for us to hear it. You can then discuss that with Sarah in terms of the agenda.

Other comments, questions? Thank you very much.

Agenda Item: Discussion of Issues (Continued)

DR. MC CABE:

Are there any other comments from members of the public? Okay, if not, then why don't we move on. Joann has an organizational structure that she has developed. Do you want to present this to us? We'll get an overhead to facilitate the communication. And I think basically what we were talking about was looking at it quickly, it appears to be sort of a reorganization of what we have with some of the categorizations that we have discussed.

DR. BOUGHMAN: Right. I called it the summary according to Wylie.

DR. MC CABE: I think what I want all of you to do though, again, looking at Joann's organization quickly, it does reorganize what we were talking about over lunch, but it's going to be very important, there is still too much to do. We're going to have to identify within these, which are more important. And it's one of those problems that all of these issues are important.

But as we begin to address and prioritize, I would urge us to go back to some of the discussion, and that is what is it that we can do that will have an impact? It's very important that we focus our efforts where there will be an impact.

DR. BOUGHMAN: As usual I can't draw it. I can't figure it out. So I was trying to listen to what I thought were some of those issues, and one of the ways that we all organize our lives, whether we recognize it or not is on the two axes of importance and urgency. And it's important to understand the difference between those, and there are some things that are urgently addressed, and we when we get them out of the way, we have the energy to spend on the things that we can in fact sustain our energy. And in fact that's really the order that I put them in. Let's some of them on and off the table, and move on.

The way I did it was categorize the things into issues where what we need is some sort of statement or comment or position, letter. And it went into three different action categories, one that we've got the essence of the discussion. The second one is we've actually got it down in the form of an approved statement or motion for the Committee, and then any follow-up.

And using the genetic discrimination letter as an example, we had our discussion. We approved the points that needed to be made. Our chairman wrote the letter. And then the chairman and staff will reissue that content, maybe with slightly different introductory statements or whatever, but we have the essence of it.

And if we go back to the transcript I think of what Pat and Victor really kind of crystallized there, I don't know how much more discussion we need, but we have not approved a formal statement yet per se. So we haven't gotten to that. I think we have decided we need to make that as some sort of position or statement, and the further steps can go on.

We also figured out that before we can take some action on some items, we need other people who are doing work to in fact present that to us so we can crystallize it. The ones I heard are the work force issues that are being addressed, and I called it an agency coalition. I wasn't as good at writing down all the acronyms that Ed was earlier.

And these are not necessarily in the order in which they will come, but we focused on them. The ELSI activities and the intellectual properties, that was pretty specific. And then the big one if you will, our continued follow-up on the development of the oversight process. We are expecting the FDA and their fellow agencies who are involved in that process to start filling in some of the detail on the steps of the process, and we wanted to have that as continuing oversight.

The Lab work group is being meeting in September, and some of the work that they will do is going to inform that process in a very direct way. And also, we have the rare diseases issue that was focused on slightly differently. That one may also fall down into the next category.

I heard three different areas where we are defining enough of a problem and an issue that we need to have full discussion, but might be better done by a subset of us, and then brought back to the Committee as a whole. One of those was the access issue, and trying to get our hands around that to decide if there are specific statements or actions that need to be taken, and we kind of wandered on that one.

Education is a huge one. We are having difficulty defining that one. It may be that what we need to find out, and I think a few people really need to focus on this, obviously my opinions enter into this organizational process, but to actually design a request of those agencies, groups, NCHPEG and the others that are out there, so that we can get a better list, or idea of what really is going on.

When we say people are doing things, that may not be enough for this Committee to know right now, who is doing what in an overview kind of process. And I think that from that we could distill for the Committee as a whole, a little bit more, what could this Committee do, and propose that, and then guide our discussion.

And then we have the consent. I brought that to consent, because we have the IRB focus as a first, but every

time we get to consent we pull in a few more issues. But once again, I think we need to figure out exactly what the questions are.

That means for full Committee agenda items that haven't been assigned out yet, the reports on the things from above it, and their distillation, the update on the oversight, and the full Committee response or filling in on our own, including what our group on consent might say. And then I still see introduction of genetic tests then to practice, and I see reimbursement falling here.

Still, not yet fully fleshed out, but while I was working on this, little did I know Michele was in fact trying to put together how she saw the issues around the introduction of tests into clinical practice. I just so happened that it fit as if it were page of what I had written. That's kind of an outline of the way the Committee as a whole might attack that kind of next step in the whole oversight process or the change of clinical practice, the laboratory oversight issue, and now the next steps out into the more general practice areas. So it doesn't do all that you requested. It does at least kind of subdivide the work.

DR. MC CABE: Well, thank you. Even though it didn't do all of our work for us, it's very helpful.

DR. LLOYD-PURYEAR: The last one was sort of a hodge-podge. I was trying to figure out what you -- because it is sort of the financing of tests, and it was health insurance issues. And I thought that was a way of actually bringing in patenting and licensing, but anyway.

DR. MC CABE: I appreciate what both of you did. It was very helpful in focusing our discussion.

MS. BARR: I just thought that there might be some way to move one of them quickly. Where you had on the first chart, patents and licensing. Then you have an ELSI activities, an intellectual property. It seems to me that if we got that at the next meeting, a presentation, then we would be able to do our letter statement on that one, and move it. It may be incorporated, just as our discrimination issue is incorporated into another report. So we could at least move that one right out.

DR. BOUGHMAN: I might suggest a little bit more than that. Given the discussion today, I think the staff might be able to pull out or highlight for us so that we could have even a proposed first rough draft of a statement. Here's the report and then refine that, rather than starting with a blank piece of paper.

MS. BARR: Do we know enough from work force already? Aren't there lots of numbers out there? Or we don't know enough about work force?

DR. BOUGHMAN: As I understand it, and correct me, everybody if I'm off base here, there has been a study done on genetic counseling as a profession, as an accredited group, or as a certified group. And there have been some attempts at least definitions of certified geneticists and so on, but there really has not been a broader look at pediatricians, and the impact of OB GYNs who do or do not have fellowship training in genetics, and hematologists, and who is going to do what kind of thing.

DR. BURKE: I feel like you have given us a framework, that with just a little bit more discussion, is going to give us a blueprint for where we go next. It's really helpful. I had just a couple of comments on how you had organized things.

The first was just as a question for us to consider whether reimbursement is already something that we could put up as the third thing after patents and licensing. And what I'm anticipating is that reimbursement is an issue of access. That we kind of already know that's an issue of access, and there isn't a lot more for us to do other than acknowledge that, and perhaps write a letter.

I think that we want to be sure that we have the appropriate discussion in full Committee, but I think it would be reasonable to put it on the list for that kind of action.

DR. MC CABE: Can I just stop, before we go on to the next one? HCFA has offered to give us a presentation on reimbursement at our next meeting.

DR. BURKE: So it looks like we could put reimbursement on that list, knowing that we'll have a presentation and discussion at the next meeting. The other, which I think is a more substantive issue is that I think what we said coming out of our discussion yesterday and this morning is that there were some substantive issues that weren't a matter of just sort of handing over the template to FDA and others and hearing back, but rather there were some issues that we felt we should continue to discuss.

And I would say that I think the rare diseases heading, which represents a complex of discussions, comes under that and ought to be under another work group. Another one which you already have is IRB. And there are two others which are question marks that possibly should be on that list. One of them is data collection, that is I just raised, should there be similarly a work group that is talking about what kind of data, what are the options, and beginning to get ideas together and organize them.

And the other is we have talked a lot about the importance of pre- and post-test information, and the need for the development of a template. I envision that there might be a work group that has major representation from professional organizations, that does some of the spade work there, and reports back.

So I really like the framework. I think if we get the content right, we're going to be very happy with it.

DR. MC CABE: Pat Charache?

DR. CHARACHE: Once again, Wylie has put the reimbursement where I was going to suggest it be put, and so on. But I wondered about fleshing out a few of these. I'd like to be sure that when we talk about patents and licensing, it's not just access, but it's quality. And that is really going to be very important to emphasize.

And under reimbursement, I wonder if we could broaden that and talk about funding, because it is not just reimbursing for the test. That's one element. But maybe it should be a separate entity. But it's also expanding the resources of HCFA and the FDA so they can meet the charges

which we are putting on their shoulders. It's a broader thing than just paying for the test itself. So I'm wondering if that should be reimbursement/funding?

And there are several others here that I think we can flesh out a little bit, but I think the placement concept is really great. Because I think things like this funding, patenting and licensing should be handled just like the discrimination letter. I think it's powerful.

DR. MC CABE: Thank you. Francis has had his hand up. When he comes back, hopefully he'll remember what he wanted to say. I saw a hand up over here.

DR. KHOURY: Wylie, can I ask you for a point of clarification of the data collection piece, in that I know we will need a lot of help along those lines. All the agencies will need a lot of help, because that piece determines to a large extent, the success of the oversight model that we proposed between yesterday and today.

So I am wondering, do you see a work group doing this, or periodic or maybe regular updates from the agencies, or some combination thereof? What do you have in mind?

DR. BURKE: My sense from the discussions we have had yesterday and today is that the first thing that needs to happen is the development of some sort of catalogue of options. Some sort of here are the different ways that data collection could go forward that are relevant to the concerns that will be raised after tests undergo premarket review.

So I think what we said is tests undergo premarket review, and some tests go on the market as a result. But we know that we want some ongoing data collection. I think at that point our conversation gets very vague and needs to be specific. So I think there needs to be a discussion on the part of an appropriate group that fleshes that out. That basically says if we are going to use existing resources, here are the kinds of things we could do, like the example you gave us about the existing survey that Bob Martin had mentioned.

But that list needs to start with what we could do with existing resources, on up to what kinds of new ventures involving new resources might we envision that would meet needs. Now I am not sure frankly -- I know there has been a lot of work going on -- whether there is already an existing group comparable to Lab Forum, that already could bring forward those kinds of ideas to this group, or whether there needs to be a working group analogous to Lab Forum perhaps, that basically does the initial brainstorming I think, and then brings those ideas back to the group for prioritization.

DR. KHOURY: We have had lots of brainstorming, but not as part of SACGT. We have had an interagency HHS working group last year. And then a consortia around two specific diseases. So I would really welcome a subgroup of this Committee that I can be actively involved with, that can maybe meet or talk for a couple of times, and bring to the full Committee, some of that option discussion for next time.

I don't know whether it needs to be as formal as the Lab Forum, but maybe an interim work group that can give you a report next time. Wylie, I suspect you will be on that team, if that's something you want.

MS. BEARDSLEY: I would like us not to lose the notion of looking at disadvantaged and small communities here. I'm not sure how it fits into this scheme. I'm not sure it's a work group, but it seems to me that we have heard a lot about this, and I know that I'm having trouble integrating it into some sort of coherent set of issues.

And I would like to see us somehow commission some work where somebody would take what's out there, and take a very disciplined look at it, and see what the issues really are here. Because the reason I think it's important is that if this groups doesn't deal with this issue, I don't know who is going to.

DR. MC CABE: Is that under the access, Joann? Would that be where that would fit? It would seem that. I guess there is some clarification. Would you see it under access?

MS. BEARDSLEY: Yes, I think it's something that could be dealt with under access. I'm not concerned about where it is.

DR. MC CABE: Okay, you just want to be sure it is captured.

DR. TUCKSON: One way of trying to get at that more simply is Judy's chairing of that group of people of color was a good group. And one of the things we want to do is not disrespect them in any way, by just consulting with them one, and then, okay, we've used you and throw them away.

But they are there, waiting. So one way we might be able to do this is for Judy to sort of convene them again by phoning and conference calls, and let them sort of percolate what they see as some of the issues. That would at least give them a template for later discussion. It would start the work concurrently.

DR. MC CABE: The other thing that was said nicely with that is as Sarah points out stigmatization, which has been on some of our lists. So it's not solely access, but other issues related to ethnic/cultural/minority communities.

DR. LLOYD-PURYEAR: It's also access to the test development process. It's just not access to the test itself. It's to make sure that test is appropriate for all populations.

DR. MC CABE: Well, access to a quality genetic test experience. That was our overarching principle this morning. So it's access to services, and certainly stigmatization could be a block to access to services, as well as size, rarity of the disorder, whatever.

DR. LEWIS: Can I just follow up on what Reed was saying? I think that's a very valuable point in terms of making sure that we stay connected with the people -- not just the people who are on the working group, but also the people who participated in the meeting in Baltimore. And just so that people know, one of the things that we are

going to be doing is talking about the process of that work at the American Public Health Association.

Sarah contacted me, so that we are going to be sharing what we learned in terms of the outreach piece in November at APHA.

DR. KOENIG: As a possible add-on to this, the other couple of pieces I still as missing, and they may just be low priorities, but we can so often against the barrier of how difficult it is to define social issues, especially how they relate to oversight. And perhaps if again, working with this group that we have already convened might be a way of moving that forward a little bit.

But that still may be one of the things that we need on our list, when Wylie was talking about which are the things that we need to continue to make a contribute to in the ongoing oversight, like the rare diseases. I think the issue of how to incorporate social and ethical concerns into technical oversight like this, since it hasn't been done that much in these forums, is something where maybe we would be making a unique contribution, if people are interested in that.

DR. MC CABE: Thank you. So if we can step aside a little bit, there are five work groups represented on this list. That's really more than I think we can take on in the immediate future. I had chosen arbitrarily two, or at the very most three this morning, and I don't know how people feel about that. If you don't feel we can on five, which I feel we can't, but if anybody wishes to argue, first of all, how many do people feel is realistic that we should take on at this time?

DR. KOENIG: Didn't we vote on one this morning.

DR. MC CABE: I don't think we voted yet.

DR. BURKE: On the IRB.

DR. MC CABE: Well, we first said that we could put together -- yes, we did. We have a vote.

MR. HILLBACK: And we certainly have an ongoing commitment on what have been working on for the last year. That's still not going to go away.

DR. MC CABE: Okay, we have the consent/IRB, and you can put an asterisk next to that. We have the ongoing commitment to oversight, and continued issues related to the report that we had already developed.

DR. BOUGHMAN: Now we are going to put that back to the full Committee?

DR. MC CABE: We had a work group that met yesterday, which was specifically in follow-up to the oversight report. The question is do you want to have a work group that continues to try and look at what needs to be done with respect to that report?

MS. BARR: Well, if we were to do that, I think actually then what you would have as a subheading, and they have to decide how much time on each, I think it actually fits with that. Rare disease fits within that. The definition of social issues fits within that. And data collection fits within that. And you are left with the other issue, which is education, which I don't think does. Now that is a reshuffle that may make it impossible to do

the work.

DR. MC CABE: Yes, I think that that would be -- those are really individual topics. It would be hard to work, and it would probably be better for the entire Committee to prioritize.

MR. HILLBACK: I would to suggest that for now, the only work group we keep going in any solid, formal way is the sort of regulatory/structure work group, i.e., the interface point with FDA, CLIA, CDC, et cetera. And not a broader work group that says we are trying to cover everything in our set of recommendations on oversight.

Basically, the work group that met yesterday, but focus on the regulatory framework that we have asked to have someone work on, and want to look at again, instead of the whole Committee, which I think needs to follow on our whole Committee report. So if we are going to keep a work group going, I would keep it with a fairly narrow charter.

DR. MC CABE: So we might want to reconstitute that, however, because my understanding of the work of the work group from yesterday is that by the end of the day today, their work is done. And that we will then generate a report as an addendum.

DR. BURKE: I would agree with that. I would say that although what I'm going to say is entirely in the spirit I think of what Elliott just said, and that is we actually had more people around the table yesterday than we do today. It was a large group. And then I think within that group, and folding in the additional people that are here today, it would be easy to divide up into smaller and much more efficient teams to address some of the specific issues that we said we want to address.

And what we call them, I don't know, but I think they would be very targeted on specific, short-term endpoints. In other words, I like the concept of brainstorming. I think there is a need for small group brainstorming on several issues, to formulate them, particularly in the context of your call for us to think about what the Committee is able to do. And sort of bring that back for discussion.

DR. TUCKSON: I'm not sure where this fits. In my mind, I think we can do three things, focus on three priorities, and a little half. The little half, which I think is an important half is the discrimination issues group, because I think that really is more of our convening and listening, as opposed to sweat equity on the front end.

I have always learned again with communities that are outside of the mainstream, it is always better to listen first and then plan, as opposed to plan and then listen. So I think it doesn't do violence to anything by saying we're not going to put a lot of work into it yet. We're going to listen, and then we'll come back and visit what they teach us. That's why I say it's a half, and doesn't require too much work. We said of course we have to do something. That's a fact. We don't mind recommending that.

The three groups that I heard are clearly, IRB. Second, I think the data group is a predicate for physician education. It's the predicate for feedback for the field

about all the stuff that we have done before, because it makes it a feedback loop. And the data stuff that is so important for quality determinations down the road I think is just key. And I would just hope that that doesn't get lost.

The third group I think absolutely has to be a focus group on patient education. That just has to deal with that question and focus on it.

DR. LEWIS: I would like to point out that what I hear us doing is keeping the same number of issues, just trying to figure out a way to sort them into the right number of groups. And we have had like four or five different attempts at taking the same number of issues and putting them into groups. I haven't heard any issues leave the table.

I have heard ways of managing the issues in efficient ways, but I haven't heard us take any issues off the table. I have heard us recategorize them into the right number of headings. And maybe I'm missing something, but haven't heard anything go away. I just want to point that out to us, that it seems to me that what we are saying is that all of these issues are critical, that they are all high priority, and that we're just trying to find a way to deal with them. With all due respect, Mr. Chairman, we are trying to take issues and fit them into your number.

MS. BARR: Well, I just want to try again in terms of what I think Wylie and I were both getting at. We, as a Committee, have done a tremendous amount of work, and we have heard a lot. Within this Committee and other resources we identified, there is a lot of expertise. So that rather than call these full working groups, with the kind of effort that went into the working groups the first time around where we had two, if we try to get some outlining committees, instead of working groups.

So if we put three or four of us together as an outlining committee on some of this stuff, to look at options, what can be done quickly, what would take a long time, we might be able to tackle all the issues, and then be able to prioritize them after that preliminary work was done.

DR. BURKE: Just to follow that up, I think part of the problem here is that we don't even quite know how to get at something like physician education. I think we need a small group to sort of look at the universe of options, and what makes sense for SACGT to do. I think the same thing applies for data collection. We need to look at the universe of data collection options, prioritize them, and bring that back to the Committee before we do a lot more work on it. I think there are some short turnaround issues that need to be worked out.

DR. MC CABE: So if we were to take then the topics that Joann has on the overhead, there are really five topics there. If you just take the top three and make them the topics for teams, that we would be talking about five of these teams. If we are talking about five, we can barely use two to three of ourselves on them, or we can be on more than one team.

So the choice is we either decrease the number that we focus on, or we decrease the number of people working on the teams. And we can certainly supplement with people who are not part of the Committee.

Sarah?

MS. CARR: I just want to ask a question about the template of pre- and post-information. That seems to be an important piece of the follow-up to the oversight. Wylie brought it up before, unless it is subsumed under something else there.

DR. BURKE: Move it if you think that is feasible. It would make sense to address those together.

MR. HILLBACK: We talked yesterday, and Wylie outlined today that one of the things we were going to do was get the professional societies to help design these templates, to help design some of these other things. But we weren't going to try and do all of that. Now I hear us start talking about we're going to try to design the templates. We're going to try and go into the level of detail. I don't know if that's what our charter is.

So I'm a little confused, but I think we have set some principles that this needs to be there. And we've got to go and keep working on that, and we can say someone else go work on it. We're going to work on some areas where we need a new initiative like the education of IRBs, because the system isn't coping with that.

DR. LLOYD-PURYEAR: Well, I don't think the role of an Advisory Committee is necessary to do all the work itself. I mean when you are talking about public education, the role of the Secretary's Advisory Committee would not be to launch I don't think, a huge public education campaign. It's to drive those efforts, to frame them, to point out the important elements of that public education campaign.

And to bring those people together, those groups and organizations together that are necessary for that campaign. And it would be the same for the data elements, because I don't think the expertise is here at the table either. You bring those groups and those individuals together to do the work, but you drive it. You drive it as a Committee.

MR. HILLBACK: Why?

DR. LLOYD-PURYEAR: Because no one else is doing that.

MR. HILLBACK: We haven't given anyone else a chance to do it yet. We put together and are going to send by the end of September, a proposal for a regulatory framework that was very much just a framework. And we are asking the regulatory authorities that are part of HHS to put something together, and use the outside world to help them. And before they even start, we are going to do some of that for them, and give it to them. I think that's what it sounds like to me.

DR. BURKE: Well, I actually think you are posing a question that we need to answer, and it's a very important one. My take on it is a little bit different than yours, although I think I agree with the general way in which you are outlining this. That is, I think at a certain point we

have done enough in advising, and then it's time to turn it over to other implementers, who will let us know what they did.

I'm not sure we're at that point in any of these arenas yet. Certainly, we have identified some as maybe more critical for our more intense input than others. The definition of rare diseases, orphan diseases would be an example. But in the setting of data templates, I think we have simply said that's what we need to have. I don't think this Committee should do the detailed work.

I do think that there is still a phase that I'm calling the brainstorming phase that takes that concept, which is a one-line concept at this point, and fleshes it out as to what do we really think and agree is in that concept? I would like to see a brainstorming group, a short turnaround group that included three or three members of this Committee, and representation from appropriate agencies and professional organizations. Do that brainstorming, bring it back to the Committee.

And at that point we say, yes, that's it. Now go work on the details. We'll be happy to hear back from you. I just think we're not quite at the stage -- you seem to feel we are.

MR. HILLBACK: Well, my suggestion is we shouldn't send the addendum forward if we are not comfortable we know what it means enough to have confidence in it. That's what I think, so you can moan or not. I surprise myself constantly by saying I think you ought to hand it over to the regulatory authorities and let them take their shot.

But we had here yesterday a number of people from the college, and from CAP and other groups, who all will tell you that through CLIA, through the college, and through all the other things there is a whole set of rules and regulations about what needs to be in this information pool, and we haven't even given them a chance to work on it yet.

If we want to define it more, that's fine. I complained two meetings ago that we were at 30,000 feet, and I guess now I'm complaining that we want to be 1 foot. But if we do, then we've got to really commit to that, and that's a different ball game, and can't be just sort of done.

DR. BURKE: I just want to register that I think the difference of opinion is not conceptual. I think we completely agree about the conceptual framework, and the sort of limits of what the Committee should take on itself, and whether it's really the dividing line between when we have done enough, and when it's time to turn it over.

DR. KHOURY: I hate to disagree with you, but I think this is one time where it's a question of a quantitative rather than a qualitative disagreement. I think the successful of this oversight paradigm that this Committee is handing to HHS for implementation, really its major success is the creation of something new, something that hasn't been done before in the government that involves the collaboration of several agencies.

And the data piece is so essential and central to it, because the success of the oversight depends on whether

we can collect the data. You know that I've been thinking about this issue for the last two years. I think this Committee or subgroups of it can still provide enough advice, enough guidance before we go implement anything.

So I don't see it at the 1 foot level, nor at the 30,000 foot level; maybe at the 15,000 foot level. So at one point you guys have to let go of it, but I agree with Wylie, we're not at that point yet. I think the next few months are going to be crucial.

DR. BOUGHMAN: I might suggest that what we are really asking for is rather than us doing the work, or us just saying our work is done, whoever want to do whatever, go do it, it is a matter of this group crystallizing the charge to groups, or invite those groups specifically. In other words, give them some sense of sanction and receipt of that information as we did by including representatives on the very large group yesterday. That made a world of difference.

DR. LEWIS: One of the things is I think that after a little more than a year of working together, that we're a really good Committee. You can almost in a sense tell what people are going to say, because you have a sense of where they are coming from. So while I don't think we need huge numbers of us on any particular work group, I think that we know what our resources are within the Committee, and within the external world to draw on them.

So I think in terms of as I hear whether or not we can have two committees with six people or six committees with two people, that in terms of the Committee, we could go either way. My concern is the amount of staff time and energy that is going to be involved in moving all these projects forward. Sarah and her staff's time is not infinite. There were many times when we were playing the conference in Baltimore, and Sarah and I were talking, and it was eight o'clock at night, and she was still at the office.

So I want to make sure that what we do is something that is doable, and that we don't even up, even though we can spread ourselves so thin that we don't take the staff we've got supporting the work that we do, and spread them so thin, that we can't accomplish what we're wanting to do.

DR. CHARACHE: I think these are a little uneven in terms of the amount of work required. And I wonder if we can't chop away at some that are fairly simple. I see for example, the first one, the consent is largely going to be what types of diseases and which diseases require it. And some examples of what the rules are to say that something requires it.

And then idea of how to communicate it. Now maybe other people see this in a different light. That's fine. But perhaps that could be handled by a small group who could define it according to whatever is meant by that word. Certainly the IRB fits that. I think just two or three of us could probably write down what it is we want the IRB to learn, and how we want to know if they have learned it, and bring it back for another meeting.

For education, probably a core segment of that is going to be a list of what we want the public to know, what we want the practitioners to know. It's the informational skeleton. That then you could decide if you have decided what you want them to know, what is the role of this group in making sure that they learn it, or finding out who can teach it, and this type of thing. So some of these are really rather defined bites that could be done by groups of three or four for the group then to use as a point for editing and elaborating.

DR. TUCKSON: I think Elliott has done us a service here. He forces us to think about how we define the purposes of these groups. At the very end of his comments I think he helped me. I don't see us as trying in way to reinvent the work that is very specific, that we have given over to the regulatory bodies to do, for example, in data. We don't want to reproduce that.

What Muin is saying, and I think that makes sense to me, is that we are trying to find new bridges and new relationships about what this stuff means, specifically for example, professional education. We could sit here all day and write pages of how important it is to get physicians to be better educated about this stuff. Great, everybody would love it.

In any meaningful term, medical education, continued professional development means ultimately the development of guidelines. But it also means the development of information about performance, about what is really going on, and feeding that back into actual practice, so it ramps up based on feedback.

Elliott has taught us a great deal in the last few days, last meetings about how burdensome he is concerned collecting data will be for the labs. I am terrified about collecting data, what it will mean by managed care companies and physicians in terms of the administrative burdens. All of those are major kinds of issues and challenges that all sort of come together across specific silos.

So I think what Muin has got me convinced of is that the charge to these sorts of groups is that you look at it as more of a whole in terms of what it ultimately means for policy issues, not for the level of specific specificity or redundancy that we have turned over to the regulatory bodies for the level one, level two scrutiny.

MS. BARR: I would agree. While I agree with Pat that IRB and consent actually can be dealt with rather efficiently, given all the work that has been done in those areas by other groups, I would just bring which issues we had to look at and how we did it different. And I also think rare diseases can probably be dealt with rather efficiently, given the amount of expertise and how many people have been working on that issue for a long time.

But that the data is huge. And I think what we can recommend to the Secretary about education I think is rather large and will take more time.

MR. HILLBACK: I guess I would just say that while I agree with some to the extent we could divide up into a lot of groups, I do get a little nervous about creating

groups of a couple of people. We have so many divergent points of view. That helps us, but it also means that the groups need to be formed that way.

But also the little groups that create something have to come back through here, the eye of the needle. But the other problem is we become the eye of the needle. And we end up with we're going to have six groups report in two days. That means we get two hours per group. And we don't do our issues justice.

I think one advantage we had yesterday in having an entire day on one topic, without other issues, without other things coming up, with a leader who really let us alone by staying tight on that, and Wylie didn't let us stray off track, not that Ed does either, but we just had one topic, and we got there.

I would hate to have six or eight of these things bubbling along and then feel that we are forced to deal with them, we create expectations. We spend an hour and a half on some, and we all leave totally frustrated that we really didn't get into the issue deeply enough to know the pitfalls, and to know which way to turn.

I think it's the danger of biting off too much at one time. I would rather be mean right now and say we're only going to do a few things, and then phase the next ones in, so that we are starting on the other ones as these are ending, or whatever. I'm very nervous that we'll wind up just getting an inch deep into some things, and being embarrassed by our output.

DR. BURKE: I certainly share your point about prioritization and being careful to give things the right attention that they need is well taken. I think we should think carefully about that.

I'm a little more optimistic than you are that I think there are a few things where I think some of us have said there is a need for a little bit more work. Now having listened to this discussion, I would define it as I think there is some collaborative work refining the charge, to make sure that what ultimately gets done is a good part of the cohesive hole.

And I think particularly the consent IRB data elements, data collection, and rare diseases pieces are all those. I think we have done a lot of the work already, and I think there is some more detailed work that needs to be done. We already know the hole that it fits into. You are absolutely right, it has to come back here, but I think there is some work in refining the charge that could be done and be brought back here, and be done justice to within a portion of the meeting.

Some of the other stuff I have a sense is sort of opening up new ground. And we either have to give it more time when the report comes back, or we have to see it as a longer term process. That is, maybe next time we'll hear back and really resolve some of these issues that are follow-up and refining charge issues, and then others we're just going to open it up. And only after that open up process occurs, can we figure out how much time it's going to take to be satisfied that we're done with it.

MR. HILLBACK: I don't disagree with you. I guess I would respond by saying if those first three items on the board there are follow-on items to clarify issues we have been talking about, then that's all we ought to take on right now, between now and our next meeting. And we ought to focus on those three things. We are going to ask Kathy Hudson to come back and give us a primer on education at the next meeting, so we can take some time at that to start to think about education.

But I would focus on those three items, the top three on the list. Figure out how we organize to do three small teams. Charter each of those. Put our process in place, and then at the next meeting work on those as our primary work, and begin our next level of our education process on the education issue.

As much as I love the education problem, and I think it's a very big problem, I'm willing to defer it another meeting if finishing this is the consensus of the group.

DR. MC CABE: Just to reiterate my understanding of what our presentations are next time, that is research on intellectual property, the ELSI research grant portfolio on intellectual property. And then also looking at reimbursement issues. So HCFA is reimbursement. So that's two or three presentations. Typically, they run 45 minutes to an hour.

Then the ones that I would agree with Elliott, the items on that list that require most acute attention, and probably can be dealt with most quickly also are the consent/IRB. Because that is really evaluation of what's out there, and developing a plan for what we should recommend.

The data elements collection, which is follow on to our report, and the rare diseases issues, which again is a follow on to the report.

The access is something that we talked about developing with Judy and the other group. So that that is something that could take a couple of meetings to really get to, to do properly.

DR. LEWIS: I was going to say, but the process needs to be put in place.

DR. MC CABE: But I think it's already been assigned to you. Thank you for volunteering.

And the education piece again, I think is a huge, huge task. There is the issue of whether it's even doable that we talked about over the day.

So I would suggest that we

MR. HILLBACK: Could I suggest that maybe on the education piece, if we wanted to do something, that we form a small team merely to scope the issue between now and the next meeting?

DR. LEWIS: If we're going to look at education, I want to make sure that we're looking at education of all the appropriate disciplines.

MR. HILLBACK: But a scoping study and nothing more.

DR. BURKE: Right, it just starts completely as an

exploratory what's there, what's in that box.

DR. MC CABE: So let's begin to put these committees together. Judy, I'm trying to remember who else from this Committee was working with you.

DR. LEWIS: Mary, Reed, Pat, Barbara, and Ann.

DR. MC CABE: That may be too large of a group at this time. So I would ask that we have two or three; you plus one or two others. What I'm going to do now is we are going to take a five minute break, and we will let the teams begin to organize themselves. I think it will be done more efficiently by that mechanism.

DR. PENCHASZADEH: What ever happened to that phase, one of the first phases you showed on a couple of topics that only required like a statement?

DR. MC CABE: I think those are still there.

Okay, a five minute break.

[Brief recess.]

Setting Priorities and Next Steps

DR. MC CABE: Sarah will now read over her understanding of these work groups. Are we going to call these work groups or teams?

MS. CARR: Whatever you want.

DR. MC CABE: Somehow it sounds like it's more of an in and out. For some of these, maybe they ought to be work groups and some should be teams.

So Sarah will tell us who's on what.

MS. CARR: Can I just say I'll do this, and then if it's not adding too much to the work load today, if we could maybe just define the questions for each these groups; the immediate question and the long-term scope maybe, because I know there are differences. If that's okay with the chairman, maybe that would be our next -- that would help staff a lot I think.

We have an education scoping team or a work group. That is going to be chaired by Joann Boughman. Members so far are Elliott, Judy Lewis, Michele, Mary Davidson, and David Lanier on education.

The IRB/consent work group or team is going to be chaired by Barbara Koenig. It is going to have Victor on it, Pat Charache, Reed Tuckson, Ed, and Kate.

The data elements/data collection work group or team is going to be chaired by Wylie. Elliott will be a member, Reed Tuckson, Victor, Muin, FDA and NIH, Ann -- not Victor, excuse me.

The access team or work group, or perhaps access is scoping out the issue -- no, access is working with the broader group on issues of small communities and minority communities. Judy Lewis is chair. Victor is on that one, Michele. This is the smallest one so far.

DR. MC CABE: I think we specifically wanted it to be small.

MS. CARR: Because we have the other group to work with.

DR. MC CABE: We want to bring in a large group representing --

MS. CARR: And Reed is ex-officio.

Then the last one is on rare diseases. It is

going to be chaired by Mary. Kate is on it, and Pat Charache so far.

DR. MC CABE: So is there anyone who is not on one of these groups? So everyone is represented on one of these groups then?

Okay, so then let's start off with the education scoping work group.

DR. BOUGHMAN: Could we give me a few more minutes?

DR. MC CABE: We'll go to IRB/consent. Barbara, are you prepared to discuss what the goals would be there?

DR. KOENIG: First, let me address a potential area of overlap with one of the other groups, because that may help clarify things. While I just talked about the fact that the whole issue of defining what we know and what we don't know, and the ideal methods of presenting that could be seen as either an essential element of data, and ongoing data collection, because it's what you are going to report back to people, as well as what you are disclosing to them, or it could be under consent.

So I think we agreed that we would first need to spend some time clarifying exactly who should do which piece of that, and stay in touch.

And the second thing in terms of the consent/IRB issues is I think of us who just met very briefly identified that one of the first things that we would want to do is make some very significant -- first be in touch with the new director of the new OPRR (OHRP). And that we would want to make a set of very specific recommendations about genetics to that group. And that that would be one of the outcomes of what we would do.

And even though we talked about the issue of doing education of IRBs, we probably would want to first think about what other efforts were going on in genetics education for IRBs, and then get involved in that.

The other task that we would identify would be the possibility of thinking of some template kind of informed consent documents that could be used at different stages of research and early introduction into clinical use of genetic tests. We might want to think about some of the issues of consent forms for panel testing. There would be a number of things that we would do.

Pat Barr actually had a slightly different list when we spoke, which I think I have all of them in my head right now. So, Pat, is there anything that you would want to add that you think that you this group should do, since you had some ideas about that?

MS. BARR: I actually think you have covered them. I think they will emerge under those subcategories anyway. That there are more specific.

DR. MC CABE: There were some other groups that we had thought about possibly including on that, PRIM&R, NBAC.

DR. KOENIG: Those need coordination. Anyone else we should be coordinating with? Are there NIH activities in this in terms of the continuation of the issue of consent beyond the individual to the family, for example? Is that an ongoing effort at NIH?

PARTICIPANT: Not that specific issue. There is a lot of interest in consent for research.

DR. KOENIG: I thought there was some specific follow-up because of the Virginia Commonwealth?

PARTICIPANT: There has been discussion of it.

DR. CHARACHE: Given the heavy responsibility that we are giving to the IRBs for oversight, in addition to learning what people are doing as far as educating IRBs, I think it would be helpful if we could define what information we want to be sure the IRB has in order to meet that responsibility.

DR. LEWIS: One of my concerns, as I said yesterday, is to make sure that we recognize that there are two processes that go on. One is signing the piece of paper, and the other is the informed consent issue that should be a part of every encounter. So I just want to make sure we don't get so focused on the template for the document, that we forget the importance of the fact that everything should have informed consent, even if you don't have to sign a piece of paper.

DR. KOENIG: So documentation versus consent. And that's extremely important in terms of the idea of some kind of template too, because there are of course many IRBs that misconstrue the regulations, and make the assumption that consent has to be documented in writing, which is not the case.

DR. LEWIS: Or the fact that the documentation of consent or applied consent, versus an act of reaching out to make sure that people know what they are sticking their arms out for.

MS. BARR: I think the one thing you need to think about is that current regulations really do not allow for agreeing to prospective research. Current regulations really do not allow for a regional or national approval that would be binding on any other group.

So I hope that you will look at sort of the very big issues that need to be addressed, and might be able to be addressed sooner rather than later, that the local IRBs get tied on. Because if you do that, then the issue of what a genetics IRB should know becomes a much easier thing to fulfill.

DR. MC CABE: Joann, are you ready?

DR. BOUGHMAN: As I have heard it, there are about three different areas that the education group should be focusing on. I've got this written out here. The first is to ascertain or collate the current status or an environment scan. One of those would be on work force analyses. That is, results of any relevant analyses that are already out there. And we know that some work that has been done, for example specific for genetic counseling.

But also to ascertain the efforts that are currently underway, either by the group of agencies. Even though the report might not be ready, let's figure out what might be out there, and/or any other activities by major organizations.

And then also parallel to the work force analysis, to try and find out who is currently developing content

guidelines for a variety of groups. This would include public education efforts, genetics professionals, and other identified health professional groups that in fact will be in this genetic services area. For example, we need to find out some more about where NCHPEG is in some of these things. That's just one example. So that the environment scan both on work force analysis, and who is doing what on content.

Secondly, to determine any specific reports or results from these things that we think that the Committee needs to hear, or we need to find more information out. And that if there are any actions -- let me back up. Or to identify groups that would need to do such reports and/or actions that SACGT could take to get them there. If that in fact is to advise the Secretary, that there needs to be something specific, or whether we could request that some of these things go on the agenda of one of our constituent agencies here on the Committee, just to clarify some of those things.

And then also to define more clearly the specific issues, the questions framed in a better way to guide specific discussions that we believe SACGT as a group needs to have, or if there are any specific action items, like one of these position statements that we think SACGT needs to go on record as making a statement about it at this time.

It seems to me that if we could get those definitions down, we could bring it back here, and then we could figure out as an entire group what our next steps were.

DR. MC CABE: So this is education of both the public and the health professionals?

DR. BOUGHMAN: That's the way I was thinking of it. At least as we initiate it, that may be one of the things that we find out. That we are missing too many things, and what we need to do is have different subgroups focused differently.

DR. MC CABE: The other thing is I just would have you make it clear, especially if you draw on people from outside of this Committee, that our charge has to do with genetic testing. It's appropriate to look at genetic professionals, because they need to be available to help interpret and counsel around genetic testing, but the focus on any work force issues really have to be relevant to genetic testing.

DR. BOUGHMAN: Well, in fact the implementation, the future of quality genetic testing as it is really going to happen out there in the real world is the way I'm looking at it. That's why the family practice or the pediatricians, and all of those. That's why the various professional organizations and their content guidelines that are now going into fellowship to medical school. All of those things I think become relevant, because people are out there doing them.

DR. MC CABE: Discussion? Yes, David?

DR. LANIER: This probably will come out anyway, but I think a research agenda in this area, I think it would important for us to either start that, or to have some other people begin to think about areas of research. It is

certainly unexplored, and I don't think we are going to come up with answers.

DR. BOUGHMAN: Well, that would better frame the second part, to try and figure out what the questions really are. Some of those would be at the scholarly research level versus who is doing what kind of thing.

DR. CHARACHE: I would urge you to also put on that list public health professionals, the laboratory directors, and leadership. They are going to have to do so much more than they have been doing it in the past. They are not going to do it unless they understand it.

DR. MC CABE: Barbara?

DR. KOENIG: I think I'll pass.

DR. MC CABE: Any other comments for this group? Okay, next is Wylie, data elements collection.

DR. BURKE: Barbara has already alluded to the fact that there is likely to be some overlap between the work of this subcommittee and the work of the informed consent subcommittee. I would see us as taking on two elements. One is the question of what does the template look like, the template that we want to lay out that explains what kind of information should be available before a test is used for documentation, and what kind of information is available with the test report.

So I would see members of this subcommittee working on some draft ideas, but then very rapidly communicating with informed consent, and figuring out whether there are some joint process that should go forward on that.

The second issue, which I think is the bigger task is the issue of trying to think through what kind of data collection options exist, and how do they address the kinds of concerns about genetic tests that are likely to arise once a test goes on the market. And I think those two questions interact with each other. What are the concerns, and what kind of data collection do they suggest?

And clearly in that conversation we have to be thinking about all of the different kinds of data collection there are. That is, start with laying out the universe, and then apply very rapidly some feasibility measures. What is realistic to do, who would do it? Pretty concrete ideas.

As we do that piece, and perhaps also as we do the first piece, I think we need to be thinking right from the beginning about what other organizations should have input into this process. That is, who is out there that ought to be part of this dialogue, in addition to the people that are already on the subcommittee. So I think that's almost an additional task of the committee, is figuring out who the stakeholders are in these questions.

DR. MC CABE: Judy on access.

DR. LEWIS: I think Reed's point about listening before we set the agenda is probably a critical one in terms of re-engaging with the members of the diverse communities that we engaged within the past, and looking at other key players who emerged during our meeting in Baltimore, and perhaps getting together once the report becomes available.

Starting with our report, and also starting by

reviewing the comments that we received that weren't addressed in our report, and re-engaging with the communities, and seeing where we are at right now, and moving forward from that perspective.

But I think that rather than us setting an agenda for them to follow, we need to develop the agenda in concert with people from outside this group, and just able to listen and hear what they have to say. And then if there are issues that emerge that are totally off our radar screen, to be able to bring those to the group, and let them know that there are concerns that we haven't even though about, because of the fact that those perspectives weren't at the table.

But also then perhaps if there are people who have key interests in some of the other areas, helping them know what the work is that is ongoing, and making some connections with the other working groups. But just to be able to maintain that liaison and the outreach and the commitment that we made to the people in Baltimore, that this wasn't the one shot deal. That we were going to be back and stay connected. That would probably be the big agenda, especially with people in the small, underserved communities.

DR. MC CABE: Comments on this?

DR. LEWIS: Are there things that I'm missing?

DR. MC CABE: Okay, and Mary on rare diseases.

MS. DAVIDSON: I think this is the rare disease/low volume group. I see that there are three tasks. The first one is the best way to come up with a number. I think we had 4,000 yesterday, with a big question mark. I would imagine that in addition to coming up with a number, we would have some sense of where that comes from.

Secondly, and these are the more substantial ones is that we are going to need to consider the special issues relative to the rare diseases and low volume tests. And I think second to that is that we need to hear some consideration for the possibilities of some alternative review process. So I was just doing diagrams. We have been diagrams for the last two days.

I would see the process for this as our really needing to go back to the patients disease organizations to really get some input from them about how they see the level one scrutiny as it is laid out, impacting their disease community's access to the test. As well as getting some input from private and public researchers.

And then thinking about a possible advisory structure, which again would bring in the interests of the conditions, specific advocacy groups, looking at their particular test when it is reviewed. And seeing if there are any possible other issues, and taking a look at this up close relative to the level one scrutiny that this group hasn't come up with yet.

With respect to the low volume tests, the non-orphan diseases, I need a little bit of help here. I know that, Pat, you and I started talking about this yesterday, where there might be some non-orphan diseases that would go into the low end group.

DR. MC CABE: Can I just clarify one thing before Pat speaks? When you were talking about structures, you were talking about structures of bringing in consumers to assist the FDA, or to provide --

MS. DAVIDSON: This is a conversation that Barbara and Wylie and I had last evening, in just thinking about how to weigh the balance between maintaining access at the same time as improving quality oversight. And that those are incredibly difficult decisions, particularly when it comes to the orphan diseases. And it makes sense to consider in those cases, and that's why I'm suggesting that this be a process that we consider, having them be involved in that review process.

DR. CHARACHE: I think this is going to be a very complex issue. It's going to be multifaceted, especially this balance between ensuring the quality of the test, and making that assurance not so burdensome that busy laboratories that are underfunded will say, the heck with this.

So we can't just ask them, what do you think about this, because they would say that's the worst thing I've ever heard of. We do have to work with some of the providers of these tests to show them that this would not burdensome, and look for other ways of ensuring quality, without compromising their major interest.

So I think we will probably have to get an iterative interaction with some of those who are at -- I think we are going to have to get some iterative dialogue with some of the people who are at greatest risk in this process, as well as figuring out again - this ties with the IRB - how they can ensure that the technology is secure, and that it really is being done in a safe manner. So I see that also in playing a role.

DR. LEWIS: One of the things I was just hearing while Mary was talking in terms of outreach to consumers was the fact that we may end up having some duplication between our groups. And I think it's going to be real important for us to stay in contact, so that we have some coordination of efforts, rather than duplication of efforts.

If we are doing some kind of organized outreach, that for example if the rare diseases is something we want to seek advice on from the access group, that we sort of do it in a way that is organized, so that we are not putting an unfair burden on the people we are consulting with outside this group, and that we are also maximizing efficiency for the staff.

So I just want to make sure that maybe one of the things we need to do after we have our initial planning, is the chairs of all the groups have a conference call, so we can lay out our plans in a way that is going to have a timeline that staff can deal with, and also if there are any activities that we could get double bang for the buck for, that we coordinate in a way that makes sense.

As I heard you talking, I wasn't sure whether or not some of that was going to be overlapped with what we are going to be reaching out to people for. So just to make sure that we have some coordination, I think is going to be

important, both for us and for the other people and the staff.

DR. BURKE: I just want to follow-up also on Pat's comments and say that I think it may be extremely valuable to go out to some of the rare disease organizations that are in your Alliance, and actually ask them to develop case histories examples of what their experience has been like. And a person who might be someone who might be helpful with this process is Bonnie Pagan or someone else involved that she might be able to identify involved in GeneTests to help make sure that you have got a good sample of rare genetic tests to sort of look at what's the experience been to date.

DR. KOENIG: As I think of this, Judy has already identified before that we are now almost able to predict, the longer we are together, everyone else is going to say, so perhaps you'll all be able to predict this. The one thing that we don't seem to have in this list of topics is something that I first brought up at our very first meeting, and that is the issue of direct-to-consumer education marketing, however you want to talk about it.

And I bring it up again just because it seems to me that it stands out. It is really something that is just a logical oversight regulation kind of topic. And we said something about it in our report, but I'm not sure if we have really integrated it into. We sort of said mostly that we would keep working on it or think about it.

DR. MC CABE: What we said in our report actually was that we encouraged the enforcement of existing regulations. It's very complex, because I think it was David who informed us that this involves commerce, as well as FDA. So that it is very difficult.

One of the issues that was brought up this morning about networking at the Cabinet level was quite appropriate here. But really a significant part of this is outside of our purview, and there is already existing statute in this area. So I think we have addressed it. We could pursue addressing it, but it is one of those things we would have to ask how much impact we could really have.

Elliott, perhaps you know more about this.

MR. HILLBACK: Well, one, I'm not worried about it as some others I guess. But I think it does fall, if you want to play a stretching game, into the data elements/data collection game in the sense that if we are transparent in telling people what we know and what we don't know, then we shouldn't be too worried about whether we tell it directly to the consumers or not.

I'm not sure Barbara totally agrees with me, but the point is I think we could at least to some degree, put at least a quick look at that issue into that data element in terms of not just what do you collect, but how do you communicate it. I think that was in the charter of this data element/data collection group is how do you present the data. And the question is when do you present the data. So maybe, Madame Chairman of that group, you could take it on.

DR. BURKE: If I could just respond to Elliott. I actually think that's an interesting idea. I think it's appropriate for us to have it on our list. But I actually

think at a certain point there will be limited degree to which we can address it.

What I would say is this. What I think is likely to come out of our conversation is going to be consensus in our subcommittee, and then bring it to the Committee for agreement. But ultimately an agreement about, as an example, here is a list of the things that a consumer would like to know that it is reasonable to provide to a consumer prior to that consumer having a test.

I think the question then will become a regulatory one outside of this regulatory framework. And that is to what extent can you require direct-to-consumer marketing to include the full list. I think on the one hand there is honesty in direct-to-consumer marketing, and I think what is in place already guarantees that. It says legally that must be the case.

And the other is completeness. And I think it is very likely that we will come up with a list of things that we think the consumer would like to know before they do a test, that includes things that a marketer would not like to tell a consumer before they have the test. So I think we shouldn't put a lot of energy into that before we figure out where we can get guidance about how much room there is for putting that kind of restriction on direct-to-consumer marketing.

MR. HILLBACK: I think you're making a big presumption though about marketing in this arena. You are not talking about very many commercial laboratories. You are talking about lots of other people that do tests. I don't think most commercial labs are interested in making a test sound something different than it really is.

DR. BURKE: We are talking about direct-to-consumer marketing though, which will apply to a very, very small subset of tests. I would argue they are the tests most likely to be the ones that the marketer wants to give only partial information about.

DR. MC CABE: The other thing I would point out is that this can really fall under a number of these different categories. I think we will do better by including it under the other topics, rather than setting it out as a single issue, because of the complexity. I think that if we look at how it impacts on a variety of aspects of genetic testing, then it gives us more reason to be concerned about it.

DR. TUCKSON: I was going to say it really clearly to me falls right down in the middle of the plate for the public education one.

DR. MC CABE: It's everywhere. So I think that we would encourage each of these committees to look and examine whether it belongs there.

DR. LEWIS: Reed made my point that I thought it could fall into multiple places, and that it sounded like consumer education around buyer beware type of thing.

MS. BARR: I just wanted to make a process suggestion to Barbara when she is thinking about consent, and what should be in consent. Even in written documents there could be that informational piece of questions, you

should consider asking your doctor about this test, that has to be given out with every kit, or given out each time the test is offered that is language appropriate and all that.

DR. MC CABE: I just wanted to ask about clarification regarding the alternate review process. Mary, you mentioned something about alternate review process.

MS. DAVIDSON: Well, let me try to reframe that. What I meant by that was, and again, it was just picking up on some late night conversations with Barbara and Wylie was thinking about, on the subject of rare diseases in particular, how to develop a collaborative process that would bring the disease-specific organizations and their test that is being evaluated to look at access and access costs and quality issues.

DR. MC CABE: I would encourage you to couch it in those terms. Terms like "review" have very specific regulatory meanings. So I think you need to explain what it is.

MS. BEARDSLEY: I was just going to go back to the direct-to-consumer advertising, and the general compliance issues about whether people are saying the right thing about tests to consumers and the public. It seems to me there may be two things we could do. One is that I think when FDA takes jurisdiction and requires approvals or clearances of these tests, it will also bring with it some requirements involving what you have to disclose in advertising. And we might want to ask FDA to tell us what those would be, for one thing.

And for another thing, we talked some I think about the FTC, and their role in this, and whether we think they might be more active in terms of going after violators. If that is the case, you might want to communicate with the FTC and tell them of our concerns. And maybe that's another letter that could be written, to try to get them on board with this.

DR. MC CABE: Could we ask FDA perhaps to make a presentation to us, and let us know, try and help to inform us better about this? Does the Committee agree that it would be helpful to learn more? But with the goal being to see is this something that we could direct the Secretary to look into among other agencies outside of Health and Human Services. Is that an appropriate restatement, Kate?

MS. BEARDSLEY: Yes.

DR. MC CABE: Could you put that together?

DR. FEIGAL: Yes, actually there is a separate unit in the Office of Compliance that deals exclusively with those types of issues. And we could probably invite someone from that unit to present information.

DR. MC CABE: Okay, and you can tell them what our specific concerns are, so that they could focus their presentation.

DR. FEIGAL: It's a very complicated process under the existing analyte specific reagent rule, leading into home brew. The agency actually, for better or for worse, prohibits the promotion of a home brew assay of any type to consumers. One of the challenges to the Office of Compliance has frankly been the Internet, which provides an

amazing spectrum of opportunity for interesting promotion.

DR. LLOYD-PURYEAR: I had a question about the rare diseases. Is there a definition of rare diseases?

DR. MC CABE: Yes, a rare disease is defined as less than 100,000 individuals affected. Is that correct?

DR. LLOYD-PURYEAR: Well, then the next one is what are the specific issues we are trying to get at with looking at rare diseases as a category for the level of scrutiny, and that's the only thing we are trying to do?

MR. HILLBACK: I thought that the issue was that there is a concern, no matter what regulatory process we put in, that we could stop both research development and provision of tests that are either for rare diseases or rare mutations of more common diseases.

DR. MC CABE: Let us also point out rare tests for a common disease.

DR. LLOYD-PURYEAR: I think it's misleading about what it is you are really talking about there by calling it rare diseases. I think you are leaving a lot of other things out. And that it's also how it gets defined. And it's confusing to the public about what's rare and what's common.

DR. MC CABE: I was going to comment about that on each one of these. I would encourage the groups to examine the titles that have been given to them relatively quickly, because some of them really don't make a whole lot of sense to anybody -- I was going to say to anybody outside of this room, but probably some of us inside the room. So you are not stuck with these titles.

On the other hand, what I would argue, and in keeping with sort of the concept of short-term and longer-term committees, I would suggest that we refer to the top three as teams, and the bottom two as work groups, indicating that we want the top three to come to conclusions fairly quickly, to do the work, and let's get it off the table. Whereas, we recognize that the bottom two are going to take longer to accomplish their goals, and will be existing through a number of meetings. Does that make sense to people, the way they are structured?

Other discussion? Is there anything that you need, Sarah, to help with additional clarification?

MS. CARR: I just want to ask about team two is education scoping, and that may change? The title for that may change?

DR. MC CABE: It's consent, data elements, and rare diseases are teams. And access and education are work groups.

Any other issues that we need to tackle? Well, I'm very impressed. I was impressed with the work that was accomplished yesterday. I was concerned whether we would be able to get through all of this today. I appreciate everyone really attending to task, being creative, and developing your own organizational patterns that helped us get through some difficult times.

Thank you and have a safe trip home.

[Whereupon, the meeting was adjourned at 3:00 p.m.]