U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

SECRETARY'S ADVISORY COMMITTEE ON GENETICS, HEALTH, AND SOCIETY

Thirteenth Meeting

Tuesday,
July 10, 2007

Room 800
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C.

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P R O C E E D I N G S (8:30 a.m.)

DR. TUCKSON: Good morning.

(No response.)

DR. TUCKSON: Good morning.

PARTICIPANTS: Good morning.

DR. TUCKSON: There we go. 8:30 exactly. We run a tight ship around here.

We want to thank everyone for attending the 13th meeting of the Secretary's Advisory Committee on Genetics, Health, and Society.

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

I want to welcome members of the public who are in attendance today, as well as the viewers who are tuning in through the webcast.

We're meeting today at the headquarters of the Department of Health and Human Services, the Humphrey Building in Washington, D.C.

Let me just make everyone aware that because of the webcast and the microphone system, that if you have the wireless stuff, your telephones and -- there it is. That's the warning. That is exactly the warning. If you put any of these electronic devices next to these microphones, you will get that horrible noise which will go out, and all of your private information will be dispensed to all the world.

(Laughter.)

DR. TUCKSON: If you don't mind that, it's okay.

A public comment session is scheduled just prior to the lunch break, and we encourage members of the public in attendance that wish to address the committee to sign up at the registration desk.

Typically our SACGHS quarterly meetings take place over a period of two full days. However, because of the importance of the charge given to us by the Secretary at our March meeting on the oversight of genetic testing, yesterday was devoted to a very special and very productive all-day working meeting of the Oversight Task Force. Later this morning, we'll hear actually from Marc Williams who will give us an update on what occurred yesterday. There was an awful lot of work and we're very proud of what they have been achieving so far.

At the March meeting, you will recall that we created a new Evaluation Task Force led by Steve Teutsch. The new priority developed as an integration of our two proposals that were presented to SACGHS: outcomes research for genetic technologies and economic implications of genomic innovations. After an in-depth study, the two study proposals were combined when it became clear that an investigation of the outcomes of gene-based applications must include their economic consequences.

Initially this new task force planned to start work immediately. However, several members of this task force also decided to join and participate in the Oversight Task Force, which has an awful lot of work to do in a short period of time.

Given that there is some overlap in the content of the two efforts, it has been decided that the Evaluation Task Force members would be more efficiently served to devote their full resources to the oversight charge first and then carry the knowledge gained from that effort on to the new task force. So work will begin on the new priority after the Oversight Task Force completes its work and delivers its report to the Secretary.

One of the things that I think is important to note is just how hard the members of this

committee work. I don't think that we probably disclosed to you, when you took on this assignment, that there would be all of these task forces and that people would be on more than one. They would be working all at the same time. But I just want you to know that the hard work is noted and it is appreciated.

On April 27th, we sent a letter to Secretary Leavitt thanking him for his leadership in addressing oversight issues and for directing our inquiry into gaps in the oversight of genetic testing. We also expressed our interest in two Senate bills that had been introduced recently that affect genetic testing: The Laboratory Test Improvement Act, Senate bill 736, and the Genomics and Personalized Medicine Act, Senate bill 976. You can find a copy of our letter in your briefing book.

Hunt Willard can't be here today, but I want to report that he was invited by the Connecticut Department of Health to give a presentation on our large population studies report. Connecticut is examining the feasibility of a statewide biobank to determine genetic and environmental factors involved in preterm births. Although what Connecticut has in mind would be on a much smaller scale than the type of study addressed in our report, given that Connecticut is a state, they wanted to learn more about the policy issues identified in our report, a number of which are relevant to biobanks in general. So we're glad that he's going to do that.

Well, today, since we're meeting just for one day and are on a tight schedule, this time I will forgo an in-depth review of the status of our strategic plan and priority issues, but for those, again, that are new members of the committee, you know that we are pretty fanatical about trying to lay out the overall strategic plan that we have and to keep tracking our progress to make sure that our stuff is just not a bunch of meetings and reports on a shelf, but that we're actually achieving a set of very defined goals. So I will forsake that today, but always we'll make sure that we keep you up to date on our strategic planning.

I do, however, want to make a quick note of developments in Congress related to the Genetic Information Nondiscrimination Act, or GINA. Genetic discrimination, of course, has been our highest priority issue, and we've been keeping close watch on the progress of this legislation since our inception.

The House bill, H.R. 493, did pass 420 to 3 on April 25th, and the Senate bill has been reported out of committee and a vote in that chamber is expected soon. After 12 years of tireless work by its supporters, a law, specifically prohibiting genetic discrimination in health insurance and employment finally seems very close to becoming a reality.

I also want to report that we have received comments from CMS on our 2006 report on coverage and reimbursement of genetic tests and services. You'll recall that we made nine recommendations in that report and several of them were related to programs and policies administered by CMS. A copy of their letter can be found in your table folders.

It was not that long ago, I guess, that we came in this very building and briefed the leadership of CMS, and we're very appreciative of their careful review and consideration of our recommendations. Marc Williams has volunteered to review these comments and to help us to determine what follow-up or next steps are needed. So if you have any thoughts, after reviewing the letter, please make sure that you work Marc to death and get to him right away.

With that, let me also welcome Dr. Madeline Ulrich from CMS. Thank you, Madeline. Dr. Ulrich is with the Coverage and Analysis Group and is sitting in today for CMS' ex officio, Dr. Barry Straube. Welcome and thank you for your diligent efforts on behalf of the committee.

I also want to report on staffing developments. Since our last meeting, Dr. Cathy Fomous has joined the Office of Biotechnologies as policy analyst, supporting both the work for SACGHS and a program aimed at harmonizing clinical research policy. Cathy has been working

intensively since the day she arrived in supporting the Oversight Task Force. So thank you. She comes to us from her position at the National Library of Medicine where she directed content development for the genetics home reference website. She's also worked as a researcher at the German Cancer Research Center in Heidelberg. Cathy is a certified genetic counselor and earned her doctoral degree in genetics from Georgetown University. Did you have anything to do with this, Kevin?

(Laughter.)

DR. TUCKSON: Natalie Vokes has joined the staff for the summer -- Natalie, where are you? Great -- as the famous intern and is working with the committee's gene patent study. We work the interns to death. So thank you, Natalie.

She graduated with a degree in chemistry from Williams College and is the recipient of a two-year fellowship to study the philosophy of science at Cambridge University. Natalie would eventually like to attend medical school and work as a physician scientist. We're happy that she's with us.

I'd like to also quickly provide an overview of today's agenda. We'll begin with an update from the chair of the Pharmacogenomics Task Force, Kevin FitzGerald, who will fill us in on the status of the public comment process. Andrea will then report out -- Marc will then report out on the work of the Oversight Task Force, given that Andrea is in recovery.

A large segment of today's meeting will focus on the work of the Gene Patents and Licensing Task Force, which is chaired by Jim Evans. Jim will provide an update on the task force's work, after which we will hear from Judge Pauline Newman who will speak on pending patent legislation in the U.S. Jim will then facilitate today's international roundtable on gene patents and licensing practices.

We are very pleased to welcome back to the table two honored SACGHS alumni, Debra Leonard and Emily Winn-Deen, who just won't go away, who are now ad hoc -- by the way, let this be a lesson to all of you.

(Laughter.)

DR. TUCKSON: There is no escape. They are now ad hoc members of the Patents Task Force. They will be participating in today's roundtable, and I know Jim will point out the other members of the task force in his remarks.

Finally, I want to welcome all of our invited speakers on gene patents, most of whom have traveled lengthy distances to join us today, and we really do look forward and appreciate your presentations.

After the patent sessions, Dr. Katrina Goddard of CDC will provide an update on public awareness of DTC tests. She'll be presenting the results of a CDC national survey and then an analysis of data from several states.

Well, now let's turn to Sarah Carr for the famous and long-appreciated reminder about the ethics rules. Ta-da.

MS. CARR: Good morning. As you know, you've been appointed to this committee as special government employees in order to serve, and though you're in a special category, you're nonetheless subject to the rules of conduct that apply to government employees. These rules are outlined in a document that you received when you started on the committee, and I'm just going to highlight two, as I do every time.

First, about conflicts of interest. Before every meeting, you provide us with information about your personal, professional, and financial interests. It's information we use to determine whether you have any real, potential, or apparent conflicts of interest that could compromise your ability to be objective in giving advice during committee meetings. While we waive conflicts of interest for general matters because we believe your ability to be objective will not be affected by your

interests in such matters, we also rely to a great degree on you to be attentive during our meetings to the possibility that an issue will arise that could affect or appear to affect your interests in a specific way.

In addition, we've provided each of you with a list of your financial interests and covered relationships that would pose a conflict for you if they became a focal point of committee deliberations, and if this happens, we ask you to recuse yourself from the discussion and leave the room.

As government employees, you're also prohibited from lobbying as individuals or as a committee. If you lobby in your professional capacity or as a private citizen, it's important that you keep that activity separate from the activities associated with this committee. Just keep in mind that we're advisory to the Secretary, not to the Congress.

Thank you, as always, for being so attentive to these rules.

DR. TUCKSON: Well, I don't know about you, but I find that to be one of the highlights of every meeting.

(Laughter.)

DR. TUCKSON: Thirteen times now.

So let's now turn to Kevin to give us an update on the status of the committee's work on pharmacogenomics. The public comments were received on our draft report, copies of which were sent to you. The Pharmacogenomics Task Force plans to review and address the comments and the time line for completion of the report. Take it away, Kevin.

+ DR. FITZGERALD: Right. Thank you, Reed. It's only going to take a few minutes this morning just to give you a brief update on where we stand with this process. Again, these are the members of this task force and not only, as Reed said, do you never, ever get to retire from this committee, but you get put on all sorts of different task forces. Right, Emily?

DR. WINN-DEEN: Yes.

DR. FITZGERALD: When you try to leave, they just give you more work.

So as you may be familiar, we had the roll-out of this draft report on March 23rd at the Personalized Medicine Coalition event where the Secretary of Health and Human Services announced his personalized health care initiative. The draft report was put up on the SACGHS website, and the SACGHS listserv was used to disseminate the draft report to the 936 people on that. In addition, there were 283 other individuals and organizations that were targeted because of their potential interest in the report, and one way we discerned that interest was to look at the people we referenced in the report. We figured they might want to know that they'd been referenced. So we sent it to them and then also to a variety of organizations which we thought would be interested and their membership might be interested. So we sent them the draft report that they might disseminate it to their members.

Public comments were received and that period ended June 1st. We received a total of 57 public comments from basically four different groups: the government, so other groups within HHS and elsewhere; companies such as Abbott, Amgen, Eli Lilly, Genzyme; and then organizations, about 18 of those, including the Blues, the Medical Association, Nursing Association, Nurses Genetics, PhRMA, and the Personalized Medicine Coalition; and then individuals representing academia, health care providers, researchers, et cetera. This was the breadth of the spectrum that we were able to get feedback from on the report.

So our time line for the future. We are now in the process of collating and analyzing the responses that we received. We will have a conference call of the task force members on August 16th to pull together the individual analyses that have been done on the responses. These analyses and this synthesis will then be worked into the draft report and the recommendations, and then that will then go out to the committee in October. You'll probably get it about the end of October, so that you'll have a couple of weeks or so before the November meeting to look at the report where, hopefully, the

recommendations will be finalized and any small editorial changes will be made. And then the target is to be able to transmit the report to the Secretary in February, and as you may well know, the Secretary has 30 days then to respond to that. So the target is for the final report to be released to the public in March of 2008.

And that's where we stand at the moment, and if there are any questions, I'd be happy to have Suzanne answer them.

(Laughter.)

DR. TUCKSON: The floor is open, please.

(No response.)

DR. TUCKSON: Well, I think, first of all, I'm encouraged by the number of people that have written in, organizations and otherwise. I do know in my normal work world this report received an awful lot of attention, and I know that there were a lot of people across the country who put a lot of energy in their responses back to this committee. So I think clearly we've touched an important element, and I think that the work stands.

I think the comments, at least that I'm aware of that you received have been favorable. I think they've given you good input, but from what I understand, I think that the work is clearly on target.

DR. FITZGERALD: Other than yours, yes.

DR. TUCKSON: Great. With that, Kevin, thank you very much.

DR. FITZGERALD: Certainly.

DR. TUCKSON: I know you've got to run out for a couple of minutes, but you'll be right back.

DR. FITZGERALD: Yet another meeting.

DR. TUCKSON: Thank you. All right, great. Appreciate it.

Now, let me turn then to the report on the Oversight Task Force. This task force is chaired by Andrea Gonzalez. Unfortunately, Andrea did have a medical emergency late last week and so she couldn't be with us for the meeting yesterday or for today.

I do want to note, though, that Andrea has been working tirelessly on behalf of the committee, and I don't know whether she's tuning in on webcast or not, but if you're out there, Andrea, we really do appreciate all that you're doing and hope that your recovery will be very quick and you'll be right back to us.

Marc Williams is standing in for Andrea today and did a terrific job yesterday of chairing a full-day meeting of the task force. So, Marc, thank you not only for your work on the committee but for filling in, and please, if you would, let us know what happened.

+ DR. WILLIAMS: Very good. To preface my remarks as one of the newer members of the SACGHS, I do want to let Reed know that I was not given full disclosure of everything that was involved or the fact that this is actually the Hotel California. So, nonetheless, here I am.

Also, just to clarify a comment that Reed made at the outset, the recovery that Andrea is experiencing -- I think I can say this without violating any HIPAA PHI -- is not directly related to the creation of this draft report. It was completely unrelated, as best as we can determine.

So at any rate, I want to start by just thanking all of the task force that has been working on this report. The amount of effort that's been put in has been incredible. As someone who has had the opportunity to chair a lot of meetings, it was really gratifying to have everybody on board and working hard and really working for the good of the entire group. So it was a fun meeting, although tiring.

So one thing you may notice is we've already kind of changed the title of this. I was

gratified to hear Reed refer to this as oversight of genetic testing because actually it had kind of started as oversight of genetic tests. One of the themes, as you're going to see as we talk about the report, is that it's difficult to contain this just around the laboratory and the tests themselves. Really laboratory testing in general is a process, and it's not limited to just what the laboratory does. So as we looked at this, we took a bit of a broader view, and I'll expand on that as we go through.

We have several members of SACGHS that are on this task force, and the people here have all been involved in chapter development and in many cases are facilitating chapters. We have a number of ad hoc members, federal experts and consultants that were brought in for specific content areas that we felt needed their input. And thank you to all of them.

So I wanted to begin with the Secretary's charge. So this is from the letter that we received in March. "Undertake the development of a comprehensive map of the steps needed for evidence development and oversight" -- and this is a critical issue in terms of what we focused on -- "for genetic and genomic tests, with improvement of health quality as the primary goal." So the things that I think are the key here are the evidence development, oversight, and improvement of health quality.

"Looking for evidence of harm attributable analytic validity, clinical validity, or clinical utility; distinctions between genetic tests and other laboratory tests; existing pathways that examine the analytic validity, clinical validity, or clinical utility; roles and responsibilities of involved agencies and private sector organizations; information provided by and resources needed for proficiency testing." And italics here, we ended up expanding this perhaps beyond what people might think was the actual specific request here to look at adequacy and transparency of proficiency testing processes. This has actually turned out to be one of the major areas of discussion that we've been having.

"Potential communication pathways to guide test use; new approaches or models for private and public/private sector engagement in demonstrating clinical validity and developing clinical utility (effectiveness measures); and added value of revisions/enhancements to government oversight." So it's a pretty broad charge, I think you'll agree.

I wanted to put this in a little bit of a historical perspective. Reed had mentioned earlier about the 12 years it's taken to get GINA along the road. Well, we're not quite to 12 years, but we're pretty darned close when it comes to oversight of genetic testing because it was in 1997 that the NIH/DOE task force issued a report assuring safe and effective genetic testing. They recommended consideration of a genetics testing specialty under CLIA, recommended that proficiency testing be mandated for all laboratories conducting genetic testing, and ultimately this report led to the formation of our predecessor committee, the SACGT.

In 2000, SACGT recommended that the FDA should be responsible for the review, approval, and labeling of all new genetic tests that have moved beyond the basic research phase using a novel, streamlined process. CLIA should be augmented with specific provisions to ensure the quality of laboratories conducting genetic tests, and data collection efforts should continue after genetic tests reach the market, and CDC should coordinate public/private sector collaboration. So you can see that a lot of things in the Secretary's request have been represented previously in reports that have been developed.

We received the response from Health and Human Services in January 2001. They accepted the recommendations and indicated that they would be implemented over time as resources allowed. FDA's oversight of genetic tests to include laboratory-developed tests and genetic test kits; post-market data collection to be performed by CDC and might be required of the test developer and other payers; and CMS to develop new CLIA regulations for expanded oversight of genetic testing laboratories.

Now, between 2001 and 2007, a few things occurred that affected that response. Questions were raised about the FDA's authority to actually regulate laboratory-developed tests. So these are what some people refer to as the home brews where the laboratory develops their own test, but it

really is not put out for commercial marketing. FDA issues guidance and they clarified that they do have a regulatory authority over analyte-specific reagents which are sometimes used in the development of laboratory-developed tests, and that they also then had review requirements for laboratory-developed IVDMIAs under their oversight for these devices.

And CMS' plans for augmentation significantly changed in 2006, and in a response I believe that was copied to this committee, they indicated that CLIA already certifies genetic testing laboratories, that if they were to develop new standards, they would be outdated before publication because of the rapidity with which this specialty is moving. Developing a genetic specialty will not solve the gap in clinical validation of laboratory-developed tests. A genetic specialty will not address concerns about the lack of proficiency testing, and the lack of data and unique problems with genetic testing laboratories and other regulations had a higher priority than these.

So the CMS plan, in lieu of developing a genetic specialty, was to provide CMS surveyors with expert guidance to assess genetic testing laboratories; develop alternative proficiency testing mechanisms, for instance, inter-laboratory comparisons; develop educational materials; maximize expertise of accreditation organizations, so those organizations that are deemed by CMS to be able to provide this information; FDA and CDC to provide guidance for review of complex and analytical test validations; and collecting data on genetic testing laboratory performance.

So that leads to March of this year where we had the request from the Secretary to take a look at this issue, and so we created the task force as I had previously noted. We have had six meetings of the full task force by teleconference, developing an outline for the report, discussing the report's scope, and then use of key terms within the report. We've had periodic meetings of the Steering Committee and the Steering Committee consisted of the five SACGHS members that are on this task force. And then we've facilitated chapter meetings, which are teams assigned to develop each chapter. They received writing assignments and virtually met as needed to refine their drafts.

And we did have a working document, this, which was clean as of Saturday, but as you can now see, has grown a bit of fuzz for our meeting yesterday. So a tremendous amount of work in a very short period of time.

The focus of the activity has been to identify gaps in knowledge of which there are many. The Secretary's letter specifically requested that we look at harms, and so we have been focusing to some degree on harms, although I'll talk a little bit about how we're trying to balance that. We also have come up with what we would consider to be real harms, meaning there's actually documentation in the literature somewhere that says that this has really happened as the result of a deficiency or a gap, and potential harms, which are the things that we can all kind of dream up to say, well, geez, if it works this way, then that could potentially cause harm but where there's really been no documentation. We think it's important to really understand what is really happening versus what we think might happen but really don't have evidence for. And then ultimately we're going to want to be developing recommendations.

So the report outline. There will be six chapters. Chapter 1 will consist of background, define the scope of the report, spectrum of harms, and overview of each chapter. Chapter 2 is going to be devoted to laboratory technologies. Three will focus on analytic validity, proficiency testing, and clinical validity. Four, clinical utility and evidence development. Five, effective communication and clinical decision support, and 6, summary of recommendations. And I want to go through each of these in a little bit more detail just to kind of give you a flavor.

So Chapter 1 is addressing an important question which is, what is oversight for the purposes of this report? We have come to the conclusion that we're using a very inclusive use of this term rather than looking at oversight from a strict regulatory perspective because, as you'll see as we go through the rest of the report, a lot of what we're talking about that's probably going to have the largest

impact on improving the quality of genetic testing are things that are traditionally not under regulatory oversight. So when you hear me use the term oversight, don't think of it in a very proscriptive, regulatory perspective because that's not our intent.

We are going to acknowledge genetic exceptionalism as a social and policy reality. GINA is, in fact, being considered by the Congress, meaning that whether or not you believe in genetic exceptionalism, there is a certain social and policy reality to that. But it is not going to necessarily drive the content or be held up as something unique or special.

The text is to be written on broad ethical issues/spectrums of harms and benefits. This is, I think, a real key issue. There was a lot of angst, if you will, among the task force members when we started talking about the Secretary's charge where there was so much focus on the harms, and we said if there wasn't benefit to these tests, we wouldn't be talking about this in the first place. It's not just harmful. So we wanted to try and present the report in such a way as to balance out benefits and harms because in some sense they're really two sides of the same coin.

As I indicate here, if we, for instance, overestimate a potential harm -- in other words, we'd say, my gosh, we're really worried about this. It's never really happened, but we're really worried about it, so we should do that -- then we may interfere with the realization of a benefit because of a perceived harm. And I think there are certainly people in this room that have argued, relating to genetic discrimination, that we have actually incurred harm in the population by having people choose not to undergo testing because of the perception that this information may be used in a discriminatory fashion. So we wanted to try and make sure that we balanced this out as best as we can.

It also will address harm due to biologic reductionism. In other words, the genome is the be all and end all, and once we know this, we'll know everything, and it will determine what will happen to people as they age. And we all know that that's fallacious, but in some cases, that is tended to be held up as the new biologic paradigm.

We are going to make an attempt to explicitly tie this report in with the Secretary's Personalized Health Care Initiative. We recognize that there's a relatively short period of time. The Secretary has a very busy agenda for those of us that not only sit on this but also sit on the AHIC and other things. There's a lot going on, and so we think that the best way to be able to accomplish things is to look for opportunities to partner with other Secretary initiatives. So we'll be looking at that.

The roles of different entities will be explicitly discussed, and I've just given you a list here that's certainly not exhaustive but gives you an idea, again, of the scope.

We are going to explicitly identify issues that are mentioned in the context of genetic testing but we believe are peripheral to the focus of the specific report. We will mention them and then state that they will not be addressed in this report so that people won't look at the report and say, well, you didn't include this, didn't include that. We'll say we didn't include it and we'll say why we didn't include it.

The status of Chapter 1 is that we have a draft outline, but the content here is really going to evolve based on the content of the other chapters since a lot of what Chapter 1 is going to do is to set the stage for each of the subsequent chapters. So that is really a very appropriate status for this particular chapter.

Chapter 2. I was hesitant. We had a little debate yesterday as to whether or not we should actually talk about the definition of genetic tests, and I elected to quote Supreme Court Justice Potter Stewart. "I shall not today attempt to further define the kinds of material I understand to be embraced, but I know it when I see it." I think that's the best definition of a genetic test. We won't specifically state that in -- and, of course, he wasn't talking about genetic testing at the time.

But be that as it may, I think the important thing that I want the committee to know

today is that we are going to define genetic test for the purposes of the report. We are using definitions that are currently in use in other settings. So we're not inventing yet another definition. But I think very importantly we're going to include intended use of the test, and we're going to provide examples of this.

One of the examples, for example, is in amino acid analysis. If you do amino acid analysis for the identification of phenylketonuria, it's clearly a genetic test because we're identifying a heritable condition. If you're doing an amino acid analysis to look at general nutritional status, that's not a genetic test. It's the same test but the intended use is entirely different. So to separate the intended use from the test methodology is really inherently important in defining genetic testing. So you'll get a chance to argue with us about that as we develop this a little bit more.

We will have a comprehensive list of the methodologies that are currently being used and considered. We're going to attempt to gaze into the crystal ball to say what's likely to appear on the horizon in the next few years that may perhaps have some differences about it that we would need to address. And the status of this is that it is near complete. And thanks to our newest staff member Cathy for really taking this bull by the horns and doing an excellent job.

Chapter 3. This is the most extensive content area and has really been quite a challenge to bring together because we've lumped together the analytic validity, proficiency testing, and clinical validity all under this one roof. So in some sense, we perhaps look at Chapter 3 and say it maybe is not quite as far along as some of the other chapters, but they clearly have the biggest task ahead of them.

So the status of Chapter 3 is that we have identified a very large number of gaps in all of these areas. We're now in the process of consolidating them, and in our meeting yesterday, we identified a couple of other content areas that we thought would be important to kind of frame Chapter 3. So we are rapidly soliciting additional input on those topics so that we can incorporate that. We're beginning the characterization of the harms and benefits and are going to use these to develop recommendations. And we believe that we're really on target to meet the time line that I'm going to be presenting in a bit.

Chapter 4. The major conclusion here is that at present there's really no regulatory oversight for clinical utility. In fact, it may not be appropriate for there to be regulatory oversight for clinical utility because this really constitutes the practice of medicine which, at the present time, is regulated at the state level. So this is where we really begin to expand the concept of what does oversight really mean.

And there are a lot of challenges relating to clinical utility. There's no existing infrastructure at the present time to look at this in a comprehensive way. It is the largest gap in realization of the benefit or value of testing. If you really don't understand the utility of testing or which tests have utility and which tests don't, then you can't allocate resources to drive the best value for the health care system. It's the biggest opportunity, though, to build processes for improvement. And notice, we're using language that was specifically in the Secretary's charge relating to health care improvement.

This group has chosen to take a very broad approach for the identification of actionable items. Again, we think this is consistent not only with the Secretary's call but with the direction for health care in the United States because we're clearly moving away from each provider is an island to the idea that we have to take a systematic approach to how we deliver things. So we're looking at quality improvement, which has made huge inroads in the areas where it's been able to be implemented in terms of improving care; evidence-based best practice; pay for performance. And I could have generated a much longer bulleted list here of the systematic approaches to improving health care. So we think, as we look at utility, that again, rather than taking a very narrow focus as has been done in the past, this really reflects what is currently happening in the health care system and this report should reflect that.

Status. We've been trying to view utility from many different perspectives, including that of patients, providers, payers, public health, quality improvement organizations, guideline developers, et cetera. We've been exploring, as charged, governmental, quasi-governmental, private, public/private partnerships for the generation, synthesis, and management of new evidence.

And the draft is written but, based on our conversations yesterday, is under rather significant revision based on the input from the meeting and the breakout session that they had. So they really had a fairly complete chapter which I think was good, but there was clearly some change in direction that is going to be reflected in the next revision. But really I think most of the things are there and will proceed rather quickly.

Chapter 5, which was my personal favorite, not because I led it or anything. We're focusing on two things. One is on effective communication. And you might say, well, what does communication have to do in an oversight document? If you think about testing and genetic testing in particular, there really has to be relatively effective communication in both the pre- and post-analytic phases. In other words, the practitioner may have to provide information to the genetic testing laboratory around issues of ethnicity or underlying medical conditions or other things for the laboratory to really be able to appropriately interpret the test.

The example we use in the chapter is if you were to do a Jewish disease panel on me, the validity and the utility of that test on myself as a non-Ashkenazi Jewish person is very different than if you were to do that Jewish disease panel on somebody of Jewish descent. So the laboratory needs to know that in order to be able to really interpret the result appropriately.

And then in the post-analytic phase, the recognition that giving the report to the practitioner and if the practitioner is unable to interpret that report in an effective way, that's going to decrease -- even in a test that has proven utility, if the practitioner doesn't understand what the report is trying to tell him, then it's going to impact and lessen the utility of that test. So communication is really a critical issue.

There are roles for the laboratory, for the provider, and increasingly there are roles for the patient. And I know we're going to hear a little bit from CDC today about some of the direct-to-consumer issues, and we will be addressing those in Chapter 5, as noted here.

And then we're looking at it from the perspective of those with genetic specialty training and those with non-genetic specialty training, both from the provider side but also from the laboratory side because, as more and more of these tests come out, particularly kits, there are going to be laboratories that do not have a specific genetic focus that are going to be getting into these tests, and they may not have some of the expertise within their system that genetics referral laboratories are currently developing. So these are all issues that will impact communication.

Then we also have been focusing on clinical decision support. There's a strong feeling among our group that really, as with other areas of medicine, providing clinical decision support to the patient or provider is going to be critically important to maximize the utility of these tests. Again, this can occur in the pre- and post-analytic phase.

Again, to use the example of the Jewish disease panel, if somebody went online and used a computerized order entry to say I want to order this, then a pop-up could come up and say is this person of Ashkenazi Jewish background. So they would be prompted to fill in the right information. In the post-analytic phase, you could embed information relating to interpretation that would be clarifying, sort of that help button that you can click on the screen and find out more information if you're not understanding.

Now, it could be passive or active. The example that I use, which is a nongenetic example, is that reference ranges that come back with laboratory reports are a passive clinical decision

support. You look at the number of the result, let's say, a carbon dioxide level and it's 40, and you say, well, the reference range is 35 to 45. So that is within the normal range.

However, there are limitations to passive systems because if I have a patient who is undergoing an acute asthmatic attack, has a respiratory rate of 40, and has significant retractions and wheezing, a CO2 of 40 in that individual is not normal. That person is actually in incipient respiratory failure even though the value falls within the normal range.

So in an active decision support mode, that system would be able to pull other relevant information and would be able to generate a message to say this is not a normal value for this individual, given the clinical parameters, high risk for incipient respiratory failure, and could perhaps even generate recommendations. So both of these systems may operate. We think there are more possibilities around active, but again, it's also more complex.

Decision support has to incorporate evidence-based clinical guidelines, and of course, if we don't have evidence-based clinical guidelines, then it's difficult to build decision support.

There's an opportunity to achieve greater impact based on experience in other sectors of health care. If you really look at the literature, if you look at some of the biggest impacts on individuals with diabetes and these sorts of things, a lot of it has to do with embedding clinical decision support in care delivery.

One of the things that's going to be critically important is really to clarify how clinical decision support is actually going to be regulated because there have been some initial instances where the FDA has looked at some of these clinical decision support algorithms as devices and has chosen to provide some regulation there. But it's not exactly clear what the scope of that will be, and it's going to be critical for us to understand how that would impact. So we're trying to get clarification on that.

Chapter 5 is written and referenced. We've delineated gaps and harms and recommendations have been developed, but we do have revisions. Based on the meeting at breakout, that will be completed.

So the development of recommendations will follow the meeting that we had yesterday. We're going to be synthesizing recommendations based on the gaps and harms and benefits. The recommendations will initially be developed within each chapter and then the Steering Committee members will review, consolidate, and prioritize those recommendations so that we don't have a list of 512 recommendations that will no go anywhere.

Here's our time line. Here's today and we're almost through this progress report. So give thanks.

From July to September, we're going to be working on developing the second draft. We will have a second face-to-face meeting of the task force on September 5th.

In September and October, task force members will be consulting with key stakeholders and gathering feedback on the report. We're going to revise that again based on the stakeholder input, and then a draft report will be sent to the SACGHS members for consideration at the November 19th to 20th meeting.

Now, you'll notice a relatively short turnaround time of 12 or perhaps 13 days, depending on which day we end up considering this. So for those of you who are sitting around the table, my colleagues and friends, at least to this point, our expectation of you is that we're going to need you to really get up to speed on this pretty quickly because we're operating on a very, very short time line, as Kevin had already mentioned.

Now, while this may be unseemly and perhaps to some degree unrealistic, I'll just point out that those of us that have actually been writing this report under a very tight time line have been putting in a tremendous amount of effort. So I think at least reading and commenting is reasonable from

my perspective. So you can throw things at me later.

The 21st to the 30th, we're going to incorporate modifications to reflect the comments and prepare the report for public comment. The public comment period will be from December 3rd to January 7th, again somewhat shorter than the typical public comment period. It is within the rules in terms of what is necessary at a minimum. The timing is unfortunate, although people have a lot of free time over the Christmas holidays and I'm sure they'll want to be spending looking at this. But in January then we're going to be analyzing public comments.

Approximately February the 15th, because we don't have the exact dates for the first meeting of SACGHS next year, we're going to meet to discuss public comments, propose revisions to the draft report, and then we're going to approve the penultimate draft for submission to the Office of the Secretary. Now, this is also a little bit of a departure from the norm, but advice that we have gotten from the Secretary's office essentially says if things don't get in by February, nothing is going to happen for the course of this administration, given the limited amount of time that they have. So thank God it's a leap year is all I can say.

(Laughter.)

DR. WILLIAMS: So we will be doing final edits and then get this penultimate draft submitted to the Office of the Secretary. So we hope that this will be very, very close to the final, but we will work in March to develop the final report and then the final review by SACGHS via email on April the 16th, with a formal submission of the final report to the Secretary on April the 30th. So hopefully this will be able to get some of the key recommendations that we have initiated with enough time to be able to accomplish something.

So that's where we're at. Since we are working at the pleasure of this committee, we wanted to reflect back some issues that had come up for your input. You don't have to feel obligated to give us input. One of the rules we operated under yesterday was silence equals agreement, which is not a bad rule, although one I have difficulty following.

So the first question is, does the report structure -- and by this, I mean the chapter organization and that sort of thing. We tried to reflect the direction that we received from the committee in March, and I just wanted to ask the question, does this report structure reflect the advice that you gave us about how to organize the report?

I see a lot of positive nods. I don't see anybody negative. So we'll assume that that's a go. That was the easy question.

One of the biggest issues, as you've no doubt perceived, is the scope of the report. Now, again, just to reflect a little bit of history here, the SACGT report addressed regulatory oversight, CLIA, FDA, but they also brought in the need for postmarket data collection. So that really, again, is beyond the scope of what would traditionally be considered oversight although they did look at a federal agency -- that is, CDC -- to do that data collection.

Outside of the context of that report, the SACGT did develop a very large focus on education. They broadly interpreted the charter that they were given and recognized that one of the barriers to effective implementation of genetic testing was the fact that the provider and patient communities were relatively poorly educated about genetics and that would limit utility of testing.

So we've chosen, as I said, to address broader issues, including communication, education, process improvement, clinical decision support, and other things. Again, we think from our perspective that this reflects the request from the Secretary in that he references specifically health care improvement, the regulatory issues, but also the communication issues.

So we think that we're on task, but we really want to get the input from the committee, which is, does this broad approach appropriately reflect the Secretary's charge to us, or have we grasped

more than we're capable of reaching?

DR. TUCKSON: Responses?

I, for one, think that you've made some very strategic and important decisions, and I think that the way you've set it up, in terms of the logic, makes all the sense in the world. I don't think you've gone too far. I think that your presentation made it pretty clear, at least to me -- but I'll be curious if others think so -- that the report wouldn't be functionally relevant in today's real world if you didn't go where you went. Otherwise, it would be a pretty report on a shelf that didn't have diddly-squat to do with actual real-life issues. So I think you set it up pretty nicely for me. But I only said that because I was waiting for somebody else to speak up.

DR. LICINIO: I think it's a wonderful plan and I think that it's very comprehensive without overreaching.

The question that I had is that because of the timing of what you said at the end with the course of the administration, that penultimate report that you're going to give to the Office of the Secretary in February -- do you think that that has an impact, or do they really have to wait for the final one?

DR. WILLIAMS: The way we have set it up -- and that's an excellent question. We think that the penultimate report is going to be substantially the same. In other words, there will not be huge differences in content between the penultimate report and the final report. The final report will probably have some editorial revisions, but there won't be major content revisions, given that all of the comments will have been received from public and from SACGHS. So at least as we envision this process moving forward, we think that the penultimate report will be sufficient for consideration, at least on an initial level.

Now, again, remember we're going to have a number of recommendations which will be prioritized. So I think it will be incumbent on us as a group to make sure that we're really solid around the top priority recommendations in that penultimate report, and if we need to tweak some of the recommendations a little bit farther down the road, that might be appropriate to consider in that two-month period between the penultimate and final report. But those are issues that we're going to have to pay very careful attention to because we cannot send a report in February that is completely different from the report that they get in April.

DR. TUCKSON: Before I get to Barbara's question, let me just follow up on that as well. One of the things I think that was encouraging from your report is that you've connected this already, the work of the committee with the personalized health work group of AHIC.

It would seem to me that the other way to make sure that even as the report gets developed and shaped, that it takes life and reality, in terms of the Secretary's time table, is to connect to the Certification Commission for Health Information Technology part of AHIC, especially as you talk about the issues of integrating effective clinical decision support and integrating evidence-based guidance. I think that's the other opportunity with that same America's Health Information Community activity where if you're plugging in now and letting them know what you are doing, you might have a better chance.

DR. WILLIAMS: Right, and I think that's a very salient comment and just from that perspective, I actually sit on the AHIC Personalized Health Care Work Group and am going to be participating -- there are three subgroups of that work group. One is on family history. One is on genetic and genomic testing and one is on clinical decision support. We have recommendations coming from the first two of those, family history and genetic testing, that are going to be presented to the AHIC as a whole at the end of this month. Clinical decision support has lagged a bit behind, but we're in the process of getting up and running.

So I'll be able to liaise between this report and what's happening there. And we also have other representatives that are working as content experts within that chapter who are also represented on that committee. So I think we've got good communication lines.

DR. TUCKSON: No, I think you do, but I just want to make sure if you can find a way maybe with some staff support, Sarah, I think we need to visit quickly with CCHIT, which is separate from the Personalized.

Again, just to make sure everybody follows all this alphabet soup, the Certification Commission for Health Information Technology is another one of the America's Health Information Community groups like the Personalized Health group. CCHIT's job is to try to get the electronic medical record certified. It's already started to certify records and it's got a time table of new elements it's going to evaluate. But one of the clear things is this whole notion of evidence-based decision support. So to try to get your ideas in, because if you don't get it into their discussion -- they're already like two years out in terms of what things will fall due. So we might want to try to at least visit with them now.

DR. WILLIAMS: I don't want to put Michael on the spot here, but you had talked a little bit yesterday in our meeting about the NISTB efforts and that sort of thing. So I don't know if you want to speak specifically to the point that Reed has mentioned from your perspective as being more involved in that infrastructure.

DR. AMOS: Sure.

DR. TUCKSON: And Barbara, you are in the queue. I haven't forgotten you.

DR. AMOS: Actually yes, NIST and the AHIC are working quite closely together to develop the standards for interoperability and intercommunication between all these electronic health record systems. There's a major effort. NIST is a small part of that, though.

DR. WILLIAMS: Okay.

DR. TUCKSON: Barbara?

DR. McGRATH: Thanks. I'm going to go back to your question whether the vision is broad enough. It seems like it's gotten broader over the last time we've seen it, and I like that.

I particularly like the part of looking to the future and potential issues because I think the charge of this committee is to look at things broadly, not just what's happening today but project into the future. So I'd like to encourage you to keep looking to this theoretical, the abstract, the over-the-horizon things that aren't there yet but we may foresee.

DR. WILLIAMS: Yes, thank you. As Niels Bohr said, "Prediction is difficult, particularly when it involves the future," but we'll do our best.

I did want to ask a more specific question than this broad question, which is, is there anything that you've seen that we've included that you really strongly believe is out of scope?

One of the areas that we discussed yesterday and I can say that we don't necessarily have a consensus around is whether provider and patient education is really within the scope of a document on oversight of genetic testing. We're still debating this. In some sense, some of the things that we've talked about relating to clinical decision support relate to educational resources that are placed in a clinical context or, if you will, a just-in-time situation. So some of us really feel that it's in some sense inextricable.

By the same token, I don't think we necessarily want to say, well, we're going to have a recommendation at AAMC to say, hey, you guys have got to do a better job of educating your docs or something of that nature.

So, again, without prejudicing the group about specifically provider education, are there things that you've seen me present that you think really shouldn't be considered in this report?

DR. TUCKSON: Committee?

I don't see how it's possible, again, in functional terms, to have an oversight process that does not inform everybody that it exists. I mean, otherwise, again, it's, gee, that's a nice report on the shelf. It's nice to know that there are people thinking about oversight. By the way, nobody knows that people are thinking about oversight, nor is there any mechanism to let people participate in the process effectively. So to me, I'm hard-pressed to take issue with the decisions the committee made, but again, I'm deliberately trying to be provocative to stimulate discussion.

It looks like you've got a consensus.

DR. WILLIAMS: Okay. The last question is -- and, again, this may be more inconceivable given how broad our scope is. Did we miss anything?

(Laughter.)

DR. WILLIAMS: Please say no, from those of us that are actually writing it.

DR. TUCKSON: Scott?

DR. McLEAN: I had a question. The focused activity includes discussion of real harms and potential harms. Which one of the chapters really focuses on real harms and potential harms? I was looking for the --

DR. WILLIAMS: The way we've actually done it, Scott, is that we've tried to embed this concept throughout all of the chapters. In fact, when we were writing our chapter -- and several other chapters have been doing this as well -- as we're writing the prose, if we make a statement and we say, well, that represents a gap, we're flagging that right there as a gap. And if we say, well, this leads to a harm, we're flagging that as a harm and we're trying to say, well, is there literature around that harm? It's a real harm. Is there not literature? It's an artificial harm.

So each of the chapters is going to be developing a list of gaps, benefits, harms, and recommendations. So it's going to be the overall job of the Steering Committee to try and consolidate those.

So I didn't talk about Chapter 6 because Chapter 6 right now is nonexistent, but that is actually going to be the summary where we try and pull it all together and say, okay, here's what we really think, here's where the summary of recommendations takes place, and try and put that into a context.

So you can imagine that while we have relatively artificially divided this report up and if you think about analytic validity and clinical validity and utility, you can't necessarily just say, well, here's where analytic validity stops and here's where clinical validity begins. They're inextricably linked. But we have to begin to carve it down in some way, shape, or form to get off the ground, and then ultimately we'll try and stitch it back together in such a way that it reads as a continuity of a process as opposed to these individual parts.

So I think, to answer your question, we're going to embed those all the way through the report, at least in its initial draft phases for the purposes of our review and then we'll begin to pull that together and make it more coherent. Does that answer your question?

DR. McLEAN: Yes, I think that answers the question. Having those concrete examples sprinkled liberally throughout, I think brings it home and makes it --

DR. WILLIAMS: I didn't put on the Secretary's charge, but one of the charges was that they wanted tangible examples. So we've been making a real concerted effort to bring real-life examples in these arenas that illustrate the various issues into the report, which I think in the long run is going to make it much more readable for a broad audience.

DR. TUCKSON: Great. Next question?

DR. WILLIAMS: That is it. Thank you very much.

DR. TUCKSON: Before you run away, let me just ask Debra. I think Debra wanted

to just ask a question.

DR. LEONARD: Can I make two comments? One is in the clinical decision support. You're talking about how you get the information to the provider and how the provider knows how to use that information, but I think there's a broader health care system that has to be approached for genetic information since a hematology physician may order a Factor V Leiden, but the surgeon may not be aware of that information and it may have implications for postsurgical DVTs or whatever is going on with the patient.

So I think that there's the broader health system aspect of the communication and use of genetic information. For pharmacogenomics or pharmacogenetics, it has broad implications for other drugs that may be affected when the testing is done for one. So I didn't see that addressed anywhere, and I don't know if that's broadening the scope too much.

DR. WILLIAMS: It's in the report. I just didn't specifically present it. Again, there is the issue there -- you know, what you're really touching on is the fact that right now we do not have -- well, first of all, we have very low implementation of electronic health records to begin with. But even those electronic health records that exist don't talk to each other.

So the issue that you're talking about is you only need to do a Factor V Leiden test once. We have some internal data that I referenced from my institution that shows that these tests are being ordered repeatedly, and there's no one around this table that would deny that that is a harm. It's wasting resources because we're repeating a test that doesn't need to be repeated.

Now, obviously, in oversight of genetic testing, that is a huge outside scope issue of how do we make interoperable electronic health records. Fortunately, AHIC exists and that is the sole reason that they exist, to create a truly interoperable United States electronic health record by 2014.

So what we have established in our recommendations is connectivity to make sure that as they address those issues of interoperability, that genetic and genomic testing doesn't get lost in the shuffle because right now there are very poor systems for actually encoding genetic and genomic results in the electronic record and communicating those between electronic health systems. So those are things we're trying to bring to the attention of the AHIC so that they can create those standards so that when we get to the point of interoperability, genetic and genomic tests will basically be treated like everything else.

DR. TUCKSON: Good.

DR. LEONARD: May I make one other point?

DR. TUCKSON: Please.

DR. LEONARD: Which may sound picky. But throughout this, you've referred to the laboratory, the provider, and the patient. But the laboratory is people, and I don't know what you want to use for the term other than laboratory, but I'm not a laboratory but I practice as a physician in a laboratory. So you may want to think about the people aspect of the laboratory in the communication.

DR. WILLIAMS: I'd have to go back and look specifically at the language that's being used, but I'm pretty sure we don't treat you as a building --

(Laughter.)

DR. WILLIAMS: -- in terms of our verbiage. But I think that's a good sensitivity comment and we will make sure that we -- we have a lot of input from the pathology community, and I think what we're trying to do is to use terminology to reflect that there are a lot of people involved in that, not just the pathologists and the technicians, but also genetics professionals that are embedded within laboratories. So we are trying to represent that in a fair way, but we'll make sure that we don't take an entity approach to that.

Again, I had a limited amount of time and wanted to try and make things as distinct as I possibly could. So I apologize for any problems from that perspective.

DR. TUCKSON: Well, Marc, you've done a terrific job. The committee has done a terrific job. Again, he held it up. Let me just remind you this is like where this report is now. People wrote this, weekends, nighttime, extra-hours effort to get us to this point. The references for some of these chapters are extraordinary. This is a textbook in many ways, and one of the things we need to do is to get it, when this is ultimately done, into the hands of the Academy so that they can use it. I mean, there are multiple utilities for this. But this is a tour de force of effort and I think the entire committee needs to be commended.

I want to also specifically note that I think you had a lot of choices to make in this report. I'm particularly gratified by the choice of emphasis of benefits in addition to harms. That was a key element of prior discussions. Emily and Debra, I remember your comments specifically on on this, but the committee as well. So I'm glad to see that you have reflected that.

I am very pleased about the intended use decision. I think that was a very important definitional one, as well as your identification of future uses. I think that's a key decision, and I hope that the committee is attentive to that.

I can imagine how tough Chapter 3 will be, the analytic validity and proficiency testing and clinical validity one. I don't envy the effort that's going to go into that.

DR. WILLIAMS: There was no blood shed yesterday. So we consider that as being positive.

DR. TUCKSON: The regulatory oversight absence for clinical utility and connecting this to quality improvement, evidence-based medicine practice, and pay for performance I think is a key decision that I commend you for.

And then, as we've already discussed, the effective communication infrastructure I think is important.

Now, if the committee is going to be able to approve, between November 7th and November 19th, the report, I think we're going to need some way of sort of providing us with a little update here and there informally of how some of your big future decisions are going so that people will be aware of them.

The reason why I wanted to go back and highlight the points I made is because I think those are the big issues, quite frankly, going forward, but I think that if we could have staff support in giving us an informal running dialogue of your dialogue, so it says, okay, we had a big argument on the last committee meeting about turn left 33 degrees versus turn right 12 degrees. This is how we resolved it. I think it is important that we know that. Then when it comes time when you get the thing, you'll say, okay, I understand what this is all about as opposed to, well, wait a minute, I got a problem with turning left 33 degrees. Deal with it sort of on time. I think then you can get this thing out and approved as opposed to going back from the very beginning. So I would urge that be considered.

Other than that, I am concerned when the people who are reporting this out on such a modern and technologically complex area are wearing a slide rule tie clasp.

(Laughter.)

DR. TUCKSON: I don't know whether that bodes poorly for vision in the future or not.

DR. WILLIAMS: What does it say about the chair that recognized it was actually a slide rule?

(Laughter.)

DR. EVANS: It just says he's old.

DR. TUCKSON: And Jim Evans, who is up next, shouldn't comment because he's got on a periodic table tie.

DR. EVANS: I wear it periodically.

DR. TUCKSON: Which he wears periodically.

(Laughter.)

DR. TUCKSON: And I think it has some outdated symbols.

By the way, thank you to the committee, and again, I do really hope that Andrea is tuning in or will get a copy of the transcript and know that our thoughts are with her as she recovers from her illness and we appreciate her leadership.

We are now going to move to the session on gene patents and licensing practices. We have some very ambitious goals for that. The task force has put together a roundtable on international patent issues, and we'll hear about some pending legislation on patents here in the United States. This information will inform us as we deliberate about the report and recommendations we will make to the Secretary.

Jim Evans will start us off with an overview of the session's goals, and so, Jim, I turn the floor over to you.

By the way, there is a break scheduled at 10:35. We're a little ahead of schedule, but just know that there is a break scheduled somewhere in there and we'll figure out the most convenient way to do it.

+ DR. EVANS: Great. I'll try to keep us ahead of schedule.

I think that this is a very timely opportunity to address issues relating to patents and licensing practices. I like to think it represents the prescience of the committee. It might just be coincidence.

But be that as it may, in the past year or so since we decided in a formal way to take up this issue as a committee, there's been a confluence of activity in this. There has been a lot of public attention to the issue of gene patents. There has been a variety of proposed legislation relating to gene patents. In fact, this week the Senate will be marking up a patent reform bill, and this has been a very active issue in the courts.

Now, the committee, as you can see, from a membership standpoint is fairly small, and we've relied very heavily on ad hoc members and agency experts. I want to especially note the return of Emily Winn-Deen and Debra Leonard. They've been very important in this task force and just show the adage that with SACGHS, you can run but you can't hide.

The history of us taking up this issue goes back several years. In the spring of 2004, the issue of gene patents and licensing was slated as a priority issue, but at that time, the National Academy of Sciences was formulating a report that was going to address at least part of this issue. So we deferred effort on our committee until that report came out.

We formed a small group in the fall of '05 to review the NAS report, and what was noticed, when that report was really looked at closely, is it's a great report. It's very important and informative. But it was really heavily focused on issues of research, on how patents will affect the research climate, how they will affect the ability to pursue things. It really did not have much in it that related to patient access and the clinical implications of the current landscape of gene patents and licensing practices. So the fact that that, of course, is the major focus of this committee -- that is, the public's health -- led us to feel that we really needed more information about that.

In June of '06, we held an informational session and decided to move forward with an in-depth study that would focus again on gene patents and -- you'll notice the two are almost always in tandem when we discuss this -- licensing practices because it's felt by many, I think, that it's there in the licensing aspects of how we deal with patents that might give us the greatest leeway to affect changes, if changes are necessary.

We began long, agonizing discussions about the study scope. So you'll see scope throughout here over the next almost year. And we established the Task Force on Gene Patents and Licensing Practices.

In October, we refined the proposed scope for the study, outlined potential approaches for the study, continued to work on the scope. We got the scope approved in November of '06, but then, as you'll see, we refined it some more. We finally finalized our approach for study at that time.

In the spring of '07, we were fortunate enough to elicit the help of the folks at Duke, and as you can see, in the spring of that year, Duke kind of dominated things, unlike in basketball at that time.

(Laughter.)

DR. EVANS: Being from Chapel Hill, I had to get that in.

In March, we heard some wonderful presentations from the Duke folks and discussed next steps. One of the linchpins of the approach is to try to use what could be vaguely classified as experiments of nature. In other words, are there situations where, for example, one clinically important gene has been patented but another has not, and can we learn from the experience through those examples about the impact of patents because one of the things we began to realize, as we looked closely at this on the task force, is that there's a lot of heat but there isn't a lot of light. There is not a lot of hard evidence and data that really inform us about the impacts of patents on what we're interested in, which is the public's access to these things and the impact on their health.

In March, we got a fantastic primer on gene patents and licensing that I think for many of us was instrumental in giving us the sufficient background and the necessary background to really understand the issues at hand.

In May, the task force discussed next steps and developed speaker lists for the session today.

The session today is going to be dominated by international considerations. Now, before we get to that in just a minute, I want to introduce Pauline Newman, but I also want to explain the task force's rationale for a focus on international patent issues. I want to assure everyone that the task force is not ignorant of the fact that patents are a part of the U.S. Constitution. We don't have leeway to do whatever we want and we can't pick and choose from the world.

On the other hand, again, harkening back to this idea of kind of experiments of nature, I think that we may well learn some important things about the impacts of patents and as long as we see those lessons, in terms of what is doable and what is not doable in the U.S., I think that we maybe able to learn a lot from the international perspective.

I would also just emphasize that we really do try to keep a focus in this task force on practicality. We're not here to tilt at windmills. We're not here to tell the Secretary that we think certain things should be done that are totally ridiculous and not doable. We really would like, at the end of the day, to come up with a set of implementable guidelines that would help the landscape of patents and licensing practices best serve the public's interest.

So here is the scope. It's short. It fits on one slide, but that belies how much work went into getting it. As we mention the scope, I would just point out to people that one of the challenges for this issue with the committee I think in some ways is unique to other things we've brought up. It is very important, like many of the things we've brought up, but it's also very controversial. The issue of genetic discrimination, at its most fundamental level, was not really controversial. We didn't have people getting up and saying we think we should have genetic discrimination.

On the other hand, there are extremely cogent arguments that people on opposite ends of the spectrum, with regard to patents, bring to bear on this subject. It is very complex and it's

controversial for a reason. It's because there are legitimate positions on both sides of the issue or on all sides of the issue.

So the scope of the study that we came to is that we want to look at both the positive and the negative effects of current gene patenting and licensing practices on patient access to genetic technologies. Our ultimate arbiter here is patient access. We want to focus on gene patents for health-related tests. That would be diagnostic tests, predictive tests or other clinical purposes. We have purposely not included in the scope in a really explicit way the issue of patents that lead, for example, to drug development. That is a different area. We are focusing primarily on issues of diagnostic testing and predictive testing.

You'll notice throughout our deliberations that we use two terms. We use "clinical access" and "patient access." Ultimately we are interested in the issue of patient access and that's self-explanatory. Clinical access, when we use it, we're really referring to the ability of physicians to order these tests, the ability of physicians to get these tests done in any kind of practical way. Clinical and patient access are, obviously, extremely overlapping but not identical.

Finally, we do feel that it's important to consider the effects of gene patents and licensing practices on translational research, on getting technologies into the clinical arena.

Here's the study plan that we came to, and I would emphasize that these are not done serially but are being pursued and will be pursued in parallel.

Part 1 is data gathering and analysis through literature review, expert consultations, case studies, and perhaps additional research. This is being spearheaded by the Duke group.

Part 2 is to gather public perspectives. As I mentioned and as you all know, this is an issue with a lot of stakeholders, an issue that a lot of people have strong feelings on. It's going to be very important to solicit public perspectives, to compile and summarize those comments for the Secretary, and hold a roundtable that is a public hearing about these things.

Part 3 is what we are in large part going to do today, which is gathering international perspectives, gathering data. Identifying experts was again spearheaded by the Duke group, the roundtable and analysis of these perspectives. We will need to, in a rather daunting task, analyze and synthesize all of this and come up with a draft report that will be released for public comment and ultimately lead to a final report to the Secretary.

So the bulk of today will be focused on international perspectives, but again, given the rapidly shifting landscape, given the dynamic nature of this subject, we felt that we would like to get some kind of background or update on what the current landscape is.

DR. TUCKSON: You're getting ready to introduce somebody.

DR. EVANS: Yes.

DR. TUCKSON: So let me just pause for 10 seconds. So a couple things I think that are key here.

One is our Duke colleagues -- some of them are here. Right?

DR. EVANS: Yes.

DR. TUCKSON: Who is here from Duke? First of all, we want to thank you very much for your effort.

(Applause.)

DR. TUCKSON: Could you introduce the Duke people? Could you introduce yourselves?

DR. EVANS: Bob, do you want to start?

DR. COOK-DEEGAN: I'm Bob Cook-Deegan, and I can't see where everybody is.

DR. TUCKSON: So Bob Cook-Deegan, and who else?

MR. POWELL: Ashton Powell.

MS. CHANDRASEKHARAN: I'm a postdoc, Subhashini Chandrasekharan, working on some of the case studies.

DR. TUCKSON: Since I can barely do Gurvaneet Randhawa --

DR. EVANS: What do you mean barely?

(Laughter.)

DR. TUCKSON: I can't do that but I'll call you "postdoctoral fellow." That's a good name.

(Laughter.)

DR. TUCKSON: And who else is here?

MS. PARSONS: I'm Deidre Parsons. I'm a graduate student.

DR. TUCKSON: Deidre Parsons. Great.

And somebody way in the back.

MS. HONG: I'm Lee Hong and I'm an undergraduate at Duke University.

DR. TUCKSON: Great.

And who else?

MS. COLAIANNI: I'm Catherine Colaianni. I just graduated from (inaudible).

DR. TUCKSON: Congratulations. It's a great school.

Who else?

MS. RYDHOLM: I'm Carla Rydholm. I'm a second-year law student and (inaudible).

DR. TUCKSON: My God, doubly smart.

And who else?

MS. PADMANABHAN: Swathi Padmanabhan (inaudible).

DR. TUCKSON: I hope you make it through the end of the year.

(Laughter.)

DR. TUCKSON: All right. You should be back studying. What are you doing here?

Who else did we miss?

MS. PRASAD: I'm Shreya Prasad. I'll be a sophomore at Duke.

DR. TUCKSON: Great. So inspiring.

So now we've got who else? Who else is here from Duke?

MS. BERGER: Elana Berger (inaudible).

DR. TUCKSON: Great. Well, listen, thank you all very much.

(Applause.)

DR. TUCKSON: I wanted, as the chairman, just to acknowledge that I am well aware, as is the committee, of how much effort Duke is putting into this, and that needs to be publicly noted.

Secondly, go back one more slide, please. Actually one more slide. There.

So I wanted to just ask you. Jim did a terrific job of giving the committee a pretty clear sense of the process that we're undergoing. So, Jim, if either you or Yvette could just give us just a couple of seconds on what was the guidance. If you look at the agenda for the next several hours, we have some of the most incredibly impressive international experts in this field who have traveled to the United States to brief us.

How do you want us again to really -- what should our notes be emphasizing? What are we listening for, other than how articulate and smart they are? But what information are we really focusing in on and what kind of guidance did you give to the speakers just so we're laser-like in terms of how we listen?

DR. EVANS: I'll address that in general terms, but maybe Yvette then wants to make specific comments.

The thing that I would really urge the committee to do is to try to filter everything that is said today through a very practical filter. Again, our ultimate goal is rather simple, deceptively so really, and that is to figure out whether there are issues that we could recommend to the Secretary that would enhance patient care, that would enhance the public's health. Are there barriers now? Are there problems because of current patent law and licensing practices, and are there things that we can learn from other countries that would be implementable? We're not interested again in pie in the sky, unrealistic type things like let's change the Constitution.

This is a subject that evokes -- I'd say second only perhaps to genetic discrimination -- really passionate responses in people, and I think that we have to be careful to be fairly dispassionate and figure out where might we be able to improve things, if improvement is needed, and what lessons can we get from other countries that would be applicable here, and those things that aren't applicable, we just have to kind of skate by.

Yvette?

DR. SEGER: I have to say whoever is staffing is doing a great job.

DR. EVANS: I agree. It's really like a Charlie McCarthy thing. I feel like the ventriloquist's dummy here.

DR. SEGER: It's basically what can we learn from other countries, what can we apply practically, again not changing the Constitution, but what's out there, and eventually we'll pull back as to what we will use in our final report. But it's definitely information-gathering and seeing how other countries have handled these issues.

DR. EVANS: So I really do have a distinct pleasure and privilege at this point and that is to introduce Judge Pauline Newman. I've actually known Judge Newman now for almost 10 years. We've worked extensively on issues regarding the education of the judiciary in scientific matters. In all of my contacts with judges across the country and throughout the world, in the course of those projects, I've rarely met anyone who commands such respect and reverence as Judge Newman.

She not only is an extremely accomplished judge, but she has her Ph.D. in chemistry. She is a circuit judge with the U.S. Court of Appeals for the Federal Circuit, and she's here to give us an update on patent reform initiatives here in the U.S., namely the patent reform bills in the House and Senate and recently federal court decisions. So a big hand of gratitude for Judge Newman for taking time out to come today.

(Applause.)

+ JUDGE NEWMAN: Thank you. I was so fascinated by that introduction.

The materials that are being handed out -- do you all have a copy -- are an outline of this very complicated topic, of which there will be barely time to scratch the surface.

What I want to emphasize, to put what's happening in Congress in the context of the things that you may find that you need to discuss, is to remind us that the purpose of patent law is to bring science and technology to the public, not to withhold it, not to put artificial barriers in its utilization, just the opposite.

(Audio system failure.)

JUDGE NEWMAN: -- of the patent system as it's come to our attention and the particular issues that we understand that you are concerned with.

But I do want to stress patents are an instrument of commerce. They are also, however, an instrument of the development of science and technology. Again, that's why they're in the Constitution, to pull the development of science, the application of science, the applied technology to

public benefit with the help of the law. So there are balances to be established, and that's what the law is supposed to do. That's what this law is trying to do.

The lawmakers, in turn, are advised, through the various political procedures, to know or at least to be told and to try and balance all of these concerns and particularly now here where there are new forms of science and technology. That's what's behind this present legislation, the evolution in what's called the knowledge economy, the digital advances, and the evolution in biotechnology and the enormous promise for public benefit that both of these technologies have brought, and to figure out whether the law does serve it adequately and whether it can serve it better, again, in the public interest.

So it's very timely, indeed, for you all to be looking at and to assure yourselves and to participate in this process.

But again, I stress that the overall purpose is to serve the public through the path of new science and technology in a capitalist economy where the role of the private sector, the profit motive is what drives, pulls, and pushes many of the scientific advances perhaps -- not only perhaps, but of course, much science evolves in the university without the intrusion of the public profit motive, but to bring it out broadly to public benefit. Unless we devise some governmental participation, we need to have very much in mind the role of the private sector, the risks involved in the realities of entrepreneurship, the complexities of the kinds of science that we're talking about, particularly in the biological sciences, and put it all together.

Well, Jim asked me about the pending legislative proposals. From the political viewpoint, a fair amount has happened in that the way things have evolved in the Congress have focused on some extremely controversial provisions that serve particular aspects of the economy. And I'm told primarily the software industry, again, what we all know as the knowledge economy, the digital procedures, have been fraught because of the potential for profit and the widespread national and international interests with commercial battles. And many of these are taking place in the courts through the patent system. To make sure that the balance is properly set is what the Congress is trying to do in reviewing this law.

I should also say, however, that the future of what I'm about to tell you about is uncertain. What I'm talking about and what's outlined in the material that I handed out is what's called a manager's amendment that was submitted by Senator Leahy on June 21st of this year as a substitute for the legislation, which had gone through the House and was languishing somewhat in the Senate because of the extreme difficulty of finding consensus and because of some of the more controversial provisions that it contained.

I also understand that two attempts at a quorum to process this amendment have failed thus far. If there are further attempts -- and I have no idea whether there will or won't be, but there are many people pressing this legislation -- I suspect that time would be very short, indeed, for further input and participation of this committee.

However, there also are a number of areas of patent law which can have an impact on the interests that I've heard mentioned this morning that you may want to think about and perhaps should think about. Some are on your agenda for later today. I noticed that both Professor Gold and Professor Straus, two international leaders in the scholarly exploration of these complex issues, will be talking with you this afternoon -- and to think about what isn't included in this legislation, as well as what is.

Well, what I have here is a very brief outline of the pros and cons for each of the currently retained, in a manager's amendment, legislation. And I've mentioned here right at the front that this compilation was made by my law clerk, Chris Katopis, who is standing in the back. Chris, raise your hand. And if you have questions of procedure or how things are working or the materials that were compiled here, I've got Chris' phone number down here.

(Laughter.)

JUDGE NEWMAN: But I've also added my personal views as to each piece of legislation. I couldn't resist having my say.

But I only have, in this limited time, time to go through a few of these, and so I'm going to start at the top with the one or two areas which are perhaps of greatest significance for what I'll call the health of the patent system.

Now, I'm not going to say the strength of the patent system because that is the foundation of this controversy. Again, I'm told that the lobbying effort -- there was enormous lobbying on all sides that's been going on here -- of the software industry has been generally overall to weaken the patent system, recognizing we've all seen some very heavy litigation, some very high stakes, some billion dollar judgments in this area, and concerns as to whether this in fact is how the system should work.

Lined up on the other side have been pretty much a combination -- a curious coalition perhaps -- of the university community, the pharmaceutical and biotech industries, and big industry in general concerned that, although there may be some developments that would move into public use, even without reliable patent support, there are many others that don't.

And one of the things for you to think about, of course, is how science and technology evolves, what are the motivations, what are the purposes, the incentives, and how will it work best to serve the public interest that we're all here to serve.

So what's considered to be the most significant change that remains in the bill or the two most significant changes have to do with fairly technical aspects of the patent law.

The first is what's called the move from the first-to-invent system to the first inventor-to-file. The current system in the United States, if there are competing patent applications because there have been authentic, concurrent inventions by different people, is for the Patent Office to run what they call an interference proceeding to find out who, in fact, was the first inventor. That person then is the one who gets the patent.

Well, this legislation would change so that the first person to reach the Patent Office, the first inventor to reach the Patent Office, would in fact get the patent. It would eliminate the patent interference procedure.

It would retain one safeguard and only one, and that is for the person who loses the race to the Patent Office to say that the guy who got there first really stole it from him or "derived" it from him is the word that's used. You don't have to show any felonious criminal activity. So that's in the system, but other than that, it is a first-to-file system.

Now, I've listed the various arguments that are presented in favor of the system. I, in fact, believe, suspect from what I see, that this may be one of the few points here which may be enacted in the current legislation.

Well, the first argument is that the rest of the world has a first-to-file system. So if we are realistic in our expectation or hope that some day there will be some kind of unified, one-patent-fits-all approach, that this current obstacle -- it's mentioned as an obstacle. I don't think it's the primary obstacle, but it's been put in that position. Anyway, this obstacle would be removed so that we'd be ready for this brave new world of one international, multinational patent.

Another argument is that today less than 1 percent, maybe one-half of 1 percent, of the patents in the Patent Office are found to have the kind of conflict which warrants the interference proceeding, and that in most of those cases, after a long, drawn-out, expensive process, the first side that filed more often than not, experience shows, prevails.

Then another argument is that the first party to file has certainty that someone else isn't going to come along and say I really invented that first and take it away after 10 years of bureaucratic

hassling in the Patent Office.

The interference proceedings are very long. They are handled in the way one might expect to make sure that there aren't any mistakes. There is a very heavily overloaded Patent Office at the moment and perhaps for the future, but these have always been notoriously long, drawn-out litigations. The polypropylene interference of some 10-20 years ago took 20 years to resolve. At that time, patents were measured from the grant date. So the patents that finally issued were dealing with old technologies and the fight continued. Even now we still see some of this litigation in our court. Now that patent life is measured from the filing date to start with, with some extension if there are internal proceedings, one might find a good deal of the patent life devoured by this bureaucratic proceeding.

And another strong argument is that in fact most entities now think internationally. Since other countries have a first-to-file system, we too, small or large business, are pretty much obliged to rush into the Patent Office before any publication in order to obtain valid patents in other countries.

Well, this sounds good, doesn't it? It sounds straightforward. How could anyone object to all this?

Well, those who object perhaps have at least as strong arguments. First, they say the overall culture would change. There would be a race to the Patent Office. It would be premature. People will file, race to the Patent Office just as soon as they reach a certain stage, not develop their science or technology a bit further as they might otherwise. One aspect is that the content of the patent application would contain less useful disclosure of the science and technology just because it hadn't yet been developed. And there are very strict rules about what's called "new matter." You can't add. You can refile perhaps, but then you lose your first date and it's very complicated. So the idea of the quality of the filings might be affected.

Then patent applications are very expensive. Figures that I heard a few years ago where that fairly simple applications were somewhere between $10,000 to $50,000 in legal fees and then the filing fees keep going up as well. This is a diversion, I think, no matter how deep a pocket you're dealing with, to have to spend this resource that you might better spend on your R&D when you aren't yet really so sure what you have, but because of the race to the Patent Office, the risks of delay are enormous, especially if you think you're onto something or maybe if you aren't sure whether you're onto something.

Then there's the question of secrecy. The first-to-file legislation proposal would also broaden. There is now recently enacted an 18-month publication rule. So your patent applications are made public after 18 months. But there used to be an exception for small inventors, or anyway, those who announced that they were interested in international filing could keep their patent application secret. Now, as part of this overall structure, whatever your invention is -- and some inventions are very hard to police, process improvements and so on, minor improvements that might give you a competitive edge -- once they're out, whether they're patentable or not, they're known to the public.

And just as a digression, we know or expect that it's going to be harder to get patents, harder to preserve patents than it has been in the past based on some judicial decisions. Those decisions seem to be attuned to the current state of science. It's too soon really to know what they're going to mean. It is an uncertainty that maybe should be factored into the larger picture.

In any event, after 18 months, if you do find that someone else has gotten there first, you have no hope, even though you were the first inventor, of salvaging your own work.

Then there's the question of the grace period, a grace period which would tolerate, authorize publication. This is something that is pressed particularly by what's called the Big 10 universities. That was the letterhead of a letter recently filed that seems to reflect the academic viewpoint quite well, that publication is, indeed, very important. There are publication days, timing, all sorts of complexities that go into the balance of the need and interest in publication and the need and interest in

filing that requires a grace period. Well, the current proposed legislation does include a one-year grace period.

Now, another argument, however, which has as a result come to the fore, has been that since the first-to-invent system of the United States has been raised by the rest of the world, particularly the European and the Asian countries, as a major obstacle to harmonization of our laws, maybe we shouldn't just give it away. Maybe we should trade it for insisting that the other laws accept a grace period, and there has been a certain movement towards acceptance of a grace period. That is, is it premature to make this unilateral concession?

Well, I go into this detail for this first issue on first-to-file/first-to-invent to stress that it's not simple, and the others are worse. So if in fact you, as I hope you will, weigh all of this and take a position reflecting the public interests, that you reflect to understand that it's not going to be easy, but to me, that's all the more reason why there should be input reflecting the public interest, as well as the various private interests which have already been brought to bear.

I should point out that small business groups that at one time powerfully opposed this change have dropped that opposition. They announced it at the meeting of the National Academy of Sciences -- I think Jim was there -- whose report has been referred to -- I assume because even small business is interested in international activities.

I do want to point out also I think this aspect is of particular relevance when the science is evolving rapidly. Rapidly evolving science can have advantages and disadvantages on both sides of this equation, but since the proposal is in the hopper and enactment may or may not take place, the delicate balance as to how it might affect, in particular, the evolution and the utilization and the practical application of genetic advances is something that ought to be considered perhaps more deeply, more profoundly than is already on the record.

Then just as another aspect of the complexities, at one time there was a proposal that a secret prior user was protected, that such a person wouldn't be forced into the patent system in order to protect a first-to-file right. The present law is sort of ambiguous as to such protection. That was initially in the legislative proposal, but that adds so many additional complexities that it was dropped. However, by dropping this proposal, it leaves unknown and uncertain where things are. Again, people always used to say that an advantage of the patent system is that if you practice the invention in secret, someone else comes along, patent -- "patent" means public -- makes it public through the disclosure in a patent application. The person who was keeping it to himself and practicing it might very well be found to be an infringer. Nobody really knew because it was secret. And so there's been very little judge-made law in this area. But it's very hard to keep secrets such as that today.

So where does it fit? Well, the Senate -- this proposal -- requests a thorough study of the practices in other countries on prior user, and I think you'll hear something about that this afternoon. Whether this legislation should be moved forward without considering that aspect is another question that would just go into the balance. There are many advantages. There are disadvantages. And how you come out -- again, I encourage you not to say it's too complicated. That just leaves the decision in other hands.

How much longer should I talk?

DR. EVANS: We want to have some time for discussion.

JUDGE NEWMAN: Let me just mention one more issue then, and then let's talk about it. And that was really why I tried to put everything that's active in here because I knew we wouldn't get to it.

It's the issue of the public participation in the patent system and particularly what I've called here the second window. It provides, in some fairly complicated ways, for the public more

formally to bring to the patent examination process information that the examiners haven't had or perhaps haven't adequately considered. That's the pre-grant submission procedure of published information that I mentioned. This is generally uncontroversial. I myself think it's a fine idea.

I think we need to be realistic about the difficulties of providing enough rapid, speedy, and qualified patent examiners to handle all of the changes in technology, not that the agency has not shown that it's capable of handling a good deal of complexity very rapidly, but because the whole patent field has gotten to be such a hot employment area, that there are far fewer career examiners and many more less experienced in the Patent Office, again leading to mistakes.

A very important aspect of the patent as a commercial aspect is that the people who are investing, whether it's an entrepreneur or your banker or some relative or just an industry's R&D activities, include weighing the various risks, the risks in a research project that it will succeed or won't succeed, how much it will cost, the risk that your investment will be recovered through market forces, the role of the patent, how well will the patent protect your market, or will it really teach your would-be competitors how to do something else, your having opened the door. What are the risks of litigation? A number of the other areas here do talk about the risks of litigation, the return, the licensing issues, particularly are of interest to university inventors who aren't going into the business themselves. They don't want to protect their business, but they need to provide enough protection for some industry to take the idea, commercialize it, and market it and return to the university whatever is fair from the product.

So the pre-grant provision of information seems to be noncontroversial. It requires, of course, the early publication that I mentioned, and that is the more difficult aspect of that, rather than just opening the door to additional information.

The debate is in what's called the second window. The first window, after the patent granted, is that for a year after the patent is granted, the legislation introduces something that corresponds roughly to what in other countries is called an opposition proceeding. Here it's called a cancellation proceeding.

But the second window would allow anytime that someone is accused of infringement to go back to the Patent Office and essentially litigate the aspects of whether the patent should have been granted or not.

Well, as with everything else, there are arguments, powerful arguments, on both sides of this, and I have mentioned some of them.

The strongest argument is that litigation is so expensive and burdensome and punitive, win or lose, and if in fact there is something wrong with the patent, whether it's too broad or shouldn't have been granted in the first place or if revised or narrowed would remove the risk for your product, there ought to be an easy, cheap, alternative way to do that. And this legislation puts a lot of rapid reaction restraints on the Patent Office. It requires them to set up another administrative tribunal to handle this. There are time limits, and it's really unobjectionable that an alternative would be helpful.

Now, at present, there is what's called an interparties reexamination proceeding that had the same goal. However, it's not being used.

People for whom the stakes are high, those who want to challenge the patent, would rather go to court on the theory that the Patent Office perhaps would be more likely to understand the issues, understand the science, and proceed to reinforce what they did before, whereas there might be a better chance at eliminating a patent in court.

But they also say to limit the unlimited challenge to one year is really too short. People have other things to do than watch every patent that comes out and see if there are flaws in it that would render it vulnerable to attack.

They also point out that no one really objected to being able to push a patent into

reexamination at any time during its life. So what's all the fuss about for a cancellation proceeding?

They also say that because of all of the complaints, a good number of safeguards have been built into the law, including the safeguard that if the patent survived such a proceeding, you can't again challenge it in court. Now, that is not the present law with the reexamination. So it would, indeed, have a strengthening effect on the patent. Critics say, therefore, people who aren't so sure how it's going to come out are not going to run the risk of reducing their chances of eliminating the patent that's in their way by using the proceeding.

The arguments on the other side are different. They say that the only patents that are ever challenged anywhere at any time are the successful ones where the inventor has made the invention or acquired it, has invested in its development, brought it to market, shown that it's profitable, and then along comes the other guy who says, oh, I'm entitled to a piece of that because there are some flaws in the first place. So they say that this would tempt such opportunistic attack. It would also tempt burdensome attack perhaps on people who are least able to afford it. They say that the possibility that I can always challenge the patent -- and remember the recent Medimmune case says that a licensee can always challenge the patent.

So the opportunity to do that can change the entire landscape of licensing negotiations because the patentee is, by definition, in a weaker position generally as a matter of law even though the specifics of that invention haven't been investigated. So they say that it's ripe for abuse and that the abuses may outweigh the advantages.

They talk about the need for a reliable asset to acquire risk capital, as well as other capital investment. They say that it's uncertain enough to have judicial review of patent validity. I suppose I'm part of that problem. Therefore, adding another area of uncertainty can shift the negotiating balance in unknown and unpredictive ways.

The Big 10 universities took a very strong position on this. What they said is if patents are to have any value, there must be some finality to the process, and that's what they were talking about. Litigation, of course, is not final. But finality to the administrative process, which was designed for benevolent reasons to be easier and cheaper to manage, they say to allow investors to develop with confidence. Well, it's complicated. It's very complicated. So I commend it to you.

I also mentioned that in foreign countries, as I understand it, the opposition period is limited to a certain amount of time after the grant of the patent. And I do know that we've all seen some horror stories of tying up such patents for their entire life. Again, the life is being measured from the filing date rather than anything else.

The absence of this second window, it said, doesn't prevent the challenge of a patent in court. If you're charged with infringement, you can bring your challenge to the court and resolve it that way. So, the opposers say, there's no need for an additional bureaucratic proceeding unless we show that it's just not working the way things are now. Well, of course, there are a lot of reasons to criticize the way things are now.

Later on -- we may not get to it. Perhaps there are technicalities of the patent law, the so-called interlocutory appeal at various stages of the patent litigation so as to try and simplify and clarify the issues as the litigation proceeds is something else that's being proposed in this legislation. Again, there's as much or more to be said against that procedure as in favor of it. But again, the interests need to be balanced, but they need to be balanced from your viewpoint, not mine as trying to settle litigation, not the viewpoint of any particular industry because the viewpoints all vary, but as far as that which you know about the development and the evolution of science and technology and its public availability, just to think about how that affects and is affected by legislative changes and whether there's anything that you should be doing.

All right. Well, then this is a good place to stop. Is it, Jim?

DR. EVANS: Yes.

JUDGE NEWMAN: Okay.

(Applause.)

+ DR. EVANS: So I'm going to take the liberty of eating into our break for just a few minutes to ask for questions or comments for Judge Newman.

I just had one question that maybe you could comment on. You alluded early on in your points about the discrepant effects of weak and strong patenting law on different parts of industry. For example, pharma would like very strong patent law. Software traditionally has argued for weakening patent law.

Do you think that that demonstration which certainly goes to within medicine that exists to some extent -- do you think that that argues for licensing practices that might remedy that type of thing? In other words, do you think that there are remedies that can be brought to bear on different aspects of patent practice that would mitigate some of that bluntness of patent law?

JUDGE NEWMAN: I have pretty much come to the conclusion, based on the power of the arguments made by the software industry, that perhaps it would be appropriate to think about whether the rules should be modified where the patentee is not in business, has not made a commercial investment. Now, that would have one impact, however, on the computer programmers who have ingenious ideas such as the idea that caused the BlackBerry producers so much grief and enter the Patent Office without a major investment. But the other side, the same principle might very well apply to scientists in universities who are seeking to license their inventions and who are not themselves exploiting and developing it.

I don't know an easy answer to that question. To strengthen the role of the licensing entity I think is very much on the table at the moment because of the new decision of the Supreme Court which says that a licensee can challenge the patent at any time. For scientists and their supporters in the universities whose interest is in licensing, not just to provide a financial return to the university, but to move the scientific development into public use, the balance of the negotiation shifts. Whether it shifts disadvantageously, I'm not so sure because, after all, if a patent can't stand --

(Audio system failure.)

JUDGE NEWMAN: -- incremental steps are no longer going to be favorably viewed by decision-makers in patenting, what will that do to the development of the science and to then the movement as the science evolves from the laboratory bench into public use and in the private sector, whether it will even get to the laboratory bench at all. All of these aspects are intertwined in a very complicated way.

DR. EVANS: And I think making our task more difficult. Something to reinforce to the committee is that arguably issues with regard to diagnostic tests and predictive tests -- we're not just talking about commerce. We're talking about another imperative too, which is patient access and the public's health. So we have to take into account the types of remedies that get to that and aren't just focused on commerce.

Thank you very much. We can have our break now, and return at 10:50. So thanks.

(Applause.)

(Recess.)

DR. TUCKSON: We have reconvened. We've got everybody now back, full attention, at their duty posts. Take it away, Jim.

DR. EVANS: Now, in just a second, I'm going to frame the questions that we have for today, and then I'm going to introduce Richard Gold.

Before that, though, I want to get a couple of comments from Debra Leonard because we've been hashing out some things during the break. So, Debra?

DR. LEONARD: I just wanted to make sure that everybody wasn't drawing a box around how to think about what we're going to be hearing by Jim's statement of we are not going to change the Constitution because I agree, we're not going to change the Constitution --

DR. EVANS: Debra is going to change the Constitution.

(Laughter.)

DR. LEONARD: No. None of us are going to change the Constitution, but we may go as far as to change the interpretation of the Constitution or how that applies to genetic testing. So I didn't want to draw too much of a box around the options that people would feel comfortable considering as we're hearing the international perspectives.

DR. EVANS: Great. And I would second that by saying that. By making that statement, I don't mean to indicate that we shouldn't be ambitious in our goals and in our recommendations. I just don't want to be so ambitious that we end up being quixotic. We need to come up with practical recommendations.

Now, with that said, I want to frame the next section here of our discussions by just letting you know about the three kind of foci of today's discussion to keep in mind while we're listening to our presenters. We're seeking to gather background information on gene patenting and licensing practices of other countries. We want to compare and contrast enforcement of intellectual property rights for patented genes in the U.S. and in countries with government-held systems, and we want to learn about the processes utilized by international groups in developing reports and recommendations on issues relating to gene patents and licensing strategies.

That said, I want to introduce now our first speaker whom I've known for some years, Richard Gold, who has been prolific in his writing about the intersection of the law, technology, commerce, and ethics. He is joining us via videocast from a meeting in Geneva. I'll bet the weather is nicer in Geneva.

(Laughter.)

DR. EVANS: Professor Gold is the Director of the Centre for Intellectual Property Policy and teaches in the area of intellectual property and technology at McGill University's Faculty of Law as the Bell Chair in e-Governance. His research focuses on the nexus between technology, commerce, and ethics, particularly with respect to biotechnology in an international context. He is the principal investigator of the Intellectual Property Modeling Group, a transdisciplinary research team investigating intellectual property regimes.

I turn the floor over to you now, Richard.

+ DR. GOLD: Well, thank you, Jim. Nice seeing you again, although you take up about a half a square inch on the screen that's far from me, so I can barely see you.

Can you hear me okay?

DR. EVANS: Yes, I believe so.

DR. GOLD: Okay, good. And do you have my slides there?

DR. EVANS: Yes, and I should mention that they're in your folder. We won't be able to show Richard and the slides at the same time. So I would direct people to their folder.

DR. GOLD: Okay. So I'll indicate when to move on.

To answer your question about the weather, no, it's actually quite poor out. It's been raining since I've come here and it's 14 degrees Celsius, which is, I'm sure, far colder than it is in Washington. So they're not enjoying their summer here. In fact, when contacting Montreal, I'm told that the --

(International audio connection lost.)

DR. GOLD: Well, thank you for inviting me. Although it may be awkward for me to know when you want to ask a question, please let's find a way for you to interrupt me if you want. I realize there will be a question period afterward.

If you can just turn to the overview, let me just take you through what I want to talk about. I realize that in the room physically present you have lots of experts from different places. So I hope that they will correct me should I make any mistakes.

What I would like to cover is --

(International audio connection lost.)

DR. EVANS: Richard, can you hear me? We've lost your feed.

DR. GOLD: Completely?

DR. EVANS: There you are. No. We got it back.

DR. GOLD: So I'm going to start off with the overview, a comparison internationally quickly. What I want to do is quickly get to a more concentrated discussion on what is the nature of the concerns, especially outside the United States, because I understand that part of the goal of this discussion is to understand what happened internationally and whether it has relevance to the U.S. So I want to isolate some of those concerns that may be different and some that are the same, talk about some of the policy responses, and in particular, the issue of licensing and how that seems to play out, and then I hope at the end of this discussion to turn to what can be learned from this experience. Since I'm again talking in the next session, I'll try to not get too far --

(International audio connection lost.)

DR. EVANS: Richard, we've lost you again. Do you have an AV person? Wait. Somehow, maybe it's when you bend over.

(Laughter.)

DR. EVANS: Can you hold your tongue just right?

DR. GOLD: Okay, I won't move.

DR. EVANS: We got you now. All right.

DR. GOLD: So on the first slide, the debate really started in the U.S. The rest of the world was, in large part, responding to developments in the United States. So I don't have to tell you about what happened in 1980 in the U.S. in terms of biotech innovation, but that's where the ball --

(International audio connection lost.)

DR. EVANS: We've lost you again.

DR. GOLD: Can you hear me?

DR. EVANS: And now suddenly we can hear you. It goes in and out.

DR. GOLD: So what I think I have to do is move enough.

DR. EVANS: Maybe that's it. You've got to be like Mohammed Ali here.

DR. GOLD: Okay. I'll sway and I'll be light as a butterfly.

So after 1980, there were some studies. And I don't know if Professor Straus is in the room, but he authored some for the OECD in this area in 1982 and '85 looking at the various countries and the patenting with respect --

(International audio connection lost.)

DR. EVANS: Richard?

DR. GOLD: Yes.

DR. EVANS: Once again, we got silence. Then when you respond --

DR. TUCKSON: So here's what we're going to do. Richard, this is Reed Tuckson, the chairman. Again, we want this to be as efficient and effective as possible. I wonder if maybe we

might take a break from your presentation. I don't know what your schedule is like. Maybe we'll do somebody that's here and have your AV people sort of help work with ours to get this fixed. Is that possible?

DR. GOLD: It's possible except that I'm also on the next panel.

DR. TUCKSON: Hold on one second, Richard.

Who is next?

DR. EVANS: Shobita Parthasarathy.

DR. TUCKSON: Is Shobita here? Shobita, are you in a position to be able to present in a few minutes?

DR. PARTHASARATHY: Sure.

DR. TUCKSON: Great.

So, Richard, do you have an AV person there?

DR. GOLD: There should be one next door to me, yes.

DR. TUCKSON: Great. I'm just trying to think how to do this. Richard, they're talking to your AV people right now here. Wait a minute.

DR. GOLD: Okay. Do you want me to continue and --

DR. TUCKSON: No. Hold on, Richard, because we're not being fair to you, and I don't want to put you in this kind of a position as a presenter. That's not fair to you.

Your people are going to redial us. So hold on for a minute. We're just going to wait. Your people are going to redial us.

DR. GOLD: Okay.

DR. TUCKSON: You're going to go off screen for a minute. We'll be back in a minute.

I appreciate everyone's patience. You're okay for the minute, Shobita. Let's do it right. So we'll just take a minute and see if we can't resolve this. I think we're all patient enough to be patient. If you stay calm, it will all be fine, but it's when people panic and go running all over the place that they just screw it up, and then the whole program gets messed up because everybody is tense and nervous. So it's just a matter of staying calm.

(Recess.)

DR. TUCKSON: Just so you know, we're calling the video now. If this doesn't work, since we already know what he looks like, we'll just do it as a teleconference. Then you can just sort of hallucinate his face.

DR. EVANS: All right. We can see you. Can we hear you?

DR. GOLD: I hope so.

DR. EVANS: We can. All right.

DR. TUCKSON: Richard, let me just say this. If we have trouble this time, what we'll do is we'll just do it as an old-fashioned telephone call.

DR. GOLD: That's fine.

DR. TUCKSON: Because we're all memorizing your face.

DR. GOLD: Okay. I'll try and put lots of expressions on in the next few minutes, so you can imagine me in different states.

DR. TUCKSON: Well, please continue and thank you.

DR. GOLD: So as I was saying, various studies following the U.S. lead in 1980 -- and the last point I think I made was the 1983 group of experts.

So moving to Europe, I'm just going to go through a few sample areas, although I will spend a little bit of time on Europe, and if Professor Straus is there, he should correct me if I --

(International audio connection lost.)

DR. EVANS: Richard, this is so strange. I think we're going to have to go to telephone. I don't understand why every time I talk we get you again.

DR. TUCKSON: Is there someone who is helping on the phone now?

Richard, apparently what they're saying to us is that if we leave our mikes on, maybe that will somehow solve the problem. We'll do one last try and we'll see whether it works. If not, we'll use the phone and we'll be quite fine. So go ahead and continue, Richard, and thank you.

DR. GOLD: Okay. Let's keep trying.

So turning to Europe, the European Commission, obviously concerned about the U.S. and Japanese lead in biotechnology and wondering why they weren't doing more, started this issue and issued a white paper in 1985 stating that it was going to act in the area of --

(International audio connection lost.)

DR. EVANS: Richard, we're going to have to go to the telephone. I really apologize.

DR. GOLD: No problem.

DR. TUCKSON: Do you all have the phone number there, Richard, to call us?

DR. GOLD: Yes.

DR. TUCKSON: I just want the members of the panel and the audience to know that these folks have been working on this for a day or so. It wasn't like people weren't attentive to detail and they didn't do their best. It's just, I guess, one of those things, but they were on this yesterday. They tested it. We would not have put the committee in a position to have your time wasted by technical glitches because of inattention to detail. Even with attention to detail, it turns out that there's a glitch. So we apologize, and we apologize to the other speakers who are pushing their time back a little bit. But we'll get through this.

AUDIO TECHNICIAN: Hello from Geneva. Can you hear us?

DR. TUCKSON: Yes.

DR. GOLD: I can loosen my tie at least, so you won't know the difference. You can pretend I'm still wearing it.

So let me go back to where I picked up. You'll have to let me know when you want me to stop, if you have a question, since I won't be able to see anything.

DR. TUCKSON: But listen, Richard, you're doing fine. Just go ahead in a normal presentation. We can hear you well and we will certainly interrupt, but you should just present in a comfortable manner. Your material is very important to us, and so please take your time and do what you would have normally done.

DR. EVANS: We now have your slides up too.

DR. GOLD: Oh, great. Okay. So you should be on the slide that says "Europe." The European Commission issued a white paper. So I talked about that.

And then they actually introduced a first draft of the directive in 1988 which dealt with all biotechnology but had specific provisions dealing with genetics that I'll get to.

From the Commission's point of view, and having talked to the person who drafted it at the Commission, this was really a technical exercise on their part to follow what was actually their view of patent law in Europe. That is, they thought it was just a technical change to make sure that they had in place a law that corresponded to the fact that biotechnology, including genes, was patentable.

However, soon after the introduction of the directive -- and there are various reasons for this, including some of the NIH early EST patents, the Harvard OncoMouse decisions, and so on, ethical concerns came out. So what had been perceived as largely a technical issue then became an ethical issue, and religious groups and ethicists joined in the debate.

In fact, the debate continued and there were also changes in the constitution at the European level that gave more power to the European Parliament. As you may know, unlike Congress in the U.S., the European Parliament is fairly weak or has been fairly weak, and over the years, through amendments to the European constitution, they've been given more and more power.

And during this period, that power has increased to the point where they were able to actually defeat the initial draft proposed by the Commission in 1995. The Commission, of course, didn't want to leave things as they were. They got the message that there were ethical issues involved, particularly around human gene patents, but more generally the relationship between owning life and who should have control on plant variety protection and so on. And they introduced a new version of the directive, similar to the original, but having more explicit recognition of some of the ethical issues in late 1995.

There was some more debate, but finally by July 1998, both the European Parliament and the Council -- and the Council is the more important body -- passed the directive with some amendments, again targeted at ethics, including a clause dealing with exceptions for patentability for things that raise moral problems. And I'll come back to that in a second.

Now, the directive itself -- the original intent had simply to say that genes are like any other chemical substance and should be patented using the exact same rules. However, the final version, because they had to address some ethical concerns about owning genes as they exist in nature, there's some ambiguous language in the directive. So Article 3.2 calls for the patentability of all artificial or isolated biotechnological material, which is in line with patent law, but then Article 5 of the directive relates particularly to gene patents. This is where we get some contradictions.

So if you're on the slide that says "Article 5 of Directive 98/44," I've given you that provision. So there should be numbers, 1, 2, and 3.

You'll see that in the first section it says that the human body, at its various stages of its formation, is not patentable, including the simple discovery of one of its elements. So the first clause seems to imply you cannot patent genes.

But then the second article, which is supposed to be harmonious with the first, but some people have argued is not, said that an element isolated from the human body that is in an artificial state, taken out of the human body and isolated, or created artificially through a technical process, even if it's a gene, can be patentable even if the structure is identical to what you would find in nature.

So there seems to be a contradiction between the first paragraph that says it's not patentable and the second that it is. The general view was the first paragraph is stating the rule that products of nature are not patentable. Paragraph two is saying, well, if you isolate it or you do something to it, it is patentable. So that's how most patent lawyers would read it. But when it got out further during parliamentary debates and other places, that was more ambiguous.

Also, what was important was the third section of Article 5 that says the industrial application, which is roughly equivalent to the utility standard in the U.S., must be disclosed in the patent application, so that you have to say this is what the gene or the protein produced by the gene does.

As you may or may not know, in Europe there's a dual system for patents. Each country or most countries issue their own patents if you file locally. Not all countries, but many. Or they all do, but anyway, I won't get into the complexity of rules there.

But there is also what is generally more used, the European Patent Convention. It so happens that the European Patent Convention and the European Patent Office are not part of the European Union. They happen to include the same states plus some others, but they're not the same institution. So in order to get an alignment between what the directive said in terms of the patentability of biotech and knowledge including patents, there had to be a corresponding change to the European Patent Convention.

However, there was some controversy. There were some countries that opposed such a maneuver, and I should say that there were some countries that opposed initially the directive as well.

So the more obvious way to have changed the Patent Convention was actually to amend it, but because there was opposition, they brought in the changes through a regulation saying all this does is clarify existing law. So on the basis that this did nothing more than clarify existing law, they passed it as a regulation which required a lesser majority to approve. So that was tough, not without some political opposition, not without some ethical groups being concerned.

One thing to remember is that the directive also called for the creation of an ethics committee to report back every five years on programs. So the ethical concern was evident both in the morality clause, the Article 5 I showed you, and more generally the fact that the directive and its operation should be surveyed periodically.

At about the same time or a little bit later, the Opposition Division -- in Europe, there's an opposition procedure for patents. It doesn't exist either in your country or in mine. During that opposition procedure, a patent was rejected based on industrial application. Now, the standard that came out will be of no particular surprise to you, but at least advanced industrial -- the way Europeans conceived of an industrial application. They said, in order for a gene to be patentable, it can't be purely speculative about what it does. There has to be some concrete evidence, and they used the formulation of specific, concrete, and credible, which obviously corresponds fairly well to the utility standard in the United States.

So you see an alignment at least in formal patent law between what was happening in Europe despite the ethical concerns and what was happening in the United States. Both were advancing at about the same pace and coming to the same conclusions. Yes, there was a gloss of ethical concerns, but those were largely outside the structure of patent law through ethical reviews. And yes, there was a morality clause, but it's very seldom used and no one expects it to be used extensively. So by and large, the two streams came together.

The one exception -- and this is where the morality clause has had the biggest effect -- is in stem cell patenting, which is not what you're looking at, but just to note that Europeans take what you in the U.S. and we in Canada would think is a fairly restrictive approach to patenting of stem cells. But I'll leave that aside.

Turning to Canada, if you turn to that slide, we have no specific legislation on gene patents. There haven't been any substantial amendments of our Patent Act, at least in this area. There have been for access to medicines. It was presumed by the Patent Office that genes were like chemicals and, therefore, patentable, and they issued patents.

It wasn't really until 2004, until we had a more or less definitive statement by the Supreme Court of Canada in a decision between Monsanto and a farmer in the prairie provinces, Schmeiser, which had to do with genetically modified canola and the seeds supposedly had spread onto Schmeiser's land and he was sued for patent infringement, and the question was did he infringe. The patents in that case were on the genes and on cells containing the genes. There was no patent issued on the plant for the very simple reason that Canada does not issue patents on whole plants or whole animals.

So the issue that was raised before the Supreme Court are gene patents valid, and the Supreme Court said yes. There wasn't an extensive analysis in the decision, but it seems clear enough that in Canada gene patents, as well as cells containing genes that aren't natural to it, are patentable.

The court went further in that case and said if you have a patent on a gene, you effectively get to control the whole plant containing that gene or the whole animal containing that gene. So, in effect, even though you cannot have a patent on an entire animal or plant in Canada, you effectively can get the same protection by patenting the gene or the cell containing the gene. I haven't

been able to figure out a situation in which you get an advantage to patenting the whole animal or plant.

If we turn now to some developing countries -- again, it's not going to be exhaustive, but let me just take Brazil, China, and India as examples.

The law in Brazil is ambiguous as to whether patents can be granted over genes. The Patent Office seems to take a view that some consider as going beyond the Patent Act in granting genes. However, this has never been tested, so we don't really know what the law of Brazil is on this point. It hasn't been challenged.

China, though, clearly does permit gene patents, and in fact, some Chinese government-owned companies have some of the largest stakes in gene patents.

Since 2005, when India reformed its Patent Act to be in compliance with the TRIPS agreement, India too permits patents over genes.

So at least in two out of the three, and probably in Brazil too, the major countries where gene type of research could lead to some commercial application, it seems that there is coverage.

We did a study for the WHO a few years ago, and we looked at the actual incidence of gene patenting in developing countries. It's fairly low. This should not be a surprise since generally gene patents are applied for by smaller biotech companies and the interest of paying extra fees and filing patents in developing countries for genetic technologies is not high. In fact, that was what was revealed. With the changes in Brazil -- at least in China and India -- will that make a difference? We'll have to see. But we do not expect broad gene patenting to occur in most developing countries unless they have a fairly significant scientific infrastructure which most don't.

Let me now move away from the history and steps taken. As I said, there seems to be an alignment of rules about the fact that genes are patentable, and the exceptions are fairly minor. There seems to be general agreement, not necessarily explicit, but that's the way things have turned out, that genes are patentable.

However, that doesn't mean there has not been very contradictory policy responses to the fact of gene patents. So if you look at the first slide that is a statement in 2002 in Canada from the House of Commons Standing Committee on Health, I'll let you read it. But essentially the committee seemed to be of the belief that there were no patents issued on DNA sequences, which was wrong at the time and is still wrong, and found it repugnant in fact. So we have some policymakers, especially those coming from a health policy perspective -- and this was a committee of legislators -- having a fairly hostile view of gene patents and not quite realizing that they existed for quite a while.

If you look at the next statement by the National Research Council, which has a mandate on doing research in the interest of Canadians and often does work with industry, you see the opposite view, that in fact, there's a recognition that patents are important to innovation, that there are clear measures of innovation. However, it might be a good time -- this was in 2004 -- to make sure that the system is completely aligned. That is, the basic principle of gene patenting, according to them, should not be put up for dispute, and I think most experts around the world agree with that. The question more is, is the system as it's presently calibrated working? And I think that's the operating premise that you're likely working under.

Let me just give you an example from the European Parliament in 2001. This relates directly to the next session on Myriad. But you get conflicting comments from the European Parliament. First, in 1998, they passed a directive which, despite the ambiguity in Article 5, seems to support the patenting of human genes. And yet, when the whole Myriad controversy was getting under way -- and as I said, I'll get into the details of that later -- they seemed to indicate that patents should not be issued on genes.

So there's a lot of contradiction. Both the House of Commons standing committee

statement and the European Parliament indicate that legislatures have a very ambiguous attitude towards gene patents, something that's probably, again, not too foreign from what you're used to.

Just to close this with a quote from BIO, this was written in the context again of Myriad and the threat by BIO to pull out -- BIO 2002 was just before that -- where they wrote a letter to the Premiere of Ontario in respect of the Myriad controversy. But you see again they're reiterating the point that from their point of view patents are essential to benefit the Canadian health care system.

So we have policymakers that go back and forth and we have those who have more experience on the commercial side, whether it be BIO or the National Research Council, promoting patents with the National Research Council taking a middle road approach and saying, well, maybe there are some aspects we want to change.

Now, that indicates that there is some controversy in the policy community. But what's the nature of those concerns? I'm going to try and relate this to the U.S. So if you can go to the slide that says "Concerns Raised."

Generally the type of general ethical concerns are the same as raised in the United States when it comes to questions of owning life. Does having a patented gene equate to owning life? So those type of questions that I'm sure you're used to, as well as questions about how gene patents affect research. Are they too extreme and so on? Again, you've got similar debates that follow those in the United States and debates about patent criteria. Is it too easy to get a gene patent? Is it too difficult? How do we interpret the utility standard? How broad a patent is issued? How many claims can be in a patent? And so on and so forth, very much in line with what's happening in the U.S.

I would say that the big difference is in the area of public health care. Since most countries, at least the OECD countries, have a public health care system, the biggest concern and the people with the biggest voice in this debate that actually tried to effect change were people coming from the health departments, people delivering health care. And there the issue was what are the effects of gene patents not only on research, but more importantly on the delivery of health care within a public system.

So they raised the issue as a general matter and various governments or institutions within a country looked at this. So there's the Australian Law Reform Commission that was mandated by the government to look specifically at the issue of genetic patents. The Canadian Biotechnology Advisory Committee on a joint mandate from Health Canada and from Industry Canada were asked again to look at the implications of gene patents both on research and on health care delivery. The WHO looked at questions of access in terms of the effect of gene patents. Nuffield Council 2002 was looking at issues of gene patents, and so on and so forth, including, as I'll talk about in the next session, a report by the Ontario government. So a lot of studies.

The general conclusion was gene patents should be around. We should keep them. Nobody came out anywhere close to strongly against gene patents, but there was a lot of discussion about how it could managed. And a lot of the discussions were about what are the levers that could be used to provide health administrators with the power to control introduction of new medicines.

Now, in terms of actual responses beyond studying it, if you turn to the next slide, generally there was little appetite for patent reform per se, some notions in the Australian Law Reform Commission about patent reforms, certainly the Nuffield Council, but generally there was not a very strong push on patent reform either in the reports and certainly not in government. We don't see any legislation that really comes out and tries to address this issue. Instead, the fight seems to be on particular issues that blew up.

And again, Myriad keeps coming back in this case. So in Europe, rather than challenging the entire patent system or introducing changes to the directive or national laws, there was an

effort to fight through the opposition process Myriad's patents, and in fact, most of them were invalidated, at least at the initial opposition stage. We're waiting to hear at the final stage.

In Canada, the response was more or less to ignore the fact that the patents existed on the basis they may not be valid or they may not apply because of other exceptions and so on. So generally in Canada, except in the Province of Quebec, no payments are made, no license exists.

There were also other responses at the international level. So if Christina Sampogna is there, she can talk to the OECD guidelines that we both worked on on the licensing of genetic inventions which tried to shift the focus from changes to patent law to changes to practice. Changes to patent law was viewed as something difficult to do, that it would be hard to get a consensus about res. Particular interventions narrowly conceived could come about, and I'm sure Christina will present you the guidelines.

But generally they aimed -- and when they were being formulated by those of us in the secretariat and working in the initial drafting stages with the committee -- to try to move beyond the Myriad debate and look at how gene patents are different and the fact that they are early stage research and so on.

So there was a general view that even though the law does not require it, it's preferable for gene patents to be nonexclusively licensed, that exclusive licenses might be justified in certain circumstances, but the default rule should be nonexclusive licenses. There should be protection for students and there certainly should be an accommodation of the interest of health care providers so that they can have control over the availability of treatment, which means having local licensees and so on so that the administrators have someone to work with.

I noticed in the notes preparatory to this session, there was some talk about, well, what about medical exceptions and how do they work here. Well, in fact, the most common types of exceptions are those covering methods of medical treatment or diagnoses, which some countries have in their patent laws. But those are read fairly narrowly for a variety of reasons to being simply in vivo. So that means the exception only applies to tests being done on animals or humans, and none of these methods really apply. They're all ex vivo, in which case the exceptions do not apply. So there's no serious contention that patents are available over genes and that they apply in this field. There's no statutory way to kick them out. So people have turned to practices.

I should mention at this point that in Europe, in terms of the transposition of the directive, some countries took a fairly narrow approach. And, again, Professor Straus may wish to talk to this. But both in France and Germany, the rule was brought in that the patents on a gene is only relation to the particular function noted in the application, and it has no general application. And there is a question about how that fits in with general patent law, but I will leave that to Professor Straus since he has written or spoken on that eloquently.

So we turn to the field of practice as opposed to patent law reform. We see again that many of the concerns are similar to those in the United States in terms of student access, in terms of ensuring that there's continued research or the development of alternative clinical therapies or diagnostic kits and so on and so forth. So really the debate in the United States for the large part matches that happening elsewhere.

But, again, the difference was in the public health care setting where the public health authorities had particular concerns about the roll-out of genetic testing in particular. What they were concerned about is whether patents get in the way of at least four things.

First, whether or not to introduce the technology. They wanted to have a technology assessment. They wanted to be able to control which technology gets introduced, how, to whom. So the first question, should we introduce the technology?

Second, how to introduce it? Do we introduce it in its gold standard or do we want to introduce it in bits and pieces? Again, the patentholder may have some say on that, and they were concerned about that.

To whom should it be offered? Should it be offered generally? Should it be offered to a restricted group? How does one contact that? Who makes the assessment? What's the role of genetic counseling? What's the integration between genetic counseling and the provision of services? And then how does one report back to the patient and so on?

So what they were concerned about is actual health care delivery, and there were several points at which a patent owner could, if they wished, intervene in the internal decisions about where to put resources when and to whom. So that was a major concern that at least the guidelines try to address but is a continuing concern in most countries.

There was also a concern about the business model that was used, and I'll get into this in much more detail when I talk about Myriad. But there was a feeling, at least among health care administrato,rs that the business model being used for genetics was the wrong one. It did not provide the flexibility to the public health care system that they needed and found that they did not have enough leverage within existing patent law to be able to go back to industry and tell them to do it differently. Yes, most countries have compulsory licensing or other provisions, but those were seen as sledgehammers that no government could rationally utilize because they would then scare off industry in much broader sectors. So they were caught with having the tools that were completely inappropriate, not allowing them to seriously negotiate because the threat was moot. No company would believe that a government would actually invoke a compulsory license in these circumstances, and so they had very little bargaining power. Their only power in the end was to act like the patent didn't exist, and that worked in the Myriad case for reasons I'll get into later.

So what can we learn from this? First, the polarization internationally was similar to that in the United States.

One group tends to be patent experts who viewed that the whole question of gene patenting and the criteria, et cetera was just part and parcel of ordinary patent law. There was nothing particularly different about this. This is about incentive for the private sector. To the extent that one is concerned about the public sector, there were other tools such as health regulation, purchasing power, and so on, and that we should not mix up apples and oranges, that patent law is really about commercial incentives to innovate. And so from their point of view, this was a purely technical matter, and yes, there would be evolution in the application of patent laws to genes, but that was natural as it happened in any field.

On the other hand, there are those who believed that gene patents raised fundamentally different issues. So there are those who come from a religious background who simply viewed that this was wrong. On the ethical front, there were concerns about commodification. Those existed in the United States too. There was nothing particularly new about that. More concerns about the nature of the public health care system and who can talk about that, so that might be slightly different.

Similar concerns as well over the effect of research. That comes up over and over again, and relatively little concern over developing countries simply because nobody really believed that there were many patents out there. There's certainly no evidence of many gene patents in developing countries.

So what can we learn? Let's continue. It seems that at least internationally -- and you can evaluate the U.S. situation better than can I -- the real concern was on the public health care administration, what's that interaction. And the feeling was, yes, licensing practices are part of the solution but not the entire solution. So we're left with ad hoc policy responses, either opposing certain

patents or ignoring certain patents rather than a comprehensive approach, whether within or outside patent law. The goal of the health care administrators is to maintain their flexibility, and there's still the open question what policy levers are required within patent law to be able to provide that type of assistance. So certainly when we get to Myriad, again I can talk about some of what was proposed.

So just let me conclude this session by saying that the U.S. debate carried on internationally, but on top of that there was the whole debate about the intersection between public health care systems and genes, but no country has found what I would consider a stable solution. There's a standoff now but nobody, I would suggest, is entirely pleased with the situation. And there seems to be a lack of willingness to undertake even modest patent reform in order to provide the policy levers that would give some comfort to the health care administrators. So we get these ad hoc responses, which frankly are fairly unfair because it targets only some companies and not others and doesn't really go to what is the appropriate balance here in terms of bargaining power.

So let me end the session now and ask you to ask whatever questions, or if you would prefer to move on to the next session because of the time, please let me know.

DR. EVANS: Great, Richard. Can you hear me?

DR. GOLD: I can, indeed.

DR. EVANS: That was fantastic. That's exactly what we needed.

In the next section, we're going to look at two case study perspectives regarding testing. Now, Richard, would it be okay with you if the other speaker went first and then we came back to you?

DR. GOLD: Either way is fine.

DR. EVANS: That would be great.

So Shobita Parthasarathy is an assistant professor of public policy at the Gerald R. Ford School of Public Policy at the University of Michigan. Dr. Parthasarathy conducts research on the politics of science and technology both in the U.S. and abroad. She's authored a very good book recently. It's titled "Building Genetic Medicine: Breast Cancer, Technology, and the Comparative Politics of Health Care." It was released earlier this spring.

And I'll turn things over to you, Dr. Parthasarathy.

+ DR. PARTHASARATHY: Thanks a lot and thank you very much for the invitation to speak to you today.

The title of my talk reflects conversations that I had with people at SACGHS about what you were interested in learning about vis-a-vis the Myriad case specifically with regard to, as Jim said, my recent book that's a comparative study of the U.S. and U.K. But I'm actually now doing some more work more generally on the comparative politics of biotech patenting broadly in the U.S. and Europe. So I'll bring in, I hope, some of those insights as well and hopefully link them to some of the comments this morning, as well as to Richard's comments earlier.

A couple of things before I begin, though. As Richard said too, please feel free to interrupt me if something is not clear or if I'm moving too fast trying to cover a lot. As you can imagine, when you've written a book on this stuff, you could go on forever, but I'll do my best to restrict my comments to just a few minutes.

In that vein, though, assuming that you guys will be interrupting me, I want to start out by at least hitting the main points of what I'm going to be talking about today. The first is that, of course, policy is important but the commercial and scientific and health care cultures that Richard alluded to just now are also extremely important in terms of how genetic testing is being built in different countries. And this is true certainly in the U.S. and Britain which I'll be focusing on today but also more broadly in Europe, which I'll also be talking about a little bit.

So you'll see, I think, in my analysis I'm going to be focusing very much on the gene patent and gene patent policy stories with regard to the development of genetic testing for breast cancer in the U.S. and Britain, but by no means are those gene patent policies the only thing that mattered in terms of the development of this technology very differently in the U.S. and Britain. And I want to sort of make that caveat clear because if it seems like I'm creating sort of an A to B story too simply, I want to assure you that that's not actually the case, but I'm just highlighting that for the purposes of the discussion today.

Furthermore, I also want to make another point, which is that we often focus, when we think about technology, on the fact that perhaps the costs might be different. Certainly we can see that that might be the case between the U.S. and other European countries that have public health care systems or that access might be different, and you'll certainly see that that is the case when we talk about the U.S. and Britain.

But I will also talk a little bit today -- and it's also in much more detail in the book -- about how, in fact, the tests themselves are different. And this goes back actually to some of the conversation that was taking place this morning that Marc was talking about in terms of what is a genetic test and the fact that the technological design and the varying importance of the lab and the clinic are different actually, I would argue, in the U.S. and in Britain, as well as the management options that come out of the different ideas of what testing is. So that's sort of one major point that I'd like to hit today.

The second is obviously that patents and patent policies play an important role in the story, but I'd also like to highlight the importance of the opposition mechanism that's come up. Richard was talking about it a little bit, and Judge Newman also talked about the possibility that in the U.S. Patent Reform Act, there will be an inclusion of an opposition type mechanism. She was talking about this as the first window for public participation, and this actually was a very important part of the Myriad case in Europe. So I want to highlight that a little bit as well and, in addition, highlight again what Richard was saying more broadly about the role that health departments can play both in terms of gene patenting and licensing practices in particular countries.

Before I go into the comparison, though, I want to review a little bit the history of the BRCA genes and the BRCA gene patents. This is probably old hat to many of you, but I think it's worth just going over just in case.

So as many of you know, the first breast cancer gene, or BRCA1, was found by Myriad Genetics in September of 1994. Many researchers thought that there was at least one other gene linked to breast and ovarian cancer and continued to look. There continued to be what many referred to as an international race to find the breast cancer genes.

And in December of 1995, a group in London announced that they had found BRCA2. Something that's important to note -- and this comes up later again -- is that Myriad disputed this priority. So Myriad also filed for a patent on BRCA2. There has been work in terms of the scientific community, who believes who actually found the gene, and that work has suggested that in terms of citations, who cites whom, in terms of who had priority. There most people believe that it was the British group that found the gene. But this goes back to the issue of when you have many groups involved in this kind of thing, you're going to get this kind of priority dispute.

As, of course, one would imagine both Myriad and the U.K. group applied for multiple patents both in the U.S. at the U.S. Patent and Trademark Office and also at the European Patent Office, or EPO. The U.K. group, which was a group that was funded by the Cancer Research Campaign filed for what they have referred to as a defensive patent, and they explicitly said, in conversations with me, that when they applied for the patent, they really wanted to make sure that groups like Myriad would not have a monopoly over what happened to the fate of the breast cancer gene patent and also the genetic test.

The British group then licensed that patent to an American company by the name of Oncormed who had also applied for patents on the BRCA1, a different consensus sequence of the BRCA1 gene, but as part of that licensing agreement, they had some very interesting provisions. And this goes back to the control that patentholders can have in terms of the licensing terms and also the licensees can have.

When they licensed that patent to Oncormed, the conditions included that the British NHS receive free access so that it would not impinge on the development of the NHS' testing systems. They also required that the patent be sublicensed, again to avoid a monopoly, and they also had a list of requirements for how individuals should be counseled. So they said you have to make sure that everyone who gets this test has to go through these particular counseling requirements. So they got really detailed into the nitty-gritty, and I haven't really seen that kind of example anywhere else in terms of really trying to influence how this genetic testing system was built both in the U.S. and, of course, in Britain where they were based.

Now, in terms of the U.S., of course, the Myriad story is a fairly familiar story probably to many of you who are involved and interested in genetic testing and patenting, but often some of the early history of the development of BRCA testing in the U.S. is lost and I think it's worth resurrecting, particularly when it comes to the gene patent story.

There are a number of providers that initially emerged. At least four were sort of major providers that were offering tests looking at the full gene sequences of both the BRCA1 and 2 genes. Some offered just simply mutation testing for the Ashkenazi Jewish panel. There are still some places that do that now, but there were basically four places that did this kind of testing early on. This is really 1996 to about 1997-1998. There were these four major providers.

I've sort of summarized them here just to give you the sense that there were actually quite different approaches to what genetic testing for breast and ovarian cancer meant in each of these groups. There were different approaches to DNA analysis but, perhaps even more importantly, different approaches to counseling in terms of whether or not you had to see a genetic counselor first, whether or not you could simply go through any primary care physician, whether or not you had to be at a certain level of high risk according to your family history. All of these kinds of things were variables in terms of the development of these different systems in the United States.

However, as many of you probably know, Myriad used its legal position, its intellectual property rights, as well as -- it would be incorrect to say it was just the intellectual property rights. It was also the fact that they had a very strong economic position, and they used that to shut down the other testing services.

The Genetics and IVF Institute closed its service fairly early along.

They sued and countersued one another, but Oncormed then folded quickly afterwards.

The University of Pennsylvania stuck it out for a little bit of time, in particular making the argument that what they were doing was in fact research and not health care. This got debated out basically, and Myriad eventually sort of adopted a pretty, broad expansive view of what a clinical service was and narrowed this definition of research. And of course, when Penn shut down their service and Myriad adopted this broad view, it also influenced the way in which we're defining research and health care, certainly when it comes to gene patenting and testing in the U.S.

So the Myriad testing system, again, I think it's worth reviewing. When I talk about the British system, it's an important comparative point I think. One of the things that's interesting about the Myriad system -- and I think Richard is going to talk about this as well a little bit -- is really what they're doing is involved in a pretty straightforward commercialization of their patented technologies. So

it's really a laboratory service that they're offering as a state-of-the-art laboratory service. In their promotional materials and educational materials, they talk about the fact that they're offering a state-of-the-art laboratory service and that is their major concern.

So they're less concerned about the clinical dimensions of the test. They're very much focused on what they can offer and what they're involved in, and what they control is the laboratory dimensions of their test. So they don't require specialized genetic counseling. The test can be offered through any physician. It's marketed fairly widely to a number of primary care physicians, for example.

And the management options, when they talk about management options, are often defined by mutation status, and they integrate into their materials the idea -- and this is something I'm not going to talk about too much, but it's important in comparative perspective that tamoxifen adds a potential management option for women who have tested positive, was quickly accepted by Myriad as a potential management option available for women, which of course, sort of going back to the questions about clinical utility, it sort of demonstrates clinical utility when you have a drug available that could potentially ameliorate these risk issues.

Their service is costly. It ranges, however, but the full sequence analysis of both breast cancer genes is approximately $3,000. This varies a little bit. It's reimbursed, but many people still choose to pay out of pocket, worried about discrimination. This may, of course, change with the new legislation.

So when we're talking about what this system looks like, we're talking about a client who sort of can demand access to the genetic testing system. They can go through a variety of physicians. The health care professional facilitates access. They're not sort of a gatekeeper, which you'll see more of in the British system. They're really involved in a facilitating role, again when you think about it in comparative perspective.

So now I want to turn to the British system, and then I'll talk a little bit more about the European situation and spend a little bit more time on that.

Just to give you a sense of the context -- obviously, the American context is probably more familiar to all of you. So it's worth reviewing where genetics sits in Britain. In particular, the genetics care and genetics testing has evolved through the National Health Service in Britain. In fact, while there is private insurance available in Britain, there are no private genetics clinics yet. So really all genetic testing is being offered through the National Health Service.

And from early on -- again, in the U.S. early on as well -- genetic testing was offered as a combined sort of laboratory and clinical service often in hospitals. Now that's started to split apart with private companies offering testing that's laboratory testing. So it splits it a little bit, whereas in the NHS, these two things, the clinical dimensions and the laboratory dimensions of testing, have really remained coupled. And the NHS has de facto control over the activities of both the clinic and the laboratory because, of course, they're funding these services.

Basically the way that it works is that there are a number of NHS regions. They're cut up across the country, and each region has a genetics clinic. These regions have considerable control over what services they provide, although most of them do provide services in particular for BRCA testing. And they get money from the national administration and they often have a lot of agency to disburse that money, although this is sort of a tension. The extent to which the national NHS administration and the regional administrations control health policy and access often differs according to the service, and it certainly became a tension in the BRCA case and I'll come back to that in a second.

I also want to add back in the sort of patent dimension of this and sort of remind you of that strain of the story, of course, since that's the focus of the orientation of my talk today. And that is that on the books there are a lot of similarities between U.K. patent policy and European patent policy and

American patent policy when it comes to these kinds of issues, as Richard was talking about before. There are some differences in terms of first-to-file/first-to-invent issues, but in terms of the books, there aren't that many differences.

However, there is an important caveat to this which shapes the way that BRCA testing was built in the U.K. and also how people in the U.K. and people in Europe responded to the Myriad patents, and that is the EU Biotech Patent Directive which, as Richard referred to, was introduced initially in 1988, but the real fever and the public controversy and discussion was in the mid to late 1990s which is, of course, exactly the same time that the Myriad patents started to become an issue, that BRCA testing was being built. So there was considerable public discussion. So these two things fed upon one another.

So the Myriad case became a major issue in the discussions around the EU Biotech Patent Directive and the general controversies around patenting biotechnology fit then also into even national debates within the U.K. over how to deal with BRCA testing and patents and gene patents and, as I'll demonstrate later, Myriad's patents, which they had to deal with eventually.

Of course, in the early days when the British were trying to develop their BRCA testing service, the patentholders weren't involved. So Myriad was not in Britain. The U.K. Cancer Research Campaign group, as I said, had wanted to stay out of it, and to the extent that they had licensed their patent to Oncormed, they had agreed with Oncormed that Oncormed would stay out of it. So the patentholders were not at all involved in the way that testing was built in Britain.

The testing first emerged in these regional genetics clinics. So different clinics had been involved in the research in varying ways. The ways in which they had been involved and been doing testing sort of then led naturally to the ways in which they offered testing initially to patients in their region.

But fairly quickly there was an attempt to create a national system. Worried that because BRCA testing was the first major genetic test for a common disease, that it would probably end up being a model or a test case, if you will, for other genetic tests that were going to be coming down the pike, there was a lot of worry and concern about making sure that they got this right.

So they wanted to develop -- a group of health care professionals, patient advocates, and scientists, as well as government officials got together and developed a national system, a national risk assessment and triage system, to dictate how genetic testing for breast cancer would be offered throughout the country. Basically what they decided to do was to create a risk stratification based on family history information.

So individuals do see their primary or secondary care physicians. A family history is taken, and then based on that family history information, they're classified into three categories: low, moderate, and high risk. The low risk individuals are deemed not to be likely to have a gene mutation, so they're reassured and turned away. Individuals at moderate and high risk are offered access to the tertiary care center. That's the regional genetics clinic. So they can have access to genetics counseling. But only individuals deemed to be high risk are offered access to testing.

However, those individuals who are deemed to be moderate risk are thought to be at increased risk of breast cancer. They're just not sure that testing is actually going to be useful for them. So they say, okay, you can have access to increased surveillance, in particular, a yearly mammographic screening. So those classified at moderate risk don't have access to DNA testing, but they do have access to increased management options, that is, increased surveillance.

DR. EVANS: Did they put a numerical figure on their risk assessments?

DR. PARTHASARATHY: So they don't put a numerical figure in terms of using the Gail model or something like that. What they do is they classified it according to the number of family members that you have and their ages and their types of cancers.

But interestingly, the initial sort of draft of this system, which was the public health genetics unit that was based in Cambridge -- they had a pretty severe threshold. It was four or more family members over age 50 for breast cancer in particular. Since then, that has been relaxed. The National Institutes of Clinical Excellence have relaxed that to three. And furthermore, one of the reasons that they've been able to get national uptake is to basically say, listen, this is a little bit flexible. In order to buy into the system, you don't have to necessarily buy into the exact criteria. So that's the basics.

So the other important thing to keep in mind in this system is that they will only test someone who has been affected by breast or ovarian cancer first. So they don't want to just do a full sequence analysis. They will only test your family if they can test someone who has been affected first so that they can link the mutation to disease incidence in the family and track it that way.

And they want to do that in order to enhance the clinical utility of the test and also to deal with some of the issues that come up often with the Myriad test, that is, the variance of uncertain significance that they're not entirely sure what the mutation means. That's one way that they try to deal with that.

But one of the things that I would argue is that this is also about the fact for them the DNA testing itself is actually not the focus of this system. The focus of the system is identifying and managing people who are at increased risk of breast cancer, which is a different kind of focus and leads to different kinds of decisions about how they'll put the technology together.

So, obviously, the focus here is on standardizing clinical care and all of this is paid through the National Health Service. So, obviously, that's a significant difference from the American system.

So then we think about this system in terms of the implications for users. The first thing I think that you see is that there is, as I said, a different kind of focus. This is about identifying and managing all of those individuals who are at risk according to family history. They want to treat those who are moderate and high risk whether or not they have a BRCA mutation. So it's sort of this kind of broad public health approach.

The testing is integrated into broader risk assessment services. It's part of this triage system where they have primary, secondary, and tertiary levels of care.

The methods of DNA analysis often vary between regions. One of the interesting things that I found in my study is that in the U.S. -- in Myriad's system, in particular -- there's a real focus on the state-of-the-art laboratory technology. Right? In Britain, what's interesting is that in this national risk assessment and triage system, the real focus was on standardizing the activities of the clinic. Much less attention was paid to standardizing the activities of the laboratory. And these are all high sensitivity methods. Whichever methods you use, the real issue is about standardizing clinical care. So the DNA analysis then I think within that kind of approach becomes an additional tool rather than the focus of the system, which I've already said.

One other thing that I want to mention. I mentioned briefly the tamoxifen approach, and I think that this is an interesting comparative point that, again, I'm not going to go into in too much detail unless you want me to. Tamoxifen is not approved in the U.K. or in the rest of Europe for that matter for treating women who have BRCA mutations. Basically the argument is that it's unproven, that it's deemed to be of increased risk and provides equivocal benefit. But there, of course, I would argue that what happens is that there there's a focus on the fact that these national health care services have to deal with providing tamoxifen over the long term. The long-term effects of tamoxifen -- those are things that they have to worry about too in making decisions about whether or not it's useful for dealing with BRCA risk.

So I think what you see here, in terms of the pure comparison between the U.S. and

Britain, is two very different systems, both in terms of the design of the two systems but also in terms of the implications for the users of these systems.

So in Britain, of course, unlike the U.S., you have a system where the client is really what we would consider a traditional patient. The doctors and the National Health Service make decisions about what kinds of services the patient has access to. They have limited ability to demand access to services, although I should also say that if somebody wants, they can pay and get access to Myriad's service in the U.S. or there are now satellite laboratories at least in Germany and I think a couple of other places are developing them as well. The health care professional seems to take on, again, a more traditional role.

But the other part that's important to keep in mind is that here too the health care consumer is not really a consumer. It's a citizen who has certain rights as being a citizen of Britain and access to the National Health Service, free access to genetic testing, provided that they qualify for it, and certainly free access to care in general.

This, however, isn't the end of the story, although I suppose there's a lot that happened in between, although this stark contrast is sort of where we end up in 2007. There's an important piece of the story that I think is very relevant to the work of this task force that happens in between, and that is that Myriad in the late 1990s and early 2000s, anticipating that their European Patent Office patents would be issued, started out in Britain and wanted to enforce the patent rights. In particular, they wanted to shut down British services or ask the National Health Service to pay royalties to the company, again anticipating their EPO patents.

However, a vigorous opposition erupted among a variety of groups, so among patient advocates, among scientists, health care professionals. And they questioned a wide variety of things. They questioned all of the differences, the accuracy of the test, their focus on clinical care, the doctor/patient relationship that was envisioned by Myriad's test, but they also questioned the legitimacy of Myriad's patent rights. And as I said, some of this opposition had already been mobilized in response to the EU directive, and this is where a lot was feeding off of one another. The opposition sort of came together. So the British Society for Human Genetics, for example, would write a press release for the directive, but also be writing in opposition to Myriad.

What I argue in the book is that there's a real clash here of different cultures of science, of health care, and of commerce that were all bound up in this Myriad opposition. And this went on for a little while, and then there was sort of a temporary resolution.

I should say that the National Health Service in Britain played a very important role in pushing back against Myriad and saying, listen, we can litigate this if you want, but we're not going to shut down the services that we have. This was, as I said, buoyed by the scientific and health care and patient communities in Britain.

They came to a resolution. Myriad initially opened a U.K. satellite laboratory by the name of Rosgen, and this satellite laboratory would offer access to Myriad's services, but still provide the NHS with free access. So it wouldn't actually affect the NHS service at all, but it would just be an add-on for people who were interested. But one of the things that was very interesting was that in the course of this conversation, Rosgen itself agreed that they would only allow access to their test if people got counseling, specialized genetic counseling, first. So here you saw even a departure from the approach that Myriad, in particular, had taken in the United States.

Now, this didn't last for very long. Rosgen eventually liquidated for reasons unrelated to the Myriad deal, but it's an interesting sort of moment in the story because it shows that there was, again, some opportunity to come to a middle ground, particularly when it came to the licensing of the BRCA patents.

Now, as this was going on, a number of scientists, health care professionals, governments, patients around Europe were watching what was going on in the U.K. but also getting involved in an opposition of their own, and they took advantage of the opposition mechanism at the European Patent Office. This was a pan-European coalition of groups, 28 opponents in all. There were 11 human genetics societies from around Europe. The Institute Curie, which is a scientific organization in Paris, took the lead, but there were a number of groups. There were four clinical genetics centers involved, three government health ministries, the European Parliament, three patient groups, one Swiss political party, and also Greenpeace. So it was a real wide variety of groups who opposed Myriad's patent at the European Patent Office.

And before I get into that in a little bit more detail, I just want to sort of explain what this opposition mechanism is because it was also mentioned this morning, and it is in the U.S. Patent Reform Act. So I think it's worth talking about a little bit, in particular how it works in Europe.

Basically the opposition mechanism is an opportunity within nine months of a patent's issue for any third party to challenge a patent. That is something that's different from the reexamination. In the American reexamination, as it currently stands, the people who can actually challenge is a very limited list, whereas here in this case, anyone can challenge a patent. The grounds are on the grounds of patentability. There's also a clause in the European Patent Convention that says that inventions that are contrary to public order or morality should not be patentable, and while this has strictly only been invoked in a couple of cases and actually been used in the OncoMouse and stem cell cases, I would argue that this sort of shapes the approach more generally in terms of whether and how third parties feel like they can get involved. This, coupled with the controversy over the EU Biotech Patent Directive, means that there's a lot of public scrutiny, and increasingly this opposition mechanism has been used by groups to shape and influence the patent process. And the Myriad case is one of them.

But in the work I've been now, I've been looking at this in a variety of different cases, and what's interesting is that while a lot of groups don't necessarily go in and use that public order or morality clause, they're often arguing about novelty or inventive step or industrial applicability, for example. In their public statements, they're almost always about public order or morality. So that's clearly what's guiding these groups, but it becomes a very technical argumentation in the opposition proceeding itself.

The opposition proceeding is an important part of the patent process in Europe because not only -- many people who are involved who are sort of dealing with this new crop of opposition from governments and civil society groups and health care professionals and scientists who may not be the traditional competitors who are used to litigating patents, what it does do is it often narrows overly broad patents because that's one of the issues that a lot of these groups are dealing with. And, of course, that's one of the issues that has come up repeatedly in terms of the patent situation in the U.S. So when there's increased scrutiny and increased public accountability, regardless of the reason, often these patents get narrowed, and that certainly happened in the Myriad case.

The Myriad opponents, as I said, in their public statements were talking about the European approach to public health and the questions about public order and morality, but when it came down to the opposition hearing room, there were very technical arguments. And they ended up being pretty successful. They were able to get a couple of the patents revoked entirely and one narrowed significantly so that now Myriad holds a patent on one BRCA2 mutation. So it's unclear how it will influence the public health services since it's only a patent on one BRCA2 mutation.

But this decision is currently under appeal. So it's not clear what will happen, but certainly in the interim these public groups have been successful in being able to narrow these patents.

So I think the opposition mechanism can provide then a couple of things that are

relevant to, I think, the charge of this committee. The first is that, obviously, it's explicit public oversight, and it allows for accountability and scrutiny. It can also allow for the narrowing of broad patents.

In fact, in Europe now there are these groups who literally sit in Munich where the EPO is based and review patents, and that's part of what they do on a daily basis, is they decide which patents they're going to oppose. I should say these are all groups that are focused on biotech patents in particular. Really these are the only kinds of patents that have been opposed by civil society groups at the EPO so far, which is also I think an interesting part of this saga as well.

So then just in conclusion, to go back over the things that I have discussed today, there are, obviously, a number of differences between the U.S. and the U.K. in particular, but also the U.S. and Europe when we think about new health care technologies. There are, obviously, health care systems, different traditions of patient advocacy. But one of those important things is different approaches to patents and patent policy both in terms of the cultural approaches -- so whether it's the legacy of the Bayh-Dole Act in the U.S. or a general sort of discomfort with gene patenting among the university science community in the U.K. and in Europe, those kinds of things end up having significant implications both for the way that these new technologies are being built -- obviously, my case focuses on BRCA testing, but I argue that it's broader than that -- but there's also these controversies that are going on in Europe generally around biotechnology. I would say that it's become a bigger topic of debate in Europe. This is in the context of debates over genetically modified organisms that are much greater in Europe than in the United States.

But the patenting debate has occupied a large space in these discussions throughout Europe and continues to do so. The European Patent Directive, although it was accepted in 1998, took a number of years for all of the European countries to get on board with it because there was considerable hesitancy on the part of governments, and there continues to be, as I said, now at the civil society level. Now they're sort of going through opposition patent by patent.

One of the other things that's important is that health departments are taking an active role, whether it's the U.K. NHS stepping into the Myriad controversy and drawing a line or the other health departments that were opponents to Myriad's patents at the European Patent Office. They have played an important role in shaping the way that these patents are being addressed in Europe as well.

While I would say that in comparative perspective there's more public controversy and over a longer period of time in Europe than there has been in the United States, I would argue that over the last few months, I've been surprised to see the number of editorials in the New York Times, for example, that addressed these kinds of questions. Michael Crichton's new book talks about this kind of stuff. So it seems like this is becoming an issue of public controversy, perhaps raising again -- this seems to ebb and flow here. Whether or not that may influence, for example, the way the opposition mechanism might get used if the patent offices performed in that way is worth considering as well.

So I will just leave it there, and if you have any questions --

DR. EVANS: Great, and let's hold off on specific questions until after Richard's second presentation.

Richard, are you there?

DR. GOLD: Can you hear me?

DR. EVANS: Yes, great.

DR. GOLD: Great.

DR. EVANS: A disembodied voice.

We have your slides up, Richard, on BRCA testing in Canada, or we're going to momentarily. You can go ahead and start.

+ DR. GOLD: Well, thank you and thanks to Shobita. I haven't met you before, but I

would like to some day since we're working on similar things.

I think my talk is complementary to her talk in a couple of respects. Not only are we dealing with the same subject and taking an international view, but we use different methodologies to do our studies and so there are different things that each one reveals. I think the true story -- in any historical story, you never really get at the truth. So by using different ways to interrogate what happened, we get a fuller picture. Then it's up to, I think, the committee and to other observers to decide what really happened or at least, maybe more importantly, what can be learned.

Let me, just before I get into the overview, just say the way we went about studying this. We started this a few years ago using the public literature. I should say at the start that I've been involved personally with some aspects of this; that is, I was an advisor to the Ontario government who was one of the main actors in Canada. And I also was an expert for the person who did the initial drafting of the OECD guidelines on the legislative genetic *. Obviously, it was the expert committee as a whole that did the actual drafting but I had the pen initially and then handed it over to Christina to take it through the internal process. So I've been involved. That's one aspect.

But what I noticed in going through this is we don't have a full picture. The literature is missing a few important voices, and that includes the voices of the policymakers but also Myriad. And to a large extent, as I'll get into, that's been the fault of Myriad. But we decided to try to resolve that and what we did is we brought together physically some of the main actors, especially in Canada but not exclusively. We brought, other than the Canadians involved, the different governments and so on, someone from the research department in France who was giving advice to the Institute Curie, as well as Bob Cook-Deegan's group down in Durham at Duke. We brought them together to try and get a discussion going about how they perceived what happened.

So what I'm going to take you through is what we heard from them. It's going to be, obviously, up to each and every person to decide whether what we were told is what really happened or it was justified after, et cetera. We had a very frank discussion, so I think people believed what they were saying, but obviously, in any methodology you have to be aware of the risks and one of the risks is that what people reported isn't exactly what happened.

So let me go through and I'll talk about the time line. Since Shobita did it to a certain extent, I'll try to do that quickly, but I'm going to highlight a few different elements and I'll especially concentrate on what happened in Canada.

I want to talk about the business model. This tended to be a very major issue in what happened. And then what were the problems? Why did this gene patent and the way it was being used become a lightning rod? That was really the question that we were trying to answer rather than what should have been the solution.

And it comes down to really three things that we identified: a lack of communication not only by Myriad, although Myriad was very poor on communication, but also by the governments involved, and internal discussions. Lack of trust was a very major issue here on both sides. And institutional failure more, I would argue, on the governmental side than anywhere else. And then I want to end with what I think are some of the implications and conclusions.

So once again, Shobita took us through some this. There was a consortium in '89 that was founded. In 1990, Marie Claire King localized the gene. Importantly, 1991 is when Myriad Genetics was spun off from the University of Utah by Marc Skolnick to get more flexibility. He got financing from Eli Lilly in '93 and there was an initial public offering in '94, which corresponded roughly to when Myriad applied for the first patent on BRCA1. There were other patents subsequently filed, as Shobita said. The Cancer Research Campaign filed a patent then on BRCA2 in 1995, followed by one by Myriad in '96. And then Myriad starts to go into business in the U.S. in 1996, and I think Shobita took us through

a little bit of that history. And they introduced a large scale rearrangements panel in 2002, and that's been one of the controversies. I'm not going to get into it terribly, but I'm happy to talk about it. But other technologies were better at doing large-scale rearrangements, and it wasn't until 2002 that Myriad offered a test capable of doing that.

So let me take you to Canada which is really the focus of what I want to do. So in about 2000 -- I don't have the exact date in front of me here -- Myriad entered into an agreement with a private company called MDS Laboratories. MDS had been in the business mostly of providing diagnostic laboratory services to the various governments. So their largest client was the Ontario government and after that, it would be the governments in various other provinces. They had started to get more into biotechnology at this time. They were trying to find new technologies to bring to market.

I guess I should give you a little bit of the Canadian history. What they saw was severe government cutbacks during the 1990s so that we could balance our budget, and a lot of that was felt in provincial government health budgets. That is, the federal government had been funding provincial governments to provide health care and a large portion of the cutbacks occurred in health care, given that it's such a significant part of the Canadian budget.

So the provincial governments had to start cutting back, and what they did is they started cutting back on services. So they either delisted some, but it was easier to just simply not add new services to the menu of services covered by public health care insurance. They more or less allowed private sector providers to provide some services that fell outside what they covered, not explicitly stated or agreed upon, but implicitly that's how MDS at least saw it. So they saw their niche at finding high quality new technologies that were not broadly available through the public system and offering them. That's where they thought they would go into it.

So they came across Myriad. And I'm not entirely sure whether it was MDS that met Myriad or vice versa. Anyway, MDS signed the agreement in around 2000.

So they started to talk with governments about providing these services, and they went to the government procurement departments within their health ministries. So in Ontario, they would have gone to that department to talk about licensing this. That unit said, well, we're used to buying kits, but this is not a kit. This is a service, and so this is unusual. And they kicked it over basically to their policy unit.

Their policy unit had lots of other things on their plates, but they had been thinking about genetic technology for some time and they were wondering, well, what are the impacts of these new genetic technologies as they come on line. This was the era where we saw all kinds of new diagnostic testing services. Eventually gene therapy, pharmacogenetics were going to come on line very soon, and so they saw this as a wave of new technologies, and they didn't really have a policy framework to deal with it. So the policy unit didn't know what the answer was.

So basically it had been kicked over to them, but they didn't have an answer. So just communication stopped with Myriad, Myriad waiting for a response, and the government not responding. *[3b flip] long time. We're getting no answer. We don't know what's happening.

So in late May/early June 2001, they had their lawyers issue cease and desist letters to four provinces, including Ontario, basically telling them we have a patent on this. You're funding hospitals that are providing laboratory services that violate our patent. Please stop or you must stop.

In August 2001, the government of Ontario, in a letter from the then-Minister of Health for Ontario, now the federal Minister of Health, Tony Clement, sent in a letter saying basically, well, our opinion is we are infringing on no valid patents. It was very vaguely stated and could either be argued that they were saying the patent is invalid or because they're only funding hospitals, they're not infringing. So that was left vague.

In response, the presidents of Myriad Laboratories and of MDS, this particular unit of MDS, asked for a meeting with the Minister of Health, and that was accorded in November 2001.

At that meeting, they presented the minister with a stack of letters, including one from your ambassador and from Senator Hatch from Utah basically saying Canada is in violation of its trade agreements, and there might be a reference to the U.S. Trade Representative because Ontario was failing to pay Myriad.

Well, this is not something that gets into the press -- the whole issue had gotten to the press around the summer of 2001. The Minister of Health said we have to have it independent and we don't necessarily think this is valid. So once all this came to the fore, that was seen as exceedingly hostile.

There were also about 100 letters from different scientists that were presented to the minister at that time.

So this was seen as a very hostile action, to threaten Canada with trade sanctions, and the government at that point said, from what we can tell -- this is me guessing, but I don't think the guess is wild -- we really can't be seen to be giving into this. The public health care system has been under some stress because of lack of funding. The principle of a public health care system, organized and controlled by the public, is paramount. If we're giving in to a U.S. private company, this would look terribly bad. So Myriad made some strategic mistakes in raising the stakes and threatening trade sanctions in my opinion.

The minister then held a policy forum in 2001 at which various people from public life, academia, from government, industry were present, and that led to the creation of a report that Ontario prepared and released at the end of January 2002. It dealt mostly with technology assessment. This was a global view of genetics and the challenges it posed. So the biggest one was coordination of technology assessment across Canada so it's not duplicated, coordination of the provision of services so that not each province duplicates everything. Just an aside, health care is provided on a province-by-province basis. So to the extent that there's coordination, they have to work together. So most of the report was concentrating on coordination. But one out of seven chapters dealt with IP and basically said, look, we need policy levers to be able to negotiate and resist what was viewed as a hostile maneuvering by Myriad.

The way that the Ontario government and others viewed it is Myriad had a one-size-fits-all type of approach to licensing. They were unwilling to budge. It wasn't well integrated into the provincial health care systems. It didn't take into account genetic counseling. It didn't allow for an implementation in phases, that is, Ontario provided another test called protein truncation as one of the things that they took into account with genetic counseling to make a decision about whether full testing should be done on the gene. But because it involved the gene, Myriad didn't like it.

So there was this tension where the government said, well, we can't administer the system the way we want. So we need policy levers both on the research side -- so it called for a research exemption, but it also called for a particular compulsory license that would be very narrowly tailored to the particular circumstances of genetic testing and so on. So it wouldn't scare off all of industry, it would be very targeted. There were some other things too like coordination and so on, tougher criteria applied, better management at the Patent Office, and so on.

All provincial governments agreed and supported the Ontario report, including Quebec, and I say including Quebec because Quebec never agrees to anything. So the fact that Quebec agreed with the rest of the provinces on a health care matter is fairly significant.

And in response to all of this BIO intervened and threatened to pull out BIO 2002 which was being held in Toronto that summer. They eventually backed down. But you can see that there

was pressure at the political level, and Myriad was politically connected, especially to Senator Hatch, but they also had Paul Cellucci, the ambassador at the time on board. They had BIO. So they thought they had -- presumably, they were getting the big guns out to say you got to do something here, and they expected Ontario to comply and say, okay, well, we made a mistake.

Well, Ontario then started a policy process between the provinces, and Health Canada participated. And Health Canada is responsible for the federal part of the health care system. But then in terms of the more general needs of technology assessment and who should be doing what -- but they also engaged in direct conversation with the unit in Industry Canada that was responsible for the Patent Act because they saw that what they needed was a policy lever. They didn't necessarily want to invoke a compulsory license, but they wanted to have it in their pocket so it was a real threat.

So Myriad knew, as everybody knew, that the existing compulsory license in Canada is, as I said before, a sledge hammer. It was not a realistic proposition that anybody would invoke it. So it wasn't a real threat.

What the provinces wanted was a real threat, not so that they would actually issue a compulsory license, which would be the improper way to think about compulsory licenses, but industry would know if they went too far, it could be invoked. So it would engage industry in negotiation. That was the goal. So there was a discussion about that and so on, which did not lead anywhere other than I think frustration on both sides.

By the spring of 2003, though, the emphasis of the policy unit on gene patents waned for the simple reason that SARS hit Toronto. So everybody in the policy unit and elsewhere suddenly switched gears and was looking at SARS in response to it. You had a real health crisis, as opposed to a potential one.

And by October 2003, the government of Ontario changed and the new government didn't have this as a particular priority. Discussions still continued, especially at the federal level between Health Canada, which took the side of the provinces, and the patent policy director within Industry Canada, which didn't want to make a change, not leading anywhere.

Eventually in the fall of 2004, a reference was made to the Canadian Biotech Advisory Committee. Now that's a very Canadian solution to things. When you can't agree between two government units, you send it out to a royal commission or some commission. This committee is of particular interest because it issues various reports on biotechnology. It reports to eight ministers, has lots of academics and industry people involved. It has issued report that are not bad but have never been implemented. And I don't even know if most of them, if any of them, have been responded to officially by the government other than to thank them. So sending this out to CBAC to my mind is a little bit of an act of desperation. I'm sure the people involved maybe agreed with that, maybe didn't. You'd have to ask them.

But CBAC did report in 2006 saying gene patents are fine but there need to be policy levers within the Patent Act and we ought to think about that.

So that's the time line in Canada.

Let me now play it out from how was this seen by the various actors. So I have to start with the U.S. because Myriad is a U.S. company, and one of their biggest faults was thinking that the rest of the world looked like the United States. And I won't make any editorial comment about how common or uncommon this may be. But they basically thought that they were entering into, in coming to Canada and I would argue Europe and elsewhere, an environment that was somewhat similar to the United States. It was clear that they didn't have much respect for public health care systems. Mark Skolnick was on record as saying he thinks public health care systems are bad. So they didn't really seem to have taken it into account.

But we have to start with the U.S. model. You have to remember Myriad was and still is operating in the red. They lose money. This particular unit has about three people doing sales for the entire world, so very short-staffed, mostly people with technical background, only one commercial person really. So the business model was to split the market between the proband testing, which was fairly expensive, about $3,000, and follow-on testing. The idea that Myriad had was for every test that we do, the full proband test, if we identify a mutation, we expect that there will be 10 family members that are likely to be tested for that mutation. And the idea was we'll license out the ability to do that testing. We'll keep the proband.

Now, given that the cost of the single-point mutation testing is about a tenth, this seemed to be roughly a split of income. Myriad had built a big lab in Salt Lake and so wanted enough coming through its facility to be able to recoup its investment. So it thought that this business plan worked.

In fact, it turned out to be about 1 to 2 for a variety of reasons that we need not get into. Most family members did not get the subsequent mutation testing. So instead of a 1 to 10 ratio, it was a 1 to 2.

In terms of what Myriad tells us -- and the story should be thought of in parallel to this because different people have different opinions -- Myriad said they had an incredibly broad view of what research was, and in fact, their view was you don't need to come to us for a license to do research. And research to them included the provision of genetic tests if it was done by the same people who were doing the research. What they didn't want, they said, is to outsource the proband testing or any of the testing. If you did it yourself, from their point of view, it was covered by the research exemption.

And the whole controversy at Pennsylvania is that the one unit that was being accused by Myriad of infringement was outsourcing it both for academics within the other departments in the institution and for others. So the institution's view was that this fell within the research exemption, but Myriad saw them as basically an outsourcer, just providing testing services and were no different than anywhere else. So I'll leave it to you to decide which one was right. But Myriad's view at least was they're doing commercial activity. They're not doing research activity. So they didn't care if data was provided to patients and so on.

In fact, if you look at what Myriad did, whenever they did come up with mutation data, they quickly made it available within the Breast Cancer Information Core Database even before sometimes they were assured they would get a patent. In fact, they contributed more mutations than anyone else. So they wanted this information public. It was in their interest, they said, for other people to contribute because it just made the test better and so on. So they had no problem with people contributing, and they had no intention, they said, of actually going after anybody who did so. What they were concerned about were bigger operations that were basically outsourcing. So, again, difference of opinion and it's up to anybody to decide whether you believe what Myriad is saying or not, but they seem to be earnest at least in what they were saying.

DR. TUCKSON: Richard, you're making your points very well. This is Reed. We may need you to truncate a couple of the last slides just a bit, but your points are getting through quite well. So if you could cut a few a little bit down, we'd appreciate it.

DR. GOLD: Okay. Well, I can go fairly quickly through the next slide.

So the international model was basically to replicate what happened in the United States, find a local licensee, and get them to do it. So they did that. They tried to do that around the world. They have gone to France and other places. Even though their model was exactly what it was in the United States, they said they were flexible towards other models. In fact, in Japan, they allowed the Japanese company to do all the testing. In France, where it's illegal to export, they were prepared to allow

it to happen there. Australia, they cross-licensed. So there was some indication that Myriad was flexible in its business plan.

Since Myriad seemed, at least from what they're saying, to be reasonable in some ways, why did this turn out the way it did? Well, the research community never heard from Myriad. Myriad never made it public that they wouldn't prosecute. So because of the previous patent battles that Shobita took us through, there's a lot of ill will. So the research community didn't believe Myriad, and so they thought by contributing to the public database, they'd be exposing themselves to patent infringement.

The public health authorities didn't like this business model because, as I said in my previous presentation, there was no ability to manage the health care system. And generally, Myriad thought its business plan was like selling chairs into Canada, and obviously, there are reasons to think that that's not the case.

So what was the health care administrator's view, going ahead a couple of slides? As I said, they were concerned about their ability to determine who should get testing when, how to integrate genetic counseling, how broad a population. And they wanted simply time. Now, they never told Myriad they wanted time, which is another problem.

So what were the failures? How did this come about?

Well, Myriad certainly never informed the research community of what they wanted.

They misinterpreted what the government was saying. The government wasn't saying we're not going to license it. It's that we need to think about it. They just didn't say so explicitly. But Myriad said, well, six months have gone by. Let's escalate it. Escalating was the exact wrong thing to do. What it did is it left the government with the impression, okay, these guys are intransigent and you can't negotiate with them. So the government felt this happened too quickly.

Also, a subtlety in the European opposition, the person who was helping on the government level said that -- the French government purposely didn't launch the opposition because if the French government launches the opposition, it means they're against gene patents in general and the French government was not. What they were signaling is that there may be a problem with this particular patent, and in general practice in Europe, launching an opposition procedure, despite all the rhetoric that was happening in the press, really is an indication, please negotiate with us because we're going to challenge your license. Let's find a solution. Myriad didn't know that. They weren't well advised or they didn't find out, and so they missed this opportunity that France was offering them. And I'm not saying all the intervenors believed that, but at least some of the main ones in France did.

Underlying all this was a lack of trust that came from the scientific community where there was a lot of lack of trust. Ontario had talked to policymakers elsewhere and all they heard was Myriad always came out with the same offer. They didn't hear options about flexibility. And then when Myriad escalated, they just said, well, that proves the point. So lack of trust there.

There was also some lack of trust between the health department and the industry department in Canada that didn't help.

In terms of institutional difficulties, there was a lack of understanding by Myriad that policymakers and people in industry work at different time speeds, and so they just didn't give enough.

Industry groups quickly shunned Myriad and said that they're the black sheep and you shouldn't blame the rest of us, instead of trying to mediate.

There was no government department that really had both the jurisdiction and the willingness to say let's mediate this. So each one sort of stuck to their turf, were unwilling to move and that didn't help.

In terms of the implications, let me move to that. Obviously, better communications would have solved a big part of this problem. Would it have been avoided? I don't know, but I think it

could have been. And what was really missing to get trust was the fact there was no honest broker. There was nobody in Industry Canada who were in charge of the Patent Act or in Health Canada who had jurisdiction to be able to broker this. So that was a problem.

I think also you cannot sell genetic testing services the way you sell chairs. It just doesn't work, especially in a public health care system. And just recently a few weeks ago at an OECD meeting in the Netherlands, the chief medical officer of Pfizer said, look, our business model doesn't work. We have to really rethink it. So I don't think it's just me saying it. I think industry is starting to realize they need to change.

There need to be tools that allow technology assessment and a roll-out of technology in a way that makes sense to the health care system.

So I'll stop there.

DR. EVANS: Great. Richard, thank you very much and thanks for also hurrying along. The technical difficulties put us behind, but I think you really got things across very well and we really appreciate it.

+ We have a very short time for a few questions to both of our presenters, and I'll just go ahead and open the floor.

DR. TUCKSON: Let me just give everybody a notice in terms of a process check. We are aware that apparently human organisms require food.

(Laughter.)

DR. TUCKSON: This has just been brought to my attention by Muin Khoury from the CDC.

(Laughter.)

DR. TUCKSON: So believe me, we're going to take a break. One of the good things about the penthouse is that the cafeteria is right next door. So what we're going to wind up doing is having a working lunch. You'll get enough time to rush over there, get some food and come back.

So just know that we haven't gone crazy. We haven't forgotten you need to eat. We're going to get that. We want to take a few minutes for questions. We're going to get a couple of the public comments in. You'll get your food and then you'll be able to eat. So just hold on. But you're tough because you're intellectually brilliant.

DR. EVANS: I thought Reed was going to declare us non-human organisms to get around that.

(Laughter.)

DR. EVANS: It looks like Julio has a question.

DR. LICINIO: I had a question for Richard Gold. In one of his first slides, it says that a patented gene gives rights over the entire organism in Canada. I wonder like, let's say, if people have genetic mutations or problems that are diagnosed in vitro, let's say, in the case of in vitro fertilization, and you put a patented gene in a person, what happens?

DR. GOLD: Well, that's never been tested. It's an interesting question. My guess is -- and as I said, there's no official policy -- that you can't get any control over a human being. So even though that would apply to a gene artificially placed into a cell of an animal or plant, I cannot see a court ever allowing that to apply to a whole human being. So I think theoretically yes. That's in accord with patent law, but I think the courts will find constitutional or other reasons to limit that. So I'm not overly worried about it.

DR. EVANS: Other questions. Yes, Gurvaneet?

DR. RANDHAWA: It's a fascinating presentation. I'm on an upward learning curve here.

The one thing that I wasn't clear about is if the research that shows a gene is linked to a disease or leads to an intervention that can improve public health, if that funding comes from the public sector, mostly or all of it, does the public sector have any leverage in terms of either the licensing or the actual patenting and how it's issued?

DR. GOLD: Who was that addressed to? Me or to Shobita?

DR. RANDHAWA: I'm sorry. Both of you.

DR. PARTHASARATHY: Richard, do you want to go ahead and I'll answer after you?

DR. GOLD: No. I just talked a lot. I'll let you do it.

(Laughter.)

DR. PARTHASARATHY: Great. Well, I'll give a partial answer then and he can fill in.

That's actually an interesting point with regard to the Myriad case in particular. First, there is the Bayh-Dole Act which allows if the government funds university research and some patentable invention results from that, the government has chosen not to take an interest in it. So they don't get involved.

However, in the Myriad case, there were actually researchers from the National Institute for Environmental Health Sciences involved in the initial BRCA1 research. And in the early days when Myriad first applied for the BRCA1 patent, the NIH in particular said, listen, you need to put our inventors on the patent or else we're going to file a counter-patent, and then this is going to be very problematic for you. So eventually Myriad did put these two individuals from NIEHS on the patent, but in conversations with them, they actually interestingly haven't really received much in terms of royalties.

But it does raise another question, which is the extent to which now NIEHS would have any kind of standing to influence how the patent was being used, licensed, et cetera. To date, they have not taken advantage of that position, but often I get asked that question. So that's a question for NIH.

Certainly the scientists, in my conversations with them, say, listen, we're done with it, and we're so annoyed by the whole situation we just don't want to have anything to do with it anymore.

But it's a policy question that I haven't yet been able to get an answer to in terms of the Myriad case in particular.

DR. GOLD: I have nothing to add on the U.S. side. In Canada, we don't have the equivalent of Bayh-Dole. Each university comes up with its own set of rules in negotiation with its researchers. Who owns it is either the university or the researcher or some combination. The federal government has really no -- even if they provide research grants, the research grants just say whatever your IP policy is applies. So the federal government has no say, and we don't have any march-in rights as exists in the U.S.

DR. EVANS: It looks like Debra Leonard has a question and then I think we'll have to finish up.

DR. LEONARD: This is addressed to Richard. On your penultimate slide of your first talk, you have a statement that licensing practices are part of the solution, but not the entire solution. So can you expand on where licensing practices would fall short if we took that approach to protecting gene patents for health care use?

DR. GOLD: Sure. Again, this is just my opinion and doesn't necessarily represent the Canadian -- if you took a sample of Canadians.

My view, in talking to especially health care administrators, is yes. Licensing guidelines are wonderful if people actually follow them and everybody acts reasonably and people

communicate well and have good trust. However, that's not always reality. There will be outliers and so on. These policy units don't have that many staff. So what they want is very targeted changes to patent law that would give them leverage in negotiations.

So one example would be a very targeted compulsory license that would say -- it could follow something like the French law. French law provides that a compulsory license is available for either a health care product or diagnostic testing. It has never been, or rarely, invoked, but its threat has been invoked and the French government uses it basically to negotiate saying, if you don't comply, we will issue it. And because it's such a narrow exception, it won't threaten the entire industry. So it's seen as a realistic threat. So things like that.

In terms of the research side, they want to see things like a research exemption. Maybe Myriad was right and they were willing to tolerate a large amount, but researchers don't know that. So even if Myriad is right, researchers are acting as if they don't have the right. A clear research exemption would allow research to proceed and preferably a wide one. There's a whole variety of approaches around the world to research exceptions and there's no indication that there's any particular harm to a broader one. And if it reassures researchers, it may be worth doing simply as a symbol. Most companies will not sue people for infringement, but a researcher may not know that. So this is a good symbolic way to do it.

So it's those type of levers that are being asked for, not a substantial change to patent law, but those levers, plus an opposition procedure.

The provinces would say, look, we don't want to have to go to court and wait for years for an answer. We would like a fairly quick procedure that would allow us to challenge issued patents. Especially in an area like genetics where the standards are changing all the time, we want to be able to get in there and have our say so that we can get rid of bad patents. And generally, in at least the Ontario government's point of view -- and I happen to think that they're right -- the Myriad patent is very weak. It is unlikely to be valid, but that's my opinion. So they want a quick way.

So those are the types of solutions that they're looking for not, I don't think, that dissimilar from what you were discussing.

DR. EVANS: So, Richard, is it fair to say -- I don't want to put words in your mouth -- that you feel that perhaps the most effective policy levers involve narrowly tailored, mandated licensing for certain applications?

DR. GOLD: I would say a combination. The way I see the levers are that they should never have to be invoked, but they have to be a real threat. So they should be narrowly conceived. But they don't work unless you know what the proper licensing practices are. I don't think this is an either/or position. I think your licensing guidelines are more likely to have an effect if the governments that are involved feel that they have this leverage in case things go wrong. Almost no government wants to invoke them. So you play on that by showing them here's a solution that people can live with. Here's a reasonable compromise, and I think it gives greater weight to actually following, in a voluntary way, the licensing guidelines. I'm sure some people in industry would disagree with that, but that's how I view it.

DR. EVANS: Great.

And the very last question because of the fact that he's the chairman and gets to interfere with our lunch is to Reed.

DR. TUCKSON: Well, you know what I'll do? I'm just going to throw this out there. Richard, if you have any answer to this, feel free. If not, we'll just discuss it later with other panelists. Shobita, I don't know. Are you staying or are you leaving?

DR. PARTHASARATHY: I'm staying.

DR. TUCKSON: So maybe I can just sort of tee it up for later. I guess with all this,

what I don't understand -- and maybe you've said it and I just haven't understood it -- is if you are a company that operates internationally, like almost every company, what rules apply? I mean, if you figure it out for Canada or you figure it out for the United States, but you decide that you're trying to market a product in Brazil or you want to market it in France or you want to market wherever, they say this rule applies. But you say, but I'm complying with the law in X. Is there any superseding or does it all work out as to international trade politics between different countries and you just basically get your country of origin to beat the hell out of some other country because you win? I mean, how does it work?

DR. GOLD: Well, I do have some comments. I'm sorry I'm keeping you from your lunch, but if it helps, you're keeping me from dinner too.

(Laughter.)

DR. GOLD: And I'm in Geneva. So there's lots of French food around.

DR. EVANS: Yes, yours is worth waiting for.

DR. GOLD: So I think the quick answer is the traditional method is to see if there's any other product, and yes, we'll call our ambassador and we'll beat people over the head if they don't comply. I think the reality is somewhat different, as my presentation and as Shobita was saying. Everybody is coming to the same basic rules. So I don't think there's a big doubt about gene patents being patentable on basically the same grounds. Yes, there might be one or two outliers.

The big question that I have, especially for U.S. companies, is they seem to lack a willingness, or whatever it is, to actually understand the context into which they're entering. Now, that might be okay for chairs. It's not okay for health care. Health care is viewed very differently even across the border in Canada and elsewhere. All of the places where this policy erupted -- and it was much bigger than the U.S. for Myriad -- are in countries where there are public health care systems. It's not a coincidence. So I think it's incumbent on U.S. companies to actually understand the environment they're entering into and that public health has a meaning. And whether they like it or not, that's the reality. The basic same factors applied in Europe, in Canada, in Australia. They were all concerned about the same thing.

So I think it's up to U.S. companies to learn that when there's a public health administration involved, they care about the way services are rolled out and who gets them when. And whether they like that or not, they have to accept that and their business plan must be modified at least internationally.

DR. PARTHASARATHY: I would just add to that that I think it's an important and interesting question, the extent to which -- especially if European and Canadian countries and Australia, countries that the United States would see as primary markets, developed countries, that have -- certainly when we're talking about genetics, genetic technologies -- often likely to have similar diseases, similar mutations to the U.S. The extent to which those kinds of public health care systems and approaches are going to inadvertently then have to shift U.S. company strategy even domestically because if they're going to take one blanket strategy, the fact that all of these other countries have public health care systems and are pressuring in a very similar way may have to shift the U.S. company strategies when it comes to health care --

DR. TUCKSON: Shobita, if you're going to be around later and another panelist, we can probably get back. I'm not going to ask you to comment on it because we've got to go to the public comments.

But the other way to view it is that I don't want us to be -- even though we are an advisory committee to the Secretary of Health of the United States, we certainly are not so provincial that we believe that all innovation in genetics is going to come from U.S.-based companies.

So the flip side of this I'm equally interested in is what happens to new innovations --

and also given just the multinational nature of companies, you can have a country that's grounded in France who decides to market in the United States. They say we passed all the rules in France. It's all clear in terms of our patent and licenses and stuff. How does that then apply flip side? So anyway, I'll just leave that as a hanging participle.

Amy Miller, are you here?

Oh, Richard, are you there?

DR. GOLD: I'm still here.

DR. TUCKSON: I have no manners. Thank you. You are wonderful. You did a terrific job. Shobita, you did a terrific job. I didn't say it right, but it's the best I could do. You did a great job and we really appreciate it. Thank you. Everybody, a round of applause for the speakers.

(Applause.)

DR. TUCKSON: Take care and have a good dinner.

DR. GOLD: Well, thank you, and have a good lunch.

DR. TUCKSON: Right. Bye now.

So Amy Miller, you are with the Personalized Medicine Coalition you know --

MS. MILLER: Yes.

DR. TUCKSON: -- of the America's Health Information Community.

+ MS. MILLER: No. I'm from the Personalized Medicine Coalition.

DR. TUCKSON: Period.

MS. MILLER: Period. I'm the Public Policy Director there, and I'm starving. So I will keep my comments very brief. I also have submitted comments earlier. So they're available to the committee.

As you know maybe, the Personalized Medicine Coalition represents academic, industrial, patient, provider, and payer groups that seek to advance the understanding and adoption of personalized medicine for the benefit of patients.

And we thank the advisory committee for the opportunity to engage in this process.

My comments focus on the draft report on pharmacogenomics, and we thank the committee for all their hard work in putting together that report. My comments are going to focus on just some issues we'd like to bring some more attention to.

The first is the development of pharmacogenomic products. We feel that business incentives for pharmacogenomic products need to be developed. As the committee, we are developing a list of incentives that we think will help advance pharmacogenomics. We welcome the opportunity to share these ideas with this group or any other public policy group.

We also recognize the importance of public education and the lack of education in the world of genetics right now. The PMC is putting together a privately funded medical education program on pharmacogenomics, and so we thank the committee for pointing out this particular gap.

Public investment in pharmacogenomic development is also important. You're not exactly the right group to say it to, but we urge full funding of the Critical Path Initiative.

As far as reimbursement goes of pharmacogenetic products, obviously, the United States is the largest single payer of health care costs. The PMC has outlined lists of payer principles when it comes to genetic- and molecular-based products. They're more fully outlined in my comments in front of you. But one thing that the report pointed out and I'd like to stress is the prevention category as a Medicare benefit. The PMC thinks this is a fantastic idea and supports the development of new policies that promote prevention as part of health care.

Also, just to remind you of who we are, we do have the power to convene groups who can speak to these issues and others from all the different stakeholders in the field, and we thank you very

much for allowing us to participate in this process.

Have a good afternoon.

DR. TUCKSON: Amy, thank you very much.

Any quick questions to Amy?

DR. FITZGERALD: Just one quick question. Could you forward us that list that you have of incentives?

MS. MILLER: We will forward a list to you very soon.

DR. FITZGERALD: All right. Thank you.

MS. MILLER: You're welcome.

DR. TUCKSON: Ever the insightful question. Thank you so much, Amy. We appreciate your being here.

Christina *Karas. Did I say it right? I finally learned to say Shobita, by the way. I did get that right now.

MR. COLWELL: I am standing in for Christina. I'm Chris Colwell with BIO, the Biotech Industry Organization.

DR. TUCKSON: Chris, how do you spell your name?

MR. COLWELL: C-o-l-w-e-l-l.

DR. TUCKSON: And you are literally standing. So go ahead.

MR. COLWELL: I am literally standing and you're literally hungry and nonviolent still, and I hope to keep it that way, so I'll be brief.

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers. We have a broad membership. It deals with health care, environmental, agricultural, and industrial companies, but within that, we also have a large number of companies that are heavily invested in research and commercialization activities and pharmacogenomics research tools and molecular diagnostics. We are becoming increasingly engaged in the policy discussions around these technologies. I appreciate the opportunity to be here today and look forward to continuing dialogue with you.

Two points that I would make, two quick comments, one with regard to today's conversations and discussions. We again are appreciative of that. It's important to have these informed discussions on intellectual property issues. I'm sure you know intellectual property protection is essential to the success and, in some instances, the survival of biotechnology companies. Having spent hundreds of millions of dollars in many cases and decades to develop a product, it's these patents that can provide the needed insurance or assurance for investors to develop these processes.

Also, a couple of quick points on the draft report, "Realizing the Promise of Pharmacogenomics." Again, very briefly. We've submitted comments on this in more detail.

First, we would recommend a more comprehensive discussion on the economic factors surrounding pharmacogenomics, particularly with some consideration or more robust consideration on appropriate reimbursement policies, which of course would be necessary for the incentives for investment and innovation.

Also, we believe that the report should indicate where enhanced congressional appropriations would be required to implement the recommended initiatives. We would particularly highlight that over the past four years funding for NIH has failed to keep pace with biomedical research inflation, and as a result, NIH has lost significant purchasing power needed to harness emerging scientific opportunities. To restore these resources, BIO and a number of other stakeholders are supporting an increase in NIH funding of up to $30.8 billion for FY 2008 and we suggest that the draft report consider the need also for enhanced public funding opportunities for companies to develop innovative diagnostic

and research tools technologies.

Thank you.

DR. TUCKSON: Terrific. Any questions, please?

DR. FITZGERALD: Same question. I'd be very happy to hear what you think are appropriate reimbursement policies because that's going to be the key thing.

MR. COLWELL: Absolutely. That's a key word, right.

DR. TUCKSON: So you will try to get back?

MR. COLWELL: We'll have a continuing dialogue with you.

DR. TUCKSON: I think that means you're going to get back?

MR. COLWELL: Yes.

DR. TUCKSON: This continuing dialogue business, I don't know. Thank you. I think, obviously, we respect what you all are doing and we really would like to get that kind of information. Thank you very much. Appreciate it. Good job.

You can pass that to Cahterine Wicklund from the National Society of Genetic Counselors.

MS. WICKLUND: Hi. Good afternoon. I'll try too to keep this short. I've got the written testimony in front of you, so if you can read the whole thing, that's fine.

I'm Cathy Wicklund, President of NSGC. And as you're aware, NSGC represents over 2,000 genetic counselors, and we practice in a variety of medical specialties, academia, research, public policy, biotech, and we're the leading voice, authority, and advocate for the profession.

We want to thank you guys for taking into account our prior testimony and comments when you're developing policies and reports.

Today we're going to talk about two issues that impact the access of genetic testing and services. First, oversight of genetic testing and second is coverage and reimbursement of genetic tests and services.

Obviously, access to quality genetic tests and services is extremely important. Genetic counselors are often among the health care providers who explain the benefits and limitations of genetic testing, as well as provide results to patients. So when a genetic test fails or is inaccurate or is misinterpreted, we're often the health care professionals who are responsible for discussing these results. As such, we definitely applaud the committee's efforts to improve regulation that ensures the analytic and clinical validity of genetic tests. And we also support regulatory regimes that will increase quality while fostering innovation, but we don't want to significantly delay breakthroughs to consumers.

We do feel it's important, though, that there is pre- and post-test consumer education and counseling and it be provided by a properly qualified individual. Proper evaluation of the family history, ordering the appropriate and correct test, and the accurate interpretation of the genetic test are critical steps in the process. We don't want to promote that we're the only genetics professionals or that only genetics professionals can provide these services. We believe it's imperative that nongenetic health care professionals have a minimum level of genetics competence if they enter into this arena and encourage that they collaborate with genetic specialists when appropriate. They should also be aware that genetic counselors work in laboratories which provide the genetic tests and are really instrumental in ensuring that the correct test is being ordered.

We also think it's critical to assess and satisfy the consumers' needs for information that empowers them in making a personal decision. We understand that the Secretary is asking for guidelines on what should be discussed when offering a genetic test, and we'd be happy to collaborate with SACGHS to develop these guidelines.

We also applaud the committee for looking at the patent issue and any effects they

have on accessing genetic tests. Obviously, it's unfortunate when individuals need genetic testing, they don't have access to it, or if there's a particular test a limited number of laboratories are performing. And coverage of tests with limited availability may also be an issue.

With the extraordinary impact of genetic information on our health and society, genetic service providers are in the position to impact the ability to deliver personalized medicine. However, without adequate coverage and reimbursement for genetic services, the full integration of these services may be difficult to attain.

In terms of coverage and access of these services, NSGC is pursuing recommendations outlined in your report of February 2006. Addressing barriers to genetic services by improving consumers' access to genetic counselors has been a top priority. As you may know, we've been successful enacting licensure bills in several states. They're listed here, most recently in Tennessee. And genetic counselors in Utah, because of this licensing, has undergone an increase in their numbers as well as coverage of their services. We're also working with policymakers in Congress to add genetic counselors as recognized CMS providers under Medicare, and we believe these are critical steps in improving access to quality genetic services.

So just in summary, we appreciate all the hard work of the committee and we hope that you'll make formal recommendations that will define regulatory regimes that ensure analytic and clinical validity of genetic tests while fostering the innovation of new tests; recognize, through support of licensure and federal legislation, nonphysician providers with expertise in genetics, as demonstrated by certification by a national credentialing organization; and support the funding of further studies to assess the value and effectiveness of genetic counseling services provided by nonphysicians.

I'd like to thank you. Our technology has progressed at an unbelievable pace, but we've definitely fallen behind, and we welcome the opportunity to continue working with you.

DR. TUCKSON: So this is terrific.

So for the committee members, you have on your table somewhere this response from CMS on our coverage and reimbursement policy thing. So recommendation 7 you should look at in the three seconds you get to eat lunch. Marc is going to take us through that. So this is like the 99th time that we've had a respected, reasoned genetic counselor, association president/leader come before us and make these points. So you've kind of got to draft of where CMS is on this, and I'll just tell you, as you fast forward reading it, it ain't the answer yet. So we're going to have to figure out how, with the scope of work that we've got, to move this forward the next time.

So we will be back in touch with you. You've done a great job of bringing this back again. You've been just as eloquent, as all of your predecessors, on the point. I feel like it's almost like water torture. Every single time you guys are going to be in here saying -- but remember this. You've got to go back and look at the notes. We asked you all for some stuff and we were pretty clear that we needed you all to come together and get everybody together and say what's the credentialing organization, what's the -- you know, everybody, all the nursing organizations need to get together and come together and work it out also. So we've got to go back and reproduce all that work. So you have been eloquent, got our attention.

Marc, pressure on you.

But I also urge again every one of the genetic counselor organizations to come together and not have the differences of opinion, because you all weren't on the same page. Who's qualified, whose board do you follow, who gets to be in charge of what, who gets paid for what, how many people get to get paid every time. You can't just keep bringing it back to us (*Tape flip, 3B to 4A) coming back in here. So I've got to keep putting the pressure back.

MS. WICKLUND: And I agree, and we've definitely been working closely with our

other organizations, and we've definitely taken strides towards, again, introducing a bill to Congress and being more specific about what we need and not relying on others.

DR. TUCKSON: But you've been great, but you all are deflecting. I'm a heat shield. (Laughter.)

DR. TUCKSON: Thank you very much.

MS. WICKLUND: Thank you.

DR. TUCKSON: By the way, Shobita is back, and I just wanted Shobita to know that I did get this figured out.

Sharon? Jonathan? Jonathan is next? Jonathan Cohen? But everything is crossed out here.

MS. CARR: No, no, not Jonathan's name.

DR. TUCKSON: But who is he talking for?

MS. CARR: He's speaking on his own behalf.

DR. TUCKSON: Jonathan Cohen, unaffiliated. He's so unaffiliated, he's not here. We'll get Jonathan later.

Now it is Sharon Terry. My God, are we glad to see Sharon, the Coalition for 21st Century Medicine this time.

MS. TERRY: Thank you for this opportunity to present brief comments on behalf of the Coalition for 21st Century Medicine, which is a coalition of innovative diagnostic companies, clinical laboratories, policymakers, researchers, physicians, venture capitalists, and more than 30 patient advocacy groups, including Genetic Alliance. We believe that access to advanced diagnostic products and services is vital to the future quality and affordability of personalized health care. We also believe that innovation and quality patient care at the keys to 21st Century medicine and that timely access to new information by physicians and patients is critical to improving the quality of care and providing more personalized medicine.

The coalition shares HHS' focus on personalized medicine and the Congress and FDA's goals of assuring that treating physicians and their patients have access to safe, accurate and reliable information to assist in decisionmaking. In light of that, we support Congress and the various agencies striking an important balance between regulation and innovation.

The coalition looks forward to FDA reissuing draft guidances for IVD MIAs and ASRs to allow all interested stakeholders an opportunity to review and comment on these documents again. We have met privately with FDA leadership in December and May. We've given comments and given the comments of us and other agencies and organizations. We believe that there's clear concern in the community regarding the draft guidance that they put out the first time. We and others expressed concern that if implemented in their current form, the draft guidances for both IVD MIAs and ASRs may result in adverse, unintended consequences. There are ambiguities in the current guidance and laboratorians will require considerably more clarity moving forward. We urge the FDA and the Department to consider the comments of the patients, providers and innovators.

There's a very real chance of Congressional action and the resulting novel or substantially modified statutory authority may ultimately supercede the draft guidances in important ways. It is important that the Department is clear in its intentions and that all entities are working toward the same end. In that regard, because of the IVD MIA and ASR, policies are inherently linked to policies on genetic testing and personalized medicine and may be appropriate for the Department to merge plans to finalize the IVD MIA and ASR guidances with plans to develop oversight policies for genetic tests and personalized medicine based on the recommendations of this committee. In the interim, the coalition will continue to educate key stakeholders about the importance of innovative diagnostics and their role in

health care.

With regard to CMS, the coalition will continue to emphasize the importance of the Clinical Laboratory Improvement Amendments of 1988, CLIA, in assuring that patients and physicians have timely access to accurate, reliable and safe advanced diagnostic medicine. The coalition believes that enhancing and strengthening existing requirements under CLIA by issuing a genetic testing specialty may address some of the recent concerns about accuracy, reliability and safety of genetic tests and laboratory-developed tests in general, particularly the genetic specialty for which a notice of intent was issued. CMS indicated in letters and in the DHHS regulatory agenda that it would proceed with a Notice of Proposed Rulemaking, but this was subsequently dropped without adequate public rationale or explanation.

The coalition also believes that any regulation of LDTs, including genetic tests, should be risk-based rather than technology-based.

We also believe that the Genetic Information Nondiscrimination Act is a critical component of personalized medicine. The bill passed the House on April 25, as you said, 20 to 3, an overwhelming bipartisan majority the likes of which has not been seen in some time on an issue of substance. Though initially it seemed stalled in the Senate, it is important to note that that chamber passed it unanimously in two previous Congresses. We respectfully ask that the SACGHS recommend that the Secretary express his strong support for the Act and encourage the Senate to vote on it as soon as possible.

We look forward to working with you and all parties on these matters of vital interest to the public health, patient safety and personalized medicine. Thank you.

DR. TUCKSON: Thank you very much.

Any questions?

(No response.)

DR. TUCKSON: As always, thank you.

Now we finally get to eat, so the deal is this. What we're going to do is at 1:45 we were scheduled and are scheduled and will have a comparison of the patent system of the U.S. and select countries, and Joe Straus has been warned to go get something to eat right away. So Joe is ready, I understand. Where is Joe? He's out eating.

(Laughter.)

DR. TUCKSON: So he took the advice.

The one thing about the food that we have is it's not noisy.

(Laughter.)

DR. TUCKSON: So you're not noisy people, and because you're intellectuals, you can eat and listen at the same time. So you're going to eat and listen at 1:45. Food is served. Our guests will run and get something. There's no line, I understand. Lunch is outside. So your lunch committee is right out there.

See you at 1:45.

(Whereupon, at 1:30 p.m., the meeting was recessed for lunch, to reconvene at 1:45 p.m.)

AFTERNOON SESSION (1:50 p.m.)

DR. TUCKSON: So I negotiated with the people in line. There are a few people in line, and the thing is that somehow or another they ran out of food at one of the stations. So everybody sort of crowded around one thing and not the other thing, and I can't control that. So I felt guilty, but I told them this. For those of you that are in the audience, I told them that when they came in, they should whisper to their neighbor who would fill them in on the parts they missed, and they all seemed happy with that.

So without further ado -

DR. FITZGERALD: You mean there are some things out of the chairman's control?

DR. TUCKSON: Exactly, the humility of the chair. You see, I had done all that lead-up to turn it back to our chair, Jim Evans, and Jim is not there, so now I've got to fill in again.

DR. SEGER: Actually, I'm standing in for Jim.

DR. TUCKSON: Oh, you're standing in for Jim?

DR. SEGER: Yes, Jim has now become a blonde woman.

DR. TUCKSON: Well, there you go. That explains what it is. Take it away.

DR. SEGER: All right. Our next session will explore how gene patents are issued, licensed and enforced outside of the U.S., with a specific focus on Europe and India, and whether these patent policies aid or hinder the availability and use of genetic tests.

Our first speaker is Dr. Joseph Straus, who is the director of the Max Planck Institute for Intellectual Property, Competition and Tax Law in Munich. He is also a professor of law at the University of Munich and has served as a visiting professor of law at many international universities. Dr. Straus has served as a consultant to the OECD, WIPO and the European Patent Organization, as well as others, and was selected as one of the 50 most influential people in intellectual property by the journal Managing Intellectual Property for the past three years.

Dr. Straus, we are delighted that you are able to join us today.

DR. STRAUS: Well, thank you so much for this, let's say, exaggerating introduction.

Ladies and gentlemen, good afternoon. It's the first experience that people have to eat and to listen. I've been told that everything is under control, nearly everything, not everything.

(Laughter.)

DR. STRAUS: Nearly everything is under control. Of course, somehow I prefer to have less audience but not a sleeping audience already digesting. So that's also one of the aspects.

Actually, this morning my colleague, Professor Gold and the lady, they actually have taken away quite a lot of information which I intended to give to you about Europe. So I can concentrate maybe on some less issues and maybe we can have more time for a discussion or for your questions.

The overview here is showing you, first of all, that there is one - I would say from the mental difference between the United States and Europe, but also the rest of the world, that we have actually a statutory approach on patenting genes in general, as reported that started with the European Directive adopted in 1989, 1998. We have therefore a number of issues in the air not actually yet decided because our courts did not have the opportunity to apply those rules in practice yet. So I will be reporting a little bit about the patent practice, the differences here, about the exploitation and enforcement, and try to summarize a few things.

Now, the first slide you have seen already, reported by Richard Gold this morning, that under the European Directive actually we have specific provisions dealing with eligibility of genes for patent protection. Here only one additional comment. He said there was a certain, let's say, disagreement; what does that mean? Does it mean that genes cannot be patented to say more specifically genomic sequences? I would say genomic sequences of course can be patented if they are not just to be viewed as a simple discovery, meaning discovering or uncovering a genomic sequence and indicating the function of that is an invention. If you have only the discovery of a simple genomic sequence, that's not enough. So that Article 5 first paragraph is actually dealing with the demarcation line between discoveries and inventions.

The second really effort of the Europeans was to make sure that gene sequences as biochemical substances can be patented is enshrined in the Paragraph 2, clearly stating that if they are isolated or technically produced, then they can be patented even if they are structurally identical to that of a natural element; in other words, genomic sequences.

Importantly, however, and that which has not yet been mentioned, is that in a recital to this directive, it is clearly stated - and that was the reaction on the original attempt of NIH and Greg Fenton to get ESTs patented, that under the European regime, a DNA sequence without indication of a function is not viewed to be a patentable invention. Simply stating the function but not necessarily the biological function is an integral part of the invention. As that has been clarified actually here only by the Federal Circuit decision in Ari v. Fisher one and a half years ago. So we had this from the very beginning in our European statutes, and also later on implemented in the national laws with some delays, but nevertheless implemented.

Now, just Newman this morning has alluded to a number of differences of more general character between the European situation and the United States situation. She mentioned first the first invented, first defined. I'm not going into that anymore. Of course, I fully agree with her that the United States should make all efforts to bring the Europeans to the point that they introduce a grace period because we had a grace period in Germany for years and had no problems. A similar grace period existed in the United Kingdom with no problems, and we have now overall some 30 countries around the world with a grace period except the Europeans. So it's a good reason to pressure on them, again, the first invent to first to file and bring them to the conclusion that having a grace period is actually a good thing.

We have, let's say, the same situation with the scientists as in your country, so we suffer from the problem that as soon as something is made publicly available it cannot be patented anymore, with one exception for the so-called misuse, but that goes too far into the detail.

Now, in addition to that, we have also a difference that's quite important for working in the area of genomics and proteomics that our relevant prior art differs from the relevant prior art in the

United States not only as far as the grace period is concerned but also that you can get a patent in Europe on a substance, a chemical substance which forms already part of the prior art but where the medical use, therapeutic or diagnostic use has not been yet forming a part of the prior art, meaning if you have a herbicide and all of a sudden that's patented or not patented but it is prior art, if somebody finds out that you can use that not very probably to cure some skin problems, you can get a patent, and that patent is actually covering all medical uses of that product. So if then a second one comes and finds out maybe that could be good for curing (inaudible), he could get a second patent on that. It's a bit complicated to explain, but the basic message is that even if a substance is already part of the prior art, it can be patented as a substance, not as a use, as a substance, and that substance patent covers all the subsequent uses whether disclosed/claimed or not. So this is quite a different situation as compared with the United States.

In addition to that, we have also a difference as far as novelty is concerned, that we in the United States in oral disclosures and public use outside of the United States is not prior art. So therefore the possibility existed to get a patent on the so-called leantree substance because that was only known in India in some places. In Europe, you cannot get a patent on such things. So oral disclosures outside of the United States, according to U.S. law, are not prior art. You still can get a patent. So if you give a lecture in London, it doesn't count. If you publish that in printing, that's prior art; otherwise not. If you use it in public, it's not prior art if it is in Salvador or Argentina or Germany. In Europe, that is all prior art, although outside the United States.

We also had as far as the second most important requirement for patentability is the inventiveness or non-obviousness, although in the law a very similar provision, there was quite a substantial difference in the practice. The European Patent Office applies a so-called could/would test, meaning that the question is whether an expert, average expert in the art would have done it, not could have done it, and the answer was he would have if there was a reasonable expectation of success; otherwise not. I'm coming to the U.S. situation in a moment. Then again, the industrial applicability in Europe is a little bit more strictly applied in this area; namely that under the law, the statute, if you claim a DNA for the production of a protein or part of a protein, then the patentability requirement is only met if the protein or partial protein is disclosed and also its function from the very beginning. Otherwise, you cannot get a patent.

Richard Gold mentioned this morning or noon that we have a decision by an opposition division of the European Patent Office applying the specific substantial and credible test. That has not been yet clarified entirely because under the statute it's quite a far-fetched, let's say, interpretation of the European statute. It may be so, but it's not yet finally clarified.

Under the U.S. law, of course, the Chakrabarty decision is known. Anything manmade under the sun can be patented. You have this much more narrow prior art, as I said, with oral disclosures, and use does not form part of that. On the other hand, the non-obviousness requirement as applied by the federal circuit was a quite low yardstick. So it was, let's say, used in parallel to the chemical substances, the so-called structural approach, and under the dual doctrine quite the substantial number of patents have been granted on DNA sequences although a partial sequence was already known, or a partial amino acid sequence was already known. The U.S. utility examination guidelines should be known and applied in a different way to the so-called first, second and third generation of genomic inventions.

More specific, much more specific in terms of the scope of protection is the European Directive and the following national statutes. Under the U.S. law you have no specific rules. You have no statutory research exemption. You have this (inaudible) exemption, the so-called safe harbor. You probably are all aware of the Merck v. Integra Supreme Court decision where the Supreme Court, my

understanding, went the limits of the interpretation of the safe harbor provision. I was in the oral hearing and had the definite impression that the justices were quite unhappy that they had to apply only this safe harbor provision instead of being asked to interpret the common law research exemption defense, which would have been much more appropriate and probably they would have clarified many other things which they were not able to clarify because of the quite strict wording of your statute.

In Europe, we have a specific provision, and this answers also the question posed to Richard Gold a couple of minutes ago that under the Directive, product protection for products containing or consisting of genetic information extends to all materials except to the human body, meaning the question was what about control of humans who would have a patented gene? Under this provision, it's clear that hopefully one day, if the gene therapy will be successful, somebody will have a patented gene, that would not be under the scope of protection of a patent. That's clarified in the Article 9 of the European Directive. However, all other materials in which that information is incorporated and in which the genetic information is also performing its function are covered. We don't have until now any court decision clarifying what does it mean "performs its function"? Is it the function claimed, disclosed, or any function which that gene performs? As you know, 40 percent of our genes are multifunctional, so we don't know actually. If that would be interpreted that only the function which was claimed, then we have quite a narrow protection. If it would be interpreted as also disclosed, it would be a little bit broader. If any function which is actually linked to that gene, we would have a quite broad scope of protection.

A big difference between the United States and Europe is also that we have a statutory search exemption which covers actually all further developments, improvements, et cetera, even if they are aimed at commercial exploitation, and it's quite clear that even in the area of so-called basic research, nothing is entirely - let's say everybody has in the end some idea of maybe how that research result should or could be commercialized. So therefore the German Federal Supreme Court in two decisions, then later on confirmed by the Federal Constitutional Courts, clarified that it's all covered by the research exemption, and I think that all the other courts in Europe would follow because the root of that statutory exemption is a convention on the community which actually never entered into force but has been enforced in many parts into the national law. So that's the big difference between the United States and Europe, also leading to the situation that patent owners are not able or willing to try to prosecute somebody for performing research with their inventions.

However, one should make it clear that this research exemption does not cover the use of research tools for the purpose for which they have been patented. So that's something we don't have any court decision, but it is the general understanding that research tools are not covered, the use of research tools for the purpose for which they have been patented is not covered. But if you go to the Integra case, it would quite clear that Merck has further developed the respective invention, and this further development/improvement itself would be covered by the research exemption.

Another question is whether the research results, then, would infringe a patent or not.

We have also another specific provision taking care maybe of multifunctionality of genes or also alternative splicing. Under the (inaudible) 25, the Directive is covering the problem that patented genes are overlapping also only in part, and under that rule if the overlap is not essential for the respective invention, the patents are independent. So again here, we don't know exactly what is essential. Is it essential that you use an axon? Then probably it would be essential, or not. But we don't have any case law so far. To my understanding, it's quite an important provision. It has to be tested in practice.

We have in some countries like Germany, Luxembourg and France, after the extensive discussion on the impact of gene patenting, especially after it has been clarified that 40 percent of our genes are multifunctional, the scientists have said, oh, it's not a good idea that a patent covers all the subsequent functions. Therefore, something has to be done. The German legislature adopted in 2006,

as you can see, quite late, a provision that in such a case, to make it short, the function must be included into the claim, meaning that that would narrow the scope of protection of that gene to the claimed function. Whether or not this will be of far-reaching impact I do not know because this will probably not have any impact on the European patents granted by the European Patent Office for the very simple reason because the national courts may invalidate a European patent designated for Germany, U.K., Spain and so forth. That's a matter for the national courts only under certain strictly set forth provisions in the European Patent Convention. It's not up to the national law how to deal with it. They have also to interpret the scope of protection under the so-called Article 69 and the respective protocol to that 69, which clearly states that for the scope of protection it is the size of the claims and taking into account the description. Now, if the European Patent Office will not force, and there is no reason for them because there is no statutory provision, the applicants to include the function into the claim, well, the national courts will probably not be able to invalidate or to narrow the scope of protection of those patents. But there is no case law so far. We will see. I could imagine that there would be some psychological influence, but legally, strictly speaking, that will not have a direct impact on the European patents. In other words, it is obvious that the applicants will choose the European route and not the national route, which is already the case now.

I witnessed this morning that this discussion is very timely. I don't know whether it is really very timely because we are witnessing actually a steep decrease of patenting in the area of genes. This is, of course, not linked only to the problem of BRCA1 and BRCA2 and the (inaudible) genes, but in general. So it's quite clear that probably after the applicants have found out that they are running ahead of the scientific and technological development, they lost really the impetus to file more and more patents; and also after the Federal Circuit's decision in Fisher and the European decision not to patent ESTs, probably we are witnessing a period of time where less and less applications are filed and less and less patents or applications are maintained, because it's also a question of paying money for annual fees, and if you file that at best you may have something in 10 years, it doesn't make much sense to spend money for that.

Here you can see the difference in the European situation as compared with the United States. We had a rising curve of applications, but you see that the numbers of patents granted for genes has been always much, much lower than in the United States, partly also because of the obstacle of non-obviousness, which was much stricter in Europe.

This just should be an illustration that in Europe, actually the patenting of genes had no - I will come to that in a moment - negative impact to my understanding, because a number of small companies quite actively cooperate with the big pharma, and I would say to the benefit of both, and not least the benefit of the public.

Let me now switch shortly to the Myriad problem. You have been informed, I would say, extensively of Myriad. They had four patents granted in the European Patent Office, methods of diagnosing a predisposition for breast and ovarian cancer. That was issued in 2001 and revoked in opposition, and I would say not really because so many stakeholders, the so-called stakeholders, were involved, but just one, namely the co-inventor from the U.K., from Cambridge. He actually testified how simple it has been to file this one in view of the prior art. Therefore, actually the revocation was based on non-obviousness, meaning that it was not really invented to find it out. So the push by others I would say maybe viewed as something that was not decisive. Then they had three other patents. Here you see the appeal is still pending. So Myriad appealed, and I asked the lawyer who is representing Myriad last week, there is no hearing yet scheduled.

The second patent was apparently in opposition with some amended claims, meaning some narrowing claims. Again, both parties appeared but no hearing yet scheduled. The same applies for

the third patent, and the last patent here related to the chromosome was upheld in 2003 and is now actually finally granted.

You should also be aware that in the final grant in the European Patent Office, meaning after the opposition, after the appeal, that doesn't mean that that patent is actually relevant because actions can be filed in all the designated member states of the European Patent Convention. So also here, nobody really knows whether or not that will be upheld.

The reactions you've heard. We had an outcry by Greenpeace, the German Federal Chamber of Medical Doctors. Patient organizations protested. The European Parliament adopted a resolution against that. The main concerns raised in Europe were, I would say, first the concern that that would be an obstacle to accessing the secrets of the human genome, a high cost of testing because of patents, and also negative impact on improvements of diagnostic methods.

We had in Europe no single request for a compulsory license, which would have been possible actually in all countries. To my knowledge, there are no court cases pending. Somehow Myriad and others have agreed to somehow cohabitate, and in Germany we had a special situation between 1996 and 2004 that Myriad allowed the German Cancer Aid to test for BRCA1 and BRCA2 in 12 centers so that more than 3,000 gene tests have been performed, but not actually using the method of Myriad. To my understanding, they have not paid any licensing fee, although there is a licensee of Myriad, Bioscientia, in Germany. The main reason for hesitations, consents, and also opposition was the idea of Myriad that all tests have to be performed in Salt Lake City and not in Europe. So that was one of the reasons why we have written this strong reaction, but after all, if there are no court cases, no requests for compulsory licenses, the impact must have not been such a tremendous one.

In the course of this debate, under my supervision our institute has performed interviews in 25 institutions, big pharma companies that house research institutes and clinics. We have not found any proof. Those interviewed have not really shared the concern of the public, whoever the public is. The majority, even to my surprise, was in favor of product patents on DNA sequences. The only critical point, and I shouldn't say the only because it's quite a critical point, was that they clearly stated as soon as they found out that there is a gene patented already, they lose their interest to search for further functions, meaning they don't want to become dependent on the patent owner.

The results cannot be viewed as entirely representative because there are still only a few products on the market, and one should be aware of the fact that if there are no products on the market, if you have a research exemption, nobody sued, and as long as you don't have a product on the market, you do not infringe. So there are some reasons for this situation, and also in Germany we had no single request for a compulsory license.

To summarize, and I hope I'm more or less on time, in the United States many more applications have been filed for the very simple reason that they filed applications also for years. From the very beginning it was quite clear that in Europe they would not get patents on ESTs. Under the old U.S. law, that has changed. There was no publication of the applications as long as no patent was granted. In Europe we have 18 months, as you have it now, too, as a general rule, meaning that if you don't get a patent and the information is disclosed, it's not a good idea to file a patent application knowing that most probably you will not get a patent. So now under your law, I guess you are all aware you also have 18 months after the filing. But if a university knows, for instance, that they have pre-published papers, they can declare that there will be no application abroad, and therefore also the American application will not be published. That's the law in the United States. So if you declare, you will not apply for a patent abroad. Your application will not be published. It will be published only as a patent if there will be a patent granted. Otherwise, there is no publication. So the idea in Europe not to grant EST patents led automatically to the hesitation to file those applications in Europe because otherwise

everybody could get the information on the EST sequence after 18 months. Now the situation is here only still in place if for any reason ever an applicant declares he or she will not apply for a patent in Europe, anywhere outside the United States.

There are more patents issued here. The question of whether they will be valid or not after the official decision, probably people will invoke the validity of patents. I don't believe that we have witnessed excessive litigation activities, not more or less than in the IT area. If you look at the IT landscape, of course we had the litigations here. I don't know about the negative impact on R&D. In Europe there are many less applications filed, less patents granted. Litigation activity I would say is relatively comparable to the United States because they are always the same actors, be it here, in Japan or in Europe. To my understanding, we cannot state and observe that we had a negative impact on R&D because of that.

So if you have any questions, I am ready to answer them.

DR. EVANS: If it would be okay, I'd like to hold off on questions until the next speaker and then have the two of you field those together, if that's all right.

DR. STRAUS: Thank you.

DR. EVANS: Thank you.

(Applause.)

DR. EVANS: Our next speaker is Dr. Bhaven Sampat, who is an assistant professor at the Department of Health Policy and Management and the International Center for Health Outcomes and Innovation Research at Columbia University's Mailman School of Public Health. Dr. Sampat's research centers on the economics of biomedical innovation, the law, and the economics of the patent system and science policy. He's currently the principal investigator on a Ford Foundation project examining patent system reform in developing countries, and he created the first freely searchable database of post-TRIPS Indian patents and applications.

Welcome.

DR. SAMPAT: Thank you very much. I stand here before you somewhat timidly because, as the introduction suggested, much to my mother's dismay, I'm neither a doctor, a lawyer, or a scientist, but a mere economist. Much of my knowledge about some of the issues relating to genetic testing was acquired over the past few hours.

(Laughter.)

DR. SAMPAT: I try to do empirical work on patenting, and what I'm going to show you today, much of what I'm going to show you today is data on DNA-related patenting in India, and then also some discussion more generally about the political economy of patent system reform in developing countries. I think that discussion will be relevant for thinking not only about DNA patents in general but also about patents on genetic tests in particular.

One last caveat before I begin. Here again, the lawyers in the room probably know a lot more than me, so I'll just sort of set the stage or fill in the blanks and correct me when I'm wrong during the Q&A. And then along the way I'll also say a few things about U.S. patent system reform in the spirit of trying to draw some lessons from India and from just innovative thinking about patent system design worldwide for the United States.

Finally, I was asked to point out that the slides I'm going to show you now are a subset of the slides you have in the handout. I thought I was over-anxious this weekend and I would never get through what's in the handout in time, so you can read that on your own time sometime.

Okay. As many of you know, the 1995 TRIPS agreement, Trade-Related Intellectual Property Rights, negotiated at the end of the Uruguay Round of the GATT, required developing countries, including India, to "modernize" their patent systems. Basically, TRIPS led to an upward harmonization

of international patent laws, meaning that countries were basically compelled to make changes to their patent laws to make them look more like those of developed countries, and in particular the United States. This led to a number of changes in India and other developing countries, including enacting a minimum patent term of 20 years; not allowing countries to discriminate across fields, so countries like India and Brazil previously didn't protect product patents on pharmaceuticals and they had to in the post-TRIPS era; and a range of other things. But generally, the notion is that patent laws got stronger and more in favor of patent holders rather than others in the post-TRIPS era.

So this is kind of interesting and has been a matter of controversy for a range of reasons. The first is just that historically all countries when they were developing basically did so by stealing intellectual property from other developed countries, including this fine nation. So for people like me who grew up in New England, you hear these stories about Samuel Slater memorizing the mill design technology from England and starting a textile industry in Pawtucket, Rhode Island. Well, that was basically theft of intellectual property rights, right?

But anyhow, the point is that a lot of things countries did before to try to catch up to the technological frontier they can potentially no longer do under TRIPS.

More importantly, in India there is concern that the granting of product patents on pharmaceuticals will lead to increase in drug prices, particularly pronounced in the HIV/AIDS context where Indian generic producers are important or had been and continue to be important producers of lost-cost generics, both for Indian consumers and for other developing countries.

Finally, from the perspective of most bodies of economic theory, it probably makes sense for developing countries to have more lax intellectual property right regimes than those of developed countries.

So (*Tape flip, 4A to 4B) important set of issues now generally and with respect to specific fields like genomics or genetic testing, is what kind of patent system should developing countries adopt. And despite the general trend towards harmonization, it appears that there might be considerable room for maneuver under TRIPS, which goes under the rubric of TRIPS flexibilities, which would allow developing countries to design their patent laws to maximize the benefits from the new regime and minimize the costs.

So what are some of these flexibilities? This was one of the points in the presentation where I really should defer to the lawyers in the audience, but at least as I read it, there is some flexibility in how countries define "inventive step" in utility. Countries can, under TRIPS, have a research exemption; India does. In some countries, including India, there are restrictions on patentable subject matter. So, for example, in India, Section 3 of the patent law excludes from patentability scientific principles, abstract theories, products of nature, new forms of old substances without increased efficacy and, relevant for this audience, processes for medicinal and diagnostic treatment of human beings.

Now, as I think was pointed out earlier today, these are just things on the books in India. The extent to which these laws actually hold up as being TRIPS compliant in the actual meaning of these exclusions and standards of patentability is still very much up in the air in India and other developing countries. So, for example, Novartis is currently challenging Section 3(d) of India's patent law, the notion that you can't patent new forms of old substances, and it's not just about how the laws are interpreted but there's also this interesting international political economy going on, so recognizing the presence of TRIPS flexibilities, groups like PhRMA and the U.S. Trade Representative are pressuring India to enact TRIPS in particular ways. The Prime Minister of India is reluctant to, for lack of a better word, offend USTR and PhRMA because he's very interested in attracting foreign direct investment. The U.S. is entering into bilateral trade agreements with a number of developing countries to try to get them to enact a patent law stronger than TRIPS, the so-called TRIPS-plus provisions, and all this is being played

out right now, and there's also not much in the way of case law in India right now. So in this context, the issue of what can be learned from India is a difficult one, but I'll try to say a few things about that in the end.

Now, before I get to talking about some data on DNA patenting, specifically let me just also put one other thing on the table, which is that all this stuff here is about de jure patent law, meaning patent law on the books, but there's also this issue of de facto patent law. So it's somewhere between ironic and paradoxical and sad that at the same time developing countries are figuring out how to enact the new patent laws that were essentially forced upon them by developed countries, there's considerable concern that developed countries' patent systems may not be doing that good of a job either.

So some of you may know that Adam Jaffe and Josh Lerner wrote a book recently channeling their inner Sigmund Freud called "Innovation and Its Discontents: How the Patent System is Broken and How to Fix It." There are all sorts of examples of patents issued that probably shouldn't have been in this country. Some of the more amusing examples include over the last 10 years a patent done on a crustless peanut butter and jelly sandwich, a patent done on a method of swinging on a swing. But more importantly, the USPTO also issues patents in highly specialized fields, including genomics and genetic testing, that would overreach as blatantly to some of you in this crowd as the peanut butter and jelly sandwich patent does to a lay person like myself. Indeed, my own cursory reading of some of the more problematic genetic test patent episodes is that the issue was not just the patent per se but that the patents were overly broad and probably shouldn't have issued as such.

So the point is just that in thinking about the impacts of TRIPS on access to genetic tests in developing countries, even in the U.S. we need to recognize that it's not just about the patents but rather also about patent quality.

So with all that, what's going on in India post-TRIPS? First some general data, and then some data on DNA patenting. So I collected data on the 60,000 or so applications filed at the Indian Patent Office in the post-TRIPS era. This just shows the distribution of applications across the top 10 international patent classes, or IPCs. The thing that stands out here is that at the top of the list are A61K and C07D, which are basically pharmaceutical classes. Also well represented is C12N or microorganisms. Some of the genomic-related patents might show up there. There's also pictorial communication patents and things like that, which might be about Bollywood; I don't know.

So who are the big applicants in India? Hopefully you can see that better than I can on my screen. The top applicant in the post-TRIPS era in India is CSIR, which is a system of publicly-funded laboratories in India that do research in a range of fields. The second largest is Hindustan Lever, which is a consumer products company that does a lot of chemicals work. But what's striking about the list of the top 20 applicants in India in the post-TRIPS era is the prominence of multinational pharmaceutical companies.

So what about DNA-related patenting in India in the post-TRIPS era? Well, that turns out to be a harder question. It turns out to be hard to identify DNA-related patents in the Indian context first because the approach that's been pioneered by Bob Cook-Deegan and others involves looking at specific U.S. patent classes and then looking at specific keywords in claims in patents within those classes. It turns out that in India, they don't use U.S. patent classes. So that's one issue. But more importantly, at this point it's impossible to get data on claims of Indian patents in any large sample. It turns out to be really, really difficult. So all we have is information on titles and abstracts and priorities and things like that.

So I tried to get around this in two ways. As a first step, I simply looked at patenting in the set of international patent classes that Verbeure et al. characterized as corresponding to DNA-related patents in their European Journal of Human Genetics article. Now, what they did is they

looked at all patents in those classes, and then they read the claims and figured out which of these are in fact DNA-related and which are not. I can't do that because I can't read the claims, so this is going to be an over-inclusive list, give you an upper bound on DNA patenting in India, and that's problematic for a few reasons, and I'll try to show you another approach which gets around that in a second.

But based on this IPC-based measure, of the 60,000 or so patent applications filed in India since 1995, about 4 percent are in DNA-related international patent classes. The top 25 patenters in these classes account for a third of patents in those classes, and they include - again, if you look at who they are, you see the prominence of multinational pharmaceutical companies. That CSIR also shows up here fourth, and also the University of California, I believe, shows up on this list, having 20 DNA-related patents in India, which is quite interesting because I believe the University of California is the biggest patenter of DNA-related stuff in the United States.

So that's one look at it. The other way which is a bit more precise is I used data on priority applications in both India and in U.S. patents. So I started by just looking at all the DNA patents issued in the United States in issue years 2000 and 2005 using this search algorithm developed by Bob Cook-Deegan and colleagues for what is now the Duke DNA Patent Database. Then I looked back at the priority application data in all of those patents and then linked that priority application data up to any Indian patents. So any time you see a DNA patent in the United States, is there a related, sort of family member patent in India?

So if we just start with the U.S. patents, there are 3,800 or so issued in the year 2000. As a previous speaker pointed out, it's declining, about 2,700 issued last year, and then mapping them over to Indian patent applications, what you see is this, that in the year 2000, which is the first row, 41 of the 3,800 or so U.S. patents had corresponding Indian applications, or about 1 percent. By 2005, that number increases to about 2.5 percent. But a relatively small share of things that are called DNA patents in this country have corresponding applications in India, although the number does appear to be increasing over time.

It turns out you can also look at whether the things based on the same priority as the U.S. patents are patented or are applications or whatever in India. The vast majority, everything but one, are pending patent applications. So there's only been one DNA-related patent granted in India since 1995.

Now, because I don't know too many things, it's unclear to me which of these are on disease gene associations or genetic tests, but I'll just point out that the number is sufficiently small that if one were interested, I could hand them to someone here and you could try to read them and figure it out. I suspect the numbers are low, but that's just my own cursory reading of them.

Who is filing the DNA patents in India? Using this measure, it looks very similar. Multinational pharmaceuticals turn out to be pretty high or pretty disproportionately represented here. So these are all the assignees that have more than one patent application on DNA-related stuff pending in India.

Finally, given the prominence of academic institutions in ownership of DNA-related patents in the United States and the fact that a number of the policy proposals that are on the table here and internationally try to leverage the fact that academic institutions own some of the key IP, I also looked at the extent to which academic owners of DNA-related patents in the United States were more or less likely to file corresponding applications in India. It turns out that non-academic owners of DNA-related patents in the United States file for corresponding Indian patents for 2.8 percent of their inventions, whereas the corresponding number for academic owners of DNA-related patents in the U.S. is 1.45 percent. So universities are, in fact, less likely to take out DNA-related patents in India.

A final thing before I wrap stuff up that I think is an interesting set of developments on the scene is that there has been all sorts of movement to enact Bayh-Dole-type legislation in India.

Even though TRIPS is silent on this, there are all sorts of interesting academic entrepreneurship in India. Some of the impetus is coming from specific institutions, but Bayh-Dole legislation is on the way. To the extent that Indian academic institutions themselves are or someday will be important producers of DNA-related inventions, this is an important development to watch. If you just look at the top 20 Indian universities, this chart shows their patenting over time. The left bar is the number of USPTO patents they're filing, and the right bar is the number of patent applications they're filing in India. You see that using both measures, academic institutions in India have increasingly begun to take out patent applications. If we were to look at the extent to which they're actually taking out DNA-related patents, however, at least at this point you don't see all that much of it. So I'll just jump to the final bullet point here.

The top 25 Indian "universities" - and I have "universities" in quotes here because they include some public sector research institutes like CSIR - they account for a relatively small share of the DNA-related patents filed in India, at least based on the international patent class-based categorization.

So where does all that leave us? I focus here on India, but I'm going to take the liberty of talking a little bit about patent system design generally here as well since one of my charges is to provide some practical thoughts for the committee. Just to sum up, very limited DNA-related patenting in India thus far. One would have to actually look at specific patent applications and trace them through to know this for sure. My sense is that most of the existing genetic tests out there are unpatented in India and probably, given their priority years, will not be patentable in India, at least the stuff that exists or is widespread right now, which underscores the somewhat obvious fact that others have raised this morning that to the extent that there's an access problem in India, and I'm not sure if there is or there isn't, but to the extent that there is, it probably reflects other stuff as well. So one of the things that we hear in pharma, which I believe is quite true, is that patents are perhaps an important barrier to access to drugs in India, but there are all sorts of other barriers to access too, including things like poor medical infrastructure, poverty and things like that. That's not to say that the patent issues are unimportant.

A second thing, and this is sort of interesting in thinking about it in parallel with pharma, is that even if genetic tests were patented in India, I'm not sure that you would see prices being as high or access being as low as you might see in the context of pharmaceutical patents, and let me just expand on that a little bit. One of the interesting questions is why pharmaceutical firms are taking out patents in India, and if those patents issue what the impacts will be on prices.

From an Economics 101 perspective you say, well, they would price discriminate if these patents issue, meaning they wouldn't want to charge U.S. prices to India. But a number of people argue that, in fact, in effect they don't price discriminate, that they charge pretty high prices for AIDS drugs and things like that in India. Why is that? The answer to me is not entirely clear, but one plausible answer and perhaps the most plausible answer that's been given to me is that they're worried about creating arbitrage opportunities. They're worried about the drugs coming over from India to here. That's less likely to be the case in the context of genetic tests, which are less embodied in pills and things like that. So price discrimination, even if it doesn't work in the context of pharma, probably would work in the context of genetic tests.

At this point, there's very little evidence that DNA-related patents in India have impeded research or any clinical applications, but you hear every once in a while at these European economic history conferences what was the worldwide economic impact of the French Revolution; it's too soon to tell.

(Laughter.)

DR. SAMPAT: And that might be the case. We're looking very early in the

post-TRIPS era. So who really knows? That notwithstanding, several policy options - India is in the process of implementing TRIPS right now, and several policy options could, I think, help limit future costs and would have little downside risk. So I'll just conclude on these.

Getting back to a theme I raised earlier, patent quality control is important. So it's not just about patents in the context of genetic tests but overly broad patents. In India, as in the U.S., we have a patent office where it's difficult to attract qualified examiners, technically competent examiners, because technically competent people want to do other things than be patent examiners in India where they get paid very little and don't have that great of a lifestyle. There's a huge backlog of applications in India, huge pressure to clear the backlog, and the infrastructure that patent examiners have for searching through prior art is very, very, very weak. So in this context, it won't be surprising if occasionally bad patents issue.

Now, India has something that's neat. We talked a bit about opposition this morning. India has a pre-grant opposition process so that anybody - well, actually, you have to have some sort of representation, but generally anybody who knows an Indian lawyer can oppose a patent after it's been published in the Patent Office Journal while it's being considered by the examiner, and there's also a post-grant opposition which can be filed by any interested party within 12 months after issue, and the grounds on which patents can be opposed include obviousness, non-patentable subject matter, anticipation, wrongful obtainment and things like that.

Now, opposition has had a number of notable successes in pharmaceuticals in India, though I put "successes" in quotes because it really depends on whether you're looking at it from the patient/activist point of view or from the pharmaceutical industry point of view, but a number of applications that have been filed in India and also filed elsewhere were in fact not granted in India because of this pre-grant opposition, yet patient advocacy groups are teaming up with generic companies and mounting these campaigns to oppose patents that they think would impose hard costs.

There are obstacles in India to opposition. One of them is that it's really hard to search Indian patents, or at least up until recently it's been really hard to search Indian patents which have been published in image PDF form. So it's really hard to go through 60,000 pictures and figure out which of these are worth opposing. Hopefully that constraint has been relaxed a bit.

At the same time, there are concerns about opposition in India. The pharmaceutical industry has argued that, in fact, the alliance between generics and the patient advocacy group is an unholy alliance in that you see groups filing serial oppositions one after another to the same patents to try to eat into patent life, which begins at filing date. So pharma, through the USTR, is trying to basically limit oppositions in India to post-grant. My own feeling is that that's not the way to go. To the extent that that is a problem, that could be fixed. For example, conditional and surviving opposition let's applicants retrieve any patent life lost through opposition, or as Mark Lindley and I have proposed to the United States, provide higher presumptions of validity to patents that have survived the opposition process, sort of gold-plate them. So the notion is that I think that a well implemented opposition system in India could help prevent harms in India, and also in other parts of the developing world, and potentially in the U.S. as well.

Finally, in the case of public sector innovations, Bayh-Dole is on the way. Bayh-Dole in India is on the way I should say. As a number of people have rightly pointed out, the issue there is not about patenting per se, or not just about patenting per se, but about licensing regimes, and my proposal here is that India and other developing countries should resist the temptation to mimic Bayh-Dole as is, but instead think about doing things that can balance technology transfer and the need to generate revenue with other goals, and ways to do that include building research exemptions into licensing contracts; perhaps, as someone mentioned today, starting with the rebuttable presumption of non-exclusive

licensing, at least for certain types of inventions.

Finally, a little shameful self-promotion, and this applies to both - this is a policy proposal that I think applies equally to the United States as well as to India. Recognizing that even for academic patents a number of the problematic cases in, let's say, the United States have been in a context where the ultimate patents that issued were too broad, again a patent quality problem, Beth Novak and I have argued recently that you might want to introduce some sort of a peer review system to review these applications. So it's similar to opposition except it's less formal and it's more diffuse.

Now, as some of you know, there is a community patent initiative that the USPTO started piloting a few weeks ago where firms like IBM and Microsoft have opted in some of their patents to open them up to a peer review process, because in the IT industry you also see these patent quality concerns. But that model relies on opt-in. But the NIH could tell all of its grantees, as a condition of taking money from us, you have to open up your patent applications to a peer review process, and you'd have to think about the right ways to design that and to implement it and things like that, but we think that that is something useful to explore not only in places like India as part of their new Bayh-Dole Act but also potentially in the United States.

Finally, it also has the virtue of, I think, being politically feasible because it would be kind of churlish for academic institutions to oppose this as they have opposed other movements toward patent system reform, like first to file, because they would essentially have to take the position that not only do we want patents but we want patents that wouldn't survive a process of peer review, which would be tough for academic institutions to do. So that's another idea that's on the table in the U.S, and we're trying to bring it to India as well.

That's it.

(Applause.)

DR. EVANS: Okay. If we could get both our speakers, Drs. Straus and Sampat, and open it up for questions, I know that Reed has the first question.

DR. TUCKSON: Right. Great. Well, again, thank you both.

Dr. Straus, I think, as I look at your slides 13 and 14, the one that sort of branches off like that, and number 14, which I couldn't read as quickly, and the print is so small on the handout that I can't quite tell - and also for you, Dr. B. -

(Laughter.)

DR. TUCKSON: You all are not going to get me again.

(Laughter.)

DR. TUCKSON: I'm trying to understand, and I think you sort of got at it as well, Dr. B., for India, but I'm trying to get a sense of is there, so far, enough experience in your countries and in Europe to tell us that not having patents stifles innovation? Companies don't want to come forward and apply for patents. They're not being granted, and therefore why bother being in the business because it's no point and we're not going to get rewarded for our intellectual capital? We're not going to get the patent, so therefore we're not going to be producing new innovation. Is that, or not, true, and how do you see that?

I think you sort of said it, Dr. B. I think the impression I got from your presentation - I may have gotten it wrong - was, again, that the unclarity, the murkiness of patent law does not seem to be stifling innovation. So that's what I'm trying to get a sense of from you all.

DR. STRAUS: Well, I would agree. I mean, it's quite clear that companies will not invest money and not try to innovate without being relatively on safe ground to get workable protection for their research results. Without that, this number 14 should just illustrate the fact that more and more big pharma is not really performing by itself the basic or, let's say, the applied research close to the basic

research but has outsourced it or is trying to enter corporation agreements with smaller companies actually based on experience which university people have had. So basically I would say yes, if the patent system does not offer a relatively - nothing is really safe in this area. You never know how you will end up. But if already the perspective is that you cannot get workable protection for your research results, that is for sure an obstacle to investment and innovation.

DR. TUCKSON: Well, is it possible that you could have a third component of the curve? Again, I'm maybe not reading it right, but patent applications are going up pretty dramatically in your curves. Therefore, people are innovating and they're continuing to do stuff and develop discoveries. The number of patents that are granted is like that. So there's a big gap. Do you have a third curve that then says the number of companies who are then investing resources, money, into innovation is going like that? Because it looks like it's going up.

DR. STRAUS: I'm not referring to the statement about the French Revolution.

(Laughter.)

DR. STRAUS: But one thing is quite clear. The first curve clearly indicates the research or scientific activity in, let's say, deciphering the human genome. More and more sequences have been, let's say, disclosed and people have filed patents for that. Then after a while, based on some experience, they found out - and I can give you just one example. The former Swiss company Sandoz paid $300 million U.S. dollars for the acquisition of Gene Therapy Institute because the Gene Therapy Institute had the exclusive license of NIH covering French, Anderson and others, covering actually all imaginable somatic gene therapy. Then they found out after eight years that they were ahead of their time, that the physiology is much more complex. They dropped. So they closed the institute after eight years because of no success.

Now, I'm just trying to explain to you that the enthusiasm by filing the patent applications at a certain point in time made people aware that the business is much more complicated. It will take much more time before they can get a product. At the same time, also the curve of granted patents reflects on the one hand a more rigid examination, but at the same time you have to apply for the examination. So people maybe got the idea they're ahead of time. They may have something different. They dropped. So maybe it's not only a third but maybe even a fourth curve.

DR. TUCKSON: So let me just be real clear. I think I understand your answer. That helps me a lot. So what we're trying to figure out here, and you're answering, both of you, the question what is the experience in other countries that we could learn from that either confirms or does not confirm that absence of patents has a stifling effect on innovation and the development of new products? What I think you are saying is that it is your suspicion that, in fact, the murkiness or absence of law in this case does stifle it and that we should not over-interpret optimistically the curve because there are other things that are going on. Am I understanding what you're saying?

DR. STRAUS: That's correct, yes.

DR. SAMPAT: Let me just add a few things to that, and actually I'll talk about what we know from the U.S. experience and then we can just say something about the international scene as well.

Fifty or sixty years ago, the economist Fritz Machlup sat before a committee like this and was asked to do - actually, he sat in front of the Senate and was asked to do an economic review of the patent system, so he asked exactly that question, which is what would happen - they were very concerned at the end of World War II about changing patent laws, and he got a lot of money, a lot more money than my $200 honorarium probably -

(Laughter.)

DR. SAMPAT: And he came back after years and years and years with the following

conclusion, which is, okay, I've reviewed the empirical evidence, and if we didn't have a patent system, it probably wouldn't make sense to institute one, but given that we do, it probably doesn't make sense to get rid of it, right? So a serious point after that. It's a difficult counterfactual because you don't see both states of the world. You don't see the same state of the world, and I think this is what he's getting at, just changing patents. All sorts of other stuff is going on.

There is a 50-year empirical legacy in economics on the impact of patents on innovation, and what's interesting there is that in most industries patents don't seem to be all that important for innovation. In pharmaceuticals, they do. Pharmaceuticals is the odd duck where patents are important for innovation, but - and this is the last point - that's really not quite the right question because nobody is really thinking about the relevant policy issue as being whether we want to turn the patent system on or off, right? But it's about changes on the margins, right?

So what we don't know is if we change the rules this way, if we tinker on the margins this way, what will happen. So the answer is we don't really know, and it's difficult to draw that lesson from other countries for genetic tests specifically, or even more generally, but just a few things on development of diagnostic and genetic tests. To the extent that a lot of the work is being done by public sector institutions, the traditional logic for patenting does not apply, which is that absent patents, firms won't have the incentives to take their money and put it into R&D, because this is already being paid for. So this is kind of a belt and suspender strategy, which is we're using the pubic funding instruments to stimulate the work, and then we're also allowing institutions to patent. So the logic that we should also allow for patents follows from the Bayh-Dole Act based on the notion that we always need exclusive licenses to facilitate technology transfer. There is absolutely no evidence anywhere to that effect, though again that's also a very difficult counterfactual.

DR. TUCKSON: Well, I hope our transcripts will capture your last comment, particularly as it relates to NIH and the fact that we are advising the Secretary. I'd be very curious to think about, when we have more time, what that means.

By the way, I hope my other colleagues are in line. If I get a chance, or if they don't ask it, I'll come back at the end and ask the question about what do you know about the relationship between patents and pricing of the products in your work. By the way, don't denigrate the patent inspector as a job. I mean, Einstein was that, so there's a precedent here.

DR. SAMPAT: That's right, but they don't make them like that anymore.

DR. EVANS: We have two other questions. I would remind the committee that there's also the flip side of the question that Reed asked, which is not just would the lack of patents stifle innovation but does the presence of patents and the way they function, does that stifle access, because that's kind of the flip side.

Emily?

DR. WINN-DEEN: I wanted to ask a question to sort of differentiate the goal of diagnostic testing, which is generally to have it widely available and locally done so that patient care can be handled in a timely way, versus a pharmaceutical, which can be distributed simply by selling bottles of pills and distributing them that way. So in a pharmaceutical model, you can have someone with a monopoly that distributes those pills to all the hospitals. But if you apply the same monopoly to a testing algorithm where labs have already invested in capital equipment so that they can run tests, and if you say only one manufacturer or whatever, one entity can offer that test, and if you are unlucky enough to have spent a quarter of a million dollars on the other guy's equipment, sorry, you won't be able to run that test, it seems to me that you're really working at cross purposes.

So I guess my question is, in the European scenario and in India, how important do you think it is for people to have this sort of locally available testing, and do patents inhibit that or help

make that more broadly available?

DR. STRAUS: Well, they probably do not help to have them more broadly available because you need a license. That's already something if you would be able to use that test without any help by the patentee, which is not always the case, then you could say they don't make them more available. But, of course, you have to take care of the source. Somebody has to invent them. That may never be lost.

I didn't mention that but I would like to make you all aware of the eBay decision of your Supreme Court recently, meaning that in cases where diagnostic patents are at hand, in your country let's say the injunctions could be forgotten because the Supreme Court under certain conditions has clearly stated that a license would be fine, even in other areas of law, because under the common law doctrine there is no mandatory provision that you must have as a patentee an injunction. So that is already something which we don't have in Europe. You have it here, not yet exercised, but the eBay decision clearly indicates that would be a possibility.

In Europe, as I said, relatively I would say easy, but it's possible to get a compulsory license, and usually, if not this quite unfortunate Myriad case, a license would be probably relatively easily available. But the resistance of the Myriad to get that done in Utah and so forth made the real problem.

I don't know, Mr. Chairman, whether I may make two additional remarks because I don't know whether I will have the opportunity anymore.

DR. EVANS: Sure, go ahead.

DR. STRAUS: India, with all due respect -- I was on mission for the WIPO, the World Intellectual Property Organization, and the Indian government last year, and the Indian examiners are not in a position to examine anything in this area. They don't have access to the search materials, they don't know exactly what the novelty is, and so forth and so on. So probably we are talking about applications, not that much patents.

DR. SAMPAT: Oh, yes. Most of the numbers I showed were on applications.

DR. STRAUS: Applications. So the application doesn't say actually anything specific. That's number one.

Number two is that after the TRIPS transformation to India and becoming mandatory to India, India had to apply the so-called mailbox system, meaning accepting patent applications immediately after 1995, not granting patents but granting the priority. Number two in those applications are Indian companies; number one the United States, number two Indian companies, Ranbaxy and others, and then quite far back the U.K., Switzerland. Germany doesn't even appear in that statistic. That should be also understood.

Maybe then the last remark, because you mentioned Machlup, I can mention von Hayek, who got a paycheck in this country when he was awarded the Nobel Prize for economics. He gave a talk about econometrics, and he said when econometrics would have been so important in his time, he would have probably never done it, but he must confess that he lived according to the principle that it is much better to know something approximately correctly than knowing something exactly but dead wrong.

(Laughter.)

DR. STRAUS: And that is the problem here. So working with statistics, not having the real parameters can lead you into some conclusions which are "more than interesting." Thank you.

DR. EVANS: Marc?

DR. WILLIAMS: This is a bit of a prosaic question compared to the others that have preceded it, but there was one part in your presentation, Dr. Straus, that I needed some clarification on.

You had indicated at the end that you had not detected in your interviews any negative impact on research and development, but then in your talk previously you had indicated that if a gene was patented, that other companies would not pursue additional functional aspects of that gene, even though as I understood the way that the patent law is written that they would have the ability to do that without infringing on the patent because it represents additional or different function. So that to me, at least, seemed to not fit together or seemed to be at odds. So if you could provide some reconciliation between those two statements, I'd appreciate it.

DR. STRAUS: Well, as I said, this was the only hint where we had the impression, yes, there may be some negative impact to that extent. But whether this is a real negative impact, I don't know because, as I pointed out - and I really think for you as a committee advising the Secretary, it should be quite clear that even finding a further function doesn't automatically tell you that you have something which you can use commercially. It takes a lot of time. So if you have a research exemption, which you don't have, at least not in clear terms, then you can perform that research, and in the end probably you will not be dependent because by the time you have some product to put on the market, the old patent will lapse. So therefore I really have a difficulty. Of course, it looks like a negative impact, and that was not the companies but the universities, institutes and so forth. But overall I would still say that the impression was and the clear statement of those interviewed was that they don't feel somehow a constraint and an obstacle by patents.

DR. EVANS: Kevin, and then we'll have to move along since we've already taken your break, you might have noticed.

DR. FITZGERALD: I don't remember getting a vote on that.

I'd like to just follow up on something that Dr. Sampat said, and I appreciate very much when you mentioned the fact that pharma seems to be somewhat different than maybe other industries in the way patents are influential for their continued survival. I'm wondering as an economist, are you aware when the analyses are done if the sort of unique status of health care in a society is taken into consideration when comparing that, say, to other areas where DNA or biological patents might be important? I mean, one could argue certainly that food is a rather unique product, but you wouldn't put it on the same status necessarily as health care, and feed may not be on the same status as food, and then you can go further down the line. All of these represent different sorts of classes of products, if you even want to call health care possibly a product.

So I worry that when we look at patents for DNA sequencing or patents for biological products, we don't make those distinctions, even economically, so I'm not quite sure we can get at the sort of data that might be most relevant to us in this discussion.

DR. SAMPAT: Just very quickly, I think that's a fair point. I think that's a very fair point. Part of what you want us to do is to make value judgments about the outputs of different industries, essentially, and economists are good at making - they're not good at but they have a comparative advantage at making value judgments in money terms. So to the extent this is brought in that we really value health - if you ask people how much they would be willing to pay for a better set of brakes on a car so they don't die, the value of health is really, really big. But that's not really exactly what you're getting at. You want to get at the unique status of health in a moral sense or at least a different normative sense than economists. We're not very good at that.

DR. EVANS: (*Tape flip, 4B to 5A) broader discussion. Thanks very much, both of you.

(Applause.)

DR. EVANS: And the last portion of the international roundtable from today is going to focus on several recent international reports that address gene patents, licensing and genetic

technologies, and how intellectual property affects genetic testing.

Our first speaker is John Barton. He's an Emeritus Professor of Law at Stanford University and co-founder of the Stanford Law School Center for Law and Technology. He specializes in international and high technology issues. He serves as a member of the Nuffield Council's study of gene patenting and was chairman of the U.K. Commission on Intellectual Property Rights and Developing Countries.

He looks far too young to be a Professor Emeritus, but I'll turn it over to you, Mr. Barton.

MR. BARTON: Thank you very much. First of all, I must own up that I'm going to deviate somewhat from the international focus, if that's acceptable. I'm going to spend some time on precisely the international focus based on work with the Nuffield Council, and then, because it seemed eminently appropriate, tell a little bit about a real-world experiment, a factual experiment that I have not published but that seemed particularly important, and then come back over to the recent Supreme Court cases because they really are producing a very fundamental change in patent law.

I don't think I need to tell you about - well, I do want to say one thing about gene patents. I think it's extremely important to remember when we talk about patents that we're talking really about particular claims, and the question is what is claimed? It's easy to say that a particular gene sequence is patented, but what does that actually mean? It usually means something like I claim the isolated sequence; in other words, in essence, so to speak, a very long oligonucleotide that has been cut off from the rest of the DNA. I claim constructs like a production organism that has those sequences put into it so you can produce a particular protein easily. I claim the proteins. Maybe I claim the research use. It's very important to distinguish between these because that really affects the effective scope of the patent.

Now, the reports that I'm prepared to talk about, and I'm going to concentrate on just the first of these, are the Nuffield Council on Bioethics, one which I was involved in about five years ago now, but note that many of the same things were said in other recent studies.

Let me say just a little bit about the Nuffield group. It was very heavily an academic group. There is an academic geneticist on it, there's an academic philosopher on it, there was a retired eminent person from the pharmaceutical industry. There was nobody who had had background in the diagnostic industry, and I think it's important to recognize that in evaluating the conclusions. We really had three themes that we were trying to put together. One was we figured it was absolutely crucial for Genentech to be able to produce TPA; i.e., a natural human protein that has a therapeutic purpose but wouldn't be practically available unless made through genetic engineering. It's absolutely important to have that kind of product.

Then at the other end, because that obviously argues for broad patenting, but then arguing in the opposite direction for some of us is the question of the research tool use, the relationship between the biotech industry, which would like to have lots of things patented in terms of research theories, genes, receptors, everything like that in order to be in a good bargaining position for raising capital with the pharmaceutical industry and then produce its products for the pharmaceutical industry. So there's a big split in the industry on that set of issues, as well as between the academic scientists and the industry.

Then, obviously, the diagnostic testing question where the tension which you've seen all through today. The tension is clearly very significant. To what extent do I want to preserve (inaudible) for preserving these diagnostic tests by expanding patentability, and to what extent do I want to preserve access by narrowing patentability?

Now, what we did was attempt to fundamentally recognize - and I'm going to read a

conclusion in a moment - fundamentally state legal principles firmly and severely in order to try to reduce the problem as much as possible. In a sense, looking at the numbers which my colleague Joseph Straus showed, looking at the numbers to a great extent, clearly Europe has done that. The number of patented gene sequences in Europe is obviously - I calculated no more than 10 percent of the number in the United States. So there is a difference there.

But then I think what was in some sense our most important insight was that we wanted, to the extent possible - and we talked about this, although it appears more as a theme than as a conclusion - we wanted to distinguish between a DNA sequence as information, which we want to keep in the public domain and useable as broadly as possible, from that sequence as a chemical, which is legitimately patentable, because that's fundamentally the distinction we tried to push. You can see immediately why I want to make sure that we emphasize what do we mean when we patent a gene, and I want to talk a little bit about claims.

So in a sense, if we could make that distinction effectively, and obviously doing so was extremely difficult, then we would have solved some of the problems. To the extent that we do make that distinction, we effectively say diagnostic tests are unpatentable when the claim is in the form I have identified this mutation as associated with that disease and I claim the use of the mutation to detect the disease. We would leave patentability - and this is the kind of direction we went in the analysis - we would leave patentability for I have a particular gene sequence which if you use it in a particular probe will be good at identifying whether or not that mutation is there, but we have left it possible for others to try to find the mutation in other ways, as for example by sequencing the genome, and that would avoid infringing the patent. So that was the clear implication of where we were going, and to give you a sense of how far this went, let me quote from the conclusions.

"We recommend that the criteria already in place within existing patent systems for the granting of patents be stringently applied to applications for product patents which assert inter alia rights over DNA sequences for use in diagnosis. If this recommendation is implemented, we expect the granting of product patents which assert rights over DNA sequences for use in diagnosis will become the rare exception rather than the norm." We conclude that the protection by use patents for specific diagnostic tests - i.e., my patent on the particular chemical, the particular sequence which you use to find the mutation - we consider the grant of use patents as a way to provide an effective means of rewarding the inventor while providing an incentive for others to develop alternative tests. We then went on and you can see clearly a strong bias towards public access to tests.

We considered that in the case of patents that had been granted for diagnostic tests based on genes, compulsory licensing may be required. Now, this is something which I think the committee would probably find quite useful. It's available at www.nuffieldbioethics.org. Obviously, it's now five years old. Nevertheless, I think we had some very good insights in it, and I think it's well worth your review, recognizing that it has to be brought up to date. I think I'll pass this given where we're going.

With that background on the Nuffield Council, I would say it was well accepted within the British community. The way a commission works in the British community is a little bit different from the way a commission works in this society, and it's a small enough society that you get feedback from all kinds of different directions on a personal basis. The feedback was quite positive.

The second point I want to talk about is the real-world experiment which I had done, and I did it in significant part while I was at NIH two or three years ago. It's unpublished, but I thought it was so relevant to you. I talked with the Duke people and I'm going to give them all my data. I felt concerned because all the critiques I'd seen of diagnostic patents take the bad side. They take the side of saying here are the cases in which access has been denied. None of them look at the other side of it, to

what extent is there an incentive. So I attempted to say in order to try to solve that problem, instead of looking at all the patents and diagnostic tests for which there are complaints or concerns, I would choose as best I could an unbiased sample of diagnostic tests, and I called up GeneTests up in Seattle and got their 10 most commonly chosen tests and their 10 most common gene review access tests and put those 10 together. There was some overlap. So based on that, I got 17 gene tests that I attempted to look at, and I looked at in each case to the extent I could what kinds of patents covered those tests, and it was clearly a nightmare. I mean, it was clearly not random. I put that forward in big, bright letters because it was an interesting game in itself in which in some cases I had essentially to go to the scientific articles that I found from the gene test area, find out whether or not their names appeared on patent applications. I mean, it was not an easy thing to do, and I found all kinds of patents. You can see again all the different kinds of focuses of these.

But what came out very interesting when I looked at them is that although the number of patents were divided roughly evenly between what I called the private world - i.e., the Myriads of the world - and the public sector - i.e., the University of California, et cetera - there was a significant focus. The private emphasis was heavily focused on hereditary hemachromatosis, on BRCA, and on spinomuscular atrophy, and almost everything else was public sector. The obvious implication, and it's kind of obvious when you step back from it, is that for what looked like the most popular, biggest market kinds of tests, patents and diagnostics work. They encourage private sector innovation. For everything else, it's done under NIH funding or Howard Hughes funding or what-have-you, and we don't really need a patent to encourage the innovation - maybe. I'm going to give a critique of that.

So the implication is the incentive effect works strong for the most common genetic diseases. For the others, we are assuming - and this is a point which I haven't heard mentioned at all today and I think is extremely crucial - we are assuming it is an easy leap from detecting the gene sequence to having an effective diagnostic test. That depends, in fact, on what the FDA does about the regulation of diagnostic tests. If the FDA makes it harder to bring a diagnostic test to market, then maybe we need a patent. I mean, I'm sure you've all heard the story which is accurate that if a university invents a new pharmaceutical product and puts it in the public domain and writes an article on it, the market product will never see the light of day. You need a period of exclusivity in order to justify the elaborate tests that are necessary in order to bring the product to market, in order to justify investing in the clinical trials. Clearly there is an interplay between the value or not of genetic patents and the regulatory standards we apply to them, and I think that's an extremely important issue which should be considered.

I might also note a couple of other nuanced differences between the old world and the new world. I mean, this study was two or three years ago. The Myriad controversy, which has taken a fair chunk of the day, was essentially five years ago. Let's look at today's issues. I actually published an article last summer in Nature Biotechnology on patents and pharmacogenomics, basically. Consider the interplay between the company which has intellectual property rights on a pharmaceutical product and the company which has IP rights on the diagnostic test which you use to decide whether or not that particular pharmaceutical is appropriately used on a particular patient. In fact, my article talks about the Herceptin example. It turns out that in the Herceptin example, a Genentech product, Genentech went and, in essence, sponsored the encouragement of some diagnostic companies. It won't necessarily go that way in the future.

There are, for example, a host of companies which are trying to claim fairly broad patent rights on P450, which is one of the key enzymes in metabolizing a variety of different drugs, and it's probably going to be very crucial in the future of pharmacogenomics. So that case might go quite differently.

I might note also that we're going to see more and more sophisticated kinds of

intellectual property that come from the big pharmacogenetic studies. We're going to see essentially the drug company finds my drug works well for this category of patients and not so well for that category of patients, and here is the elaborate mathematical function which is based on a zillion different mutations found or SNPs, depending on how the study has been done. Here's the elaborate mathematical function which is going to draw the line between the effective and the ineffective cases, and we're going to see people obviously claiming intellectual property on that. Is that a diagnostic test? That's part of the future.

I should admit a conflict of interest here because I've done some work for Affymetrix. The question of arrays in which you have a zillion different diagnostic tests based on one chip, clearly horrible problems if the marketing of a chip to, let us say, detect different sub-forms of cancer or different sub-forms of HIV which can be treated with which drugs and so forth, if some of those can be held up by patents on the use of individual sequences, it's going to be a very complicated life. So I simply kind of want to suggest as part of your thinking, make sure you look at these problems as well as at the other ones you've talked about.

Now, the final point, and I think I feel appropriate bringing this one in, is a little bit further data on how the law has changed since 2005. There are several major law-changing centers in this city within a very few blocks of where we sit, and the Supreme Court has really decided - and I think I may as well put it straightforwardly - the Supreme Court has really decided that it does not like the direction that the Court of Appeals for the Federal Circuit has taken patent law in. I think that's pretty clearly what has happened. I think every one of these cases that I'm listing, plus a couple more - and I'll have to drop the second one from the list, as will be clear in a minute - are cases in which the Supreme Court has reversed the Court of Appeals for the Federal Circuit. Every one of them makes a major change in patent law, and we're talking within the last two or three years. Let me just kind of walk through them very quickly, spending most time on coming back to LabCorp, which I think is the crucial one for our discussions here.

Merck v. Integra, this said, in essence, that the statutory research exemption can be applied very, very broadly. In my judgment, although I think there are people who disagree with me, in my judgment it has radically changed the balance between the pharmaceutical industry and the biotech industry. It has told the pharmaceutical industry you can infringe a lot of biotech industry patents as long as you are doing so as part of a regulatory process. That's extremely significant for the research tool set of questions, which are of course another part of this genomic patent issue but clearly is not your focus.

eBay v. Mercantile Exchange decided last year that the standards for deciding when an injunction should be issued should be a lot more narrow than the Court of Appeals for the Federal Circuit had had it, and the clear implication is no longer is an injunction automatic. There are now two sides to that debate, and to take a serious example, suppose my gene chip has your patented test on it along with a zillion others that are important to a particular diagnosis. Can you get an injunction to keep my chip off the market? It's not crystal clear at all, but very likely that since eBay, you cannot. You can get a right (inaudible) for damages, but obviously that doesn't bring you nearly the bargaining power that the injunction does. But I do note that there was a case interpreting this one in Texas just about three weeks ago in which the question was can CSI Arrow, which is the Australian analog of the National Science Foundation or the Indian Council for Science and Industrial Research, can it get an injunction prohibiting use of, in this case, a technology involved in a standard for the wireless phones or something like that, some electronic standard? Can it get an injunction in that context, and the trial court said yes. It hasn't worked up the ladder, but the trial court said yes, even though obviously this company's only interest is in - the Canadian research institute's ultimate interest is not in producing a product but in obtaining a royalty. So there are some questions about that one.

Then the KSR International case just this last term has radically changed and radically

tightened the standards of non-obviousness in the United States, making us look very different from where we were.

But now I want to come back to LabCorp, and here again I own up to the conflict of interest. I co-authored a brief here and co-filed it together with Affymetrix, and I think the briefs for this case are something which you all may want to look at, as are the decisions. The case fundamentally involved a correlation, and I must admit I always forget what the two compounds are involved in the correlation, but it involved a correlation between two chemicals in the human body and use of that correlation for diagnostic purposes. One of the components was folic acid.

So it said, in essence, if you measure compound X and use it to infer that there is a deficiency of compound Y in the body, you're infringing my patent. The initial trial case was brought literally on the grounds that said doctors were infringing the patent every time they did this analysis, and then the company which provided the diagnostic test to help the doctors was a contributory infringer and should therefore be sued. That's a fairly standard kind of game in terms of how you find a defendant in the patent business.

Well, this was something which under today's law, as interpreted by the courts for probably the last 20 years, was clearly patentable. This was anything under the sun, to go back to Chakrabarty. This was clearly patentable, but on the other hand this was very close, going back to my Nuffield Council report, this was very close to the information. This was very close to a discovery rather than an invention, and that point had just kind of been passed over in the law of the past 20 years. We had assumed that it had been conceded, and the case was being appealed to the Supreme Court on other grounds, and the Supreme Court issued a very surprising memo that said we aren't interested in those grounds; we want to hear about subject matter grounds. I'm paraphrasing, of course, but isn't this really a discovery, not an invention? Please tell us about that. That's what we really want to hear about.

Now, first of all, it's very odd and unusual for the Supreme Court to do anything like that. Second, this issue hadn't been discussed at all at the lower court level because everyone assumed that the law had been settled. As a sense of how much everyone assumed that the law had been settled, the Department of Justice or the Solicitor General, whoever it was, the U.S. government came in with one of its amicus curiae briefs saying, look, you change this body of law and you're going to upset zillions of existing patents and settled expectations based on those patents. Obviously, the government didn't go on to say that. This may or may not have been an invoking interpretation of law 25 years ago, but the law has kind of crept in this direction and we don't think you should go to bat quite so dramatically given how much people relied on the old law.

The Supreme Court went ahead, heard the case, and then it came down with a very cryptic opinion. First, the majority opinion was we granted cert improvidently. In other words, we shouldn't have heard the case, we're not deciding it. Three judges dissented and said this invention should have been struck down as non-patentable. This is really a discovery. It is abundantly clear - and this is why it's crucial for you all - that if those three judges prevail, gene diagnostic patents are toast. They're gone.

So the real question, then, is what this bizarre situation means, and let me give you three possible interpretations. First, the hornbook interpretation. You are not supposed to draw any conclusions at all from the fact that the Supreme Court has not granted cert in a case. That's simply a procedural thing and you're not supposed to pay any attention to it, and therefore the law remains what it has been for the last 20 or 25 years, and the diagnostic test is patentable. Alternative 2, at least six judges didn't want to hear the case. Maybe they all felt gene tests with diagnostic correlations were patentable, and therefore gene patents stand. Version 3, three judges expressed this position. The other five judges decided that in this very bizarre and unusual patent, it wasn't appropriate to go ahead and bring the case to

judgment. Let there come up a case in which the issue has been debated at the trial level and we get all the arguments and so forth, so that at least some of those six judges were coming out the other way on procedural grounds rather than on substantive grounds. We have no idea, of course, which of these versions is right.

But the net result is, I would say, the amount of money that I can obtain as a royalty for a diagnostic patent has shrunk radically. Clearly, these patents are in question. Maybe, in essence, the court has sent a signal saying the next time we get one of these cases, we're going to come down the other way. But precisely because this amounts to such a change in the law, we want to do it with a little bit of warning.

Now, before you go on to say whether or not that warning will really work or anything, consider the incentives for people to bring the litigation. I am a company which has some diagnostic patents. You infringe them. How much do I want to bring the issue to the U.S. Supreme Court? Probably only a little more than you do, and neither of us wants to spend the money doing it. So what I want to suggest is that it may well be that the effective business implication of this will be to leave diagnostic gene patents in a kind of limbo which may last forever. We may never get a Supreme Court decision on it, but in a kind of limbo where they're clearly a lot less valuable than they were not too long ago. And then even if I won the case, if I'm suing you on a gene patent, pretty clearly the extent to which I can get a remedy is going to be cut down by the eBay case, whether or not I can get an injunction, and whether I can get an injunction against you on the research tool context is going to be cut down by the Merck case, and whether or not the invention was obvious in the first place is going to be cut down by the KSR case. In other words, there is a very good chance that in its (inaudible) reform program, the Supreme Court has changed the law in exactly the direction that the Nuffield Council report wanted to go.

Thank you.

(Applause.)

DR. EVANS: Thank you very much. That was a great talk, very illuminating and very helpful.

Our next speaker is Christina Sampogna. She serves as a lawyer at the Organization for Economic Cooperation and Development, its Biotechnology Division. In this role, Ms. Sampogna manages initiatives pertaining to the life sciences, including intellectual property, R&D, innovation, human genetics and genomics, and counterfeiting. Previously Ms. Sampogna managed the unit that developed the Canadian government's patent policy for the field of biotechnology which required legislative reform, and she's provided legal and policy advice to governments and expert committees on a broad range of topics.

Today she's going to tell us about the OECD's guidelines for the licensing of genetic inventions.

MS. SAMPOGNA: Thank you, and thank you to the organizers for inviting me. I was actually going to thank the organizers for inviting me to a very sunny city, since in Paris it's 11 degrees and rainy. If I had spoken this morning, I could have said that. Right now I can't anymore. So thank you, Mr. Chairman.

As the Chairman indicated, I'm going to be speaking about the OECD guidelines on the licensing of genetic inventions. I understand that the purpose of this meeting is to look at a number of these related issues in the sense of to look at licensing, patents on genetic material and especially the field of diagnostics.

Just briefly, the point of the OECD guidelines is really to address a number of issues when we were developing them in terms of the stifling of innovation, the stifling of research and the stifling of access to technologies, and especially therapies and diagnostics. So they offer a set of

principles and best practices in terms of fostering research, fostering delivery and accessibility of products and commercialization, and they do this in a balanced way. What they aim to do is sort of take into account the multitude of factors that have been mentioned all of today that come into play. So what they try to do, they try to actually balance the different competing interests that are in the marketplace, so balance the interests between the researchers and the need to commercialize technologies, the different interests between the private sector and the public sector, and between fostering R&D and facilitating access to technology.

I was going to go through and explain what the OECD was, but given our timing I'll just skip that. I'm going to quickly go through in terms of some of the challenges that are arising in the life sciences. I'll speak to a bit of the context of the guidelines in terms of what was going on when they were being developed and why are they relevant today. Then I'll provide a very brief overview of the guidelines that are actually quite detailed, and there are quite a bit of annotations, and you've all received copies of them I understand. So I won't really go into details. What I'll do is I'll try to highlight some of the key concerns that each of the sections aims to address and some of the points that might be relevant to the deliberations of this committee. Then I'll speak to the issue of implementation of the guidelines and the impacts, which I understand is also of interest to this committee in terms of, again, how can they be useful in the American context. Then just before I conclude I want to speak about a new initiative that kind of flows from a lot of this about Collaborative Mechanisms for IP. The idea there is just how do we use intellectual property and intellectual property rights in a different way. How do we leverage it differently so as to move research forward, stimulate innovation, and possibly provide greater access to technology?

So just really quickly, these are two graphs that actually show the amount of investment in the pharmaceutical industry, but really all I wanted to highlight on these graphs were the points that investment in R&D has actually been increasing. The graph on the left-hand side is the from the FDA report on stagnation and innovation, and it's mirrored in the chart on the right-hand side, which comes from actually PhRMA's annual report for, I believe, 2006. So they kind of just show an increase in investment in R&D over roughly the same period, and what's interesting is that while investment in R&D has increased for that same 10-year period, actually what the FDA found was that the new products that were brought to market had actually decreased. So the new NMEs brought to market or applied for, actually, if you look at the chart on the left-hand side, had actually decreased, and then what's called Figure 3 here on the right-hand side, again the FDA found that the cost had actually increased of bringing the product to market. It's a more complicated issue than just being captured in two or three graphs, but just this idea of we're investing a lot of money in life sciences and are we really getting value for it, and how do we get better value for the investment that's going into this sector.

So those are some of the challenges and, as I said, those are actually challenges that we're looking at in the new initiative called Collaborative Mechanisms that I'll just briefly cover later on. But another set of challenges, and there's been a lot of talk about this today, so I'm certainly not going to go over it again, but just this idea of patents and the trend in patents and the fact that really there is an increase in the number of patents being applied for. This is a chart that's a little bit dated. It's from the World Intellectual Property Organization, and it just shows the number of patents filed in the biotech industry for roughly about 15 years. Yes, we saw a lot of data today about how the trend is sort of tapering off and there are changes, but I don't think we can say today that overall there will be no more patents on genes that will be applied for or filed. I think that would be rather unrealistic. So we still have to contend with future patents, but importantly we also have to contend with the patents that have already been granted. They're still out there and they're still going to be applicable.

This was just a chart to show trends in patenting both in terms of filed and in terms of

granted globally from the World Intellectual Property Organization.

So the context of the guidelines. What do they actually do? Well, this is their main purpose. They try to address the issues pertaining to the licensing and the technology transfer of genetic inventions with the aim of fostering R&D, stimulating innovation, increasing access and diffusion. Really, they provide guidance to the marketplace in terms of encouraging access for the delivery of health care products and services, for research, and for commercialization purposes.

The guidelines were adopted by the OECD Council. That's our highest decisionmaking body, and it's the official body of the organization. It takes the senior decisions. In fact, what it does is it can take legally binding decisions and non-legally binding decisions. There are very, very few legally binding decisions because they become international treaties. There are also very few non-legally binding determinations because they speak to a strong moral commitment on the part of the OECD member countries, and I'll just mention that the OECD member countries are the 30 most industrialized countries in the world. So these were adopted at the Council level, which means there's a strong moral commitment to their implementation.

They were also developed with a wide breadth of stakeholders. We did public consultations with over 200 stakeholders around the world, including developing countries, and they provided very useful input. So their implementation also should involve the wide breadth of stakeholders. So I'll just quickly go through the guidelines themselves and try to give a sense of some of the points that could be useful for the deliberations of this committee.

The guidelines are actually intended to be quite broad. I mean, there's an actual definition of the scope of the guidelines, but really that's just more useful in terms of trying to determine what they apply to. But they're also intended to be forward-looking in terms of future developments and future innovations that weren't yet feasible when they were adopted last year. They're divided into five sections, and I'll go through each of the five sections really quickly.

The first one is actually the licensing generally. So there are a slew of principles and best practices generally applied to the field. Really what it does is this part of the document sets the tone for the rest of the sections. I put up here - I'm not going to go through every single one of them, so rest assured. The very first one I think is the one I put up here, and for a very good reason, that it actually sort of sets out the key objectives in a very simple way in terms of fostering innovation for the development of new genetic products and services, and at the same time ensuring access to those products and services, and on a reasonable basis.

I think those are some of the key elements to the point that there's both a balance, and even within access there's a balance between reasonable commercialization and then ensuring reasonable access.

Pricing had been one of the issues that was of concern when these guidelines were being developed. There was anecdotal evidence that, of course, there were situations that had arisen where there was difficulty in obtaining access to products and technologies, and in addition sometimes there was difficulty due to the fee that was being charged. That's why the principle was put in there.

The next element that this section covered was this issue of stifling research and stifling access to research. What the Principle 1B encourages is it tries to balance this need between the rapid dissemination of information and research, especially from a researcher's perspective, with the needs of the private sector in terms of commercialization. So it does that in a number of ways, which are in the best practices.

The second part speaks about health care and genetic inventions. This section is really about this balance between access and choice in the sense of trying, again, not to limit the choice of patients and health care providers, and it also creates a balance between the needs of health care providers

and patients. So it entreats licensees and licensors to not restrict choice of product and services. It entreats them to make them available to both patients and health care providers and to allow health care providers to have the flexibility to determine what is the best product for their patients so that, again, there is a clear choice.

Then another really important point that this section covers is with respect to privacy. Professor Barton had actually spoken about genetic testing and someone had mentioned, one of the committee members had mentioned genetic testing should be done locally. In fact, we've actually carried out a really extensive survey across 18 countries on genetic testing, and what we found is that most of the testing wasn't actually done locally. Most of the testing crossed borders. One of the key issues in that was the concerns of privacy, concerns of quality, and concerns of reporting back were quite significant. There are a number of different issues with that, and in fact we actually have just published guidelines on quality assurance for molecular genetic testing which just were published actually last week.

So these guidelines actually address the issue of privacy, which is a really important issue for patients, and we entreat, again, licensees and licensors to allow the highest applicable standard to be employed.

Research freedom is the third part of the guidelines, and it's really about, again, this balance between the need for academics, for researchers to publish and to get the information out there versus the needs of the private sector often to delay publishing or to restrict the publishing of some information or some data, and how do you find that balance between them. So there are a number of points that are made in this section about confidentiality, about trying to reduce their scope, and in terms of how do you balance that with the needs for commercialization. Of course, one of the points which is very important was that commercialization should certainly not hinder educational training.

Section 4 was actually about commercial development. The idea wasn't really to restrain it but really to identify practices that had been identified and that were being carried out in the marketplace and that were having undesired effects. So what the Section 4 does in terms of commercial development is it tries to identify a number of behaviors that, while not illegal or illicit and therefore permitted in the marketplace, certainly in the context of biotechnology and in the context of genetic inventions and genetic testing should be avoided or should not be favored because of the effects that they may have produced or had produced in terms of anecdotal incidences. Some of them were already mentioned.

I'll just quickly go through them. Royalty stacking and multiple licensees were some of the practices where, again, not in and of themselves, but these sort of create hurdles. When someone wants to commercialize or develop a technology and there are many, many patents, there are a number of issues that arise with that. Identifying the patents is one of the biggest obstacles, and then obviously negotiating to obtain the license with all of those patent holders is quite complex and involves quite high transaction costs, and then the licenses themselves. So the licensing fee, the royalties, can be quite high, especially if you accumulate all of them. So these are some of the issues that we addressed in several proposed different approaches and make recommendations on.

Another issue that has actually also been mentioned earlier is this issue of reach-through rights. Of course, there are situations where reach-through rights are actually quite useful, but there seem to be some issues around reach-through rights reaching through to the final product which creates, again, a disincentive for innovation.

Then another key point that has been mentioned is exclusive licensing. Of course, it is recognized that exclusive licensing is sometimes very useful for the commercialization of technologies and of products, but there needs to be a balance in terms of when is it useful and when is it not useful, and how to actually limit the effects of exclusive licensing. So there are different ways to do it, and some of

these are enumerated in the guidelines.

Then the final section is on competition and competition law. Of course, it entreats licensees and licensors to actually comply with competition law, but more than that, it actually indicates that while some of the behaviors like tied selling, non-compete clauses and the breadth of exclusive rights are permitted, that really in the context of genetic inventions they should be avoided because of the effects that they have.

Then finally, in terms of one of the key points is this fundamental genetic inventions, that they should be licensed non-exclusively. Really, what we had contemplated when we thought of this notion of fundamental genetic inventions is that we were thinking of fundamental inventions like PCR, like research tools.

So one of the issues that I was asked to think about is the implementation and the impact of the guidelines and how can they be useful for the American context. As I mentioned, the guidelines were adopted last year, in 2006, so many countries are actually working through how to implement the guidelines. One of the things that I think would make a significant contribution to their uptake, if you want, is that governments actually support them, and there are different ways of doing it. For example, depending on the resources, of course, some countries, like the Czech and the Polish governments, have actually distributed in English the guidelines to a large segment of the government, of the private sector, and of the public sector.

With that type of diffusion, it's very simple in some ways, just providing information to market players. But what it does, coming from a government entity, is it actually sort of tells the market participants what the government considers to be good corporate behavior. In business law, we have this notion of corporate social responsibility, and I think in the biotech licensing field the guidelines can be used in a way to generate corporate social licensing, how best to license to again retain a return on investment but at the same time not stifle others, not stifle innovation.

Other governments have actually translated the guidelines. They've been translated into French, Japanese and Italian, and they're now being translated under the guidance of Professor Straus into German, and I should mention that actually Professor Straus was the chair of the expert group that worked on these guidelines, and so we actually owe him quite a lot.

Of course, translation isn't an issue in the United States since they're in English, but the other interesting thing that governments have done is they've actually made them available on their websites, and I think that's also a good tool in terms of communicating.

Then there are funding policies. What do I mean by funding policies? NIH was really good at this. They actually developed the Best Practices for the Licensing of Genomic Inventions and published them in 2005. What's really interesting is that actually both of these two sets of guidelines were developed in parallel. The people who developed the NIH guidelines were actually involved in the work of the OECD, and the NIH guidelines have been incorporated into the funding policies and therefore are involved in any of the grants that the NIH makes. Given the amount of grants that the NIH makes, it is actually quite impressive in terms of the full potential that it might have to impact them.

But the NIH is not the only one. There are other funding agencies, whether public or private, that could adopt similar sets of guidelines and therefore have a fuller impact. There are also government research centers, not necessarily the ones funded by NIH but other research centers that are government or public that could also adopt, again, either the guidelines or similar guidelines based on these.

(*Tape flip, 5A to 5B) social licensing becomes really interesting in the sense that industry can adopt the OECD guidelines. Again, they would be guidelines, they would be guiding principles, but they could actually take them and use them as their guiding principles. This has been done

in Japan, where the Japanese Biotechnology Association has actually done that. They put the guidelines up on their website. They made them available both in English and in Japanese. They've actually printed booklets of the guidelines in English and in Japanese and distributed it to all of their members, including the pharmaceutical sector, and they're developing additional guidelines based on the OECD guidelines.

In terms of diffusion, as I just mentioned the JBA, the Japanese Biotechnology Association, actually did quite a lot. But in terms of the equivalent being done in the United States, we can think of BIO association during a similar activity in terms of either, again, distributing the guidelines directly or an adapted version of the guidelines to their members, and again adopting them as sort of guiding principles.

Some of the elements in the guidelines are actually quite practical and they can be implemented directly. Others are more stated as an objective of what good corporate licensing and behavior should be.

Now, the public sector. Obviously, the largest public sector that would be of interest would be the universities, and there are a number of best practices and principles in the guidelines that can be implemented directly by universities in their technology transfer practices, but I think they can also be adopted at a higher level as guiding principles. I was really interested in the nine points that were issued by the 11 universities and the AAMCs just a few months ago here in the United States. I think that's an excellent initiative and I think, again, other universities can adopt the same approach, or an association such as AUTM can adopt a similar approach in developing guiding principles.

So these are some of my thoughts on how the OECD guidelines may be taken out, deployed, diffused and hopefully change the corporate behavior. Just before I conclude, I said I did want to mention this Collaborative Mechanisms for IP. Part of the background research and what we heard in terms of doing work on the IP guidelines was this idea of there being many patents and how do you deal with that and all the uncertainties around that. So what this project is about is exactly that. I don't have a pointer, but it's this idea that there are a number of different mechanisms out there and how do you create these mechanisms for leveraging IP.

Now, most of these mechanisms have actually been used, but they've been used in other industries and not very often in the life sciences. So the scope of this project is to actually see how they can be used in the life sciences. So the blue circle with all the little patent documents is a patent pool, and the reason I have a radio there is because Radio Corporation of America was actually first founded as a patent pool, and it was a very successful pool. In fact, it set many of the standards both for radio and radio frequencies, as well as the standards for the follow-on technology, like TVs and so on.

MPEG LA is actually a patent pool, a more modern patent pool that was put in place in the 1990s. It's been very successful and it's actually moved the industry forward. There are a number of those patent pools that have moved the industry forward. Again, they're not in the life sciences. They're in the IT communications and electronic consumer industries.

On the right-hand side of the screen there's ASCAP and SESAC. They're clearinghouses for, again, music, films, that type of thing, and the idea behind the clearinghouse is you have many consumers, you have many purchasers, and how do you bring them together? So if we think of a song, any song, in a very simple way every time somebody wants to play Song A in every city - well, let's start even smaller than that - in every train station, in every radio station, in every hotel, in every nightclub, in every city, in every country around the world, they would have to go and negotiate with the songwriter, the producer, the performer. It becomes unmanageable. So that's why these societies came into being, because you actually buy the rights through the societies and it facilitates the exchange of rights.

So the idea is could you not do this in the life sciences where you have many patents,

many IP rights, and instead of going and negotiating with every single one of them and not knowing who all they are, couldn't you do it through some other mechanism like a patent clearinghouse? We don't have all the answers yet. They're just some of the questions we're asking.

There are other mechanisms. There's a whole slew of different mechanisms, and a report will come out later this year. I have the International HapMap there because actually the way they were set up and the way the SNP Consortium was set up was very interesting as well, because it brought in different interests.

So simply in conclusion, there are a couple of points I did want to make. I think this is a very complicated field. I'm certainly not going to sum it up, but I think one of the things that is really the key message I'd like to be the take-home message of the day is that behavior will be influenced to change when the entire community, when government, when the private sector, when the public sector, when civil society acts in a coherent manner to affect change so it changes the way they're thinking and the way they approach the problems. It's quite a challenge; I recognize that. But I think that's what documents like the guidelines and discussions like these actually do, that they allow the dialogue and they allow the movement forward. Thank you.

(Applause.)

DR. EVANS: Great. Thank you. That was great.

If we could get the last two speakers up to answer questions, and then we'll quickly move on to our general discussion. So for Mr. Barton and Ms. Sampogna, if we could have any specific questions, we'll keep it fairly short and then get on with our discussion.

Julio?

DR. LICINIO: For Ms. Sampogna, this idea of a clearinghouse for the life sciences is very intriguing and it's one of the issues that we discussed before in terms of individual patents, how can you develop a (inaudible) if you have to deal individually with a lot of people. So is it more than an idea? Who else is talking about this, and is this going anywhere?

DR. SEGER: Push to talk.

MS. SAMPOGNA: Thank you, and thank you for the help with the technology.

DR. EVANS: It's patented.

MS. SAMPOGNA: It's not always diffused.

That's an excellent question. Actually, there's a lot of interest and there's a lot of enthusiasm about the idea. It's obviously very complicated. They're not easy to set up, and if I look at the ones that were set up in the IT field, it took many years. So this isn't something that is feasible in six months. But there are a number of government reports that have actually recommended the development of this. There are a number of industry players, both big and small and medium-sized companies, that are interested in this and that are interested in working with us to develop this initiative, and we have a lot of countries beyond the reports that are published that are actually very interested in working with us to develop this initiative.

It's a very interesting, it's a very intriguing, it's a very exciting initiative, but I think there are a lot of challenges, so I don't want to over-simplify the issue in terms of saying it's feasible with this type of thing. I don't think it's that simple. But yes, I think there's a lot of interest.

DR. EVANS: Along those same lines, what are the types of incentives that can be implemented, say by government, to encourage the formation of patent pools or clearinghouses? Because these are voluntary things, and I think to some extent the different corporations and et cetera are driven to it by necessity in the end. But are there ways of incentivizing it?

MS. SAMPOGNA: Again, that's also an excellent question. It's one of the issues we're looking at. Actually, I have an entire two-hour presentation I can give on that topic, which

obviously I didn't, and I won't. Some of the pools that were formed were compulsory license pools. So the government stepped in and said the industry is not working properly. We need this technology and we need it developed, and they actually sort of brought all the pools into them. The example that many people are familiar with is the one in aircraft industry at the beginning of the 1900s, during World War I.

Many of the others are actually volunteer, and it's not clear why. I mean, sometimes it is, because they need to do business. That was true for the DVD pool, for example. They needed to do business and they were blocking each other, but that's not always the case. So there are a couple of really key challenges, and one is obviously what are the incentives for these being formed? Another one is a standards issue. A lot of the pools that have been formed are around the development of a standard, either an existing standard or the actual development of a standard for that particular sub-sector of the industry. It's a bit more complicated in the life sciences to develop standards. There aren't that many in many ways. So that's another challenge, because although historically there have been standards associated with patent pools, one of the issues is do we actually need a standard? Again, that's one of the issues that we're looking at. Other issues that are quite complicated are the competition law issues because, of course, there have been a number of patent pools that have been formed but they were anti-competitive or they were there for price fixing or whatever, and those have been invalidated.

Now, what's really interesting and encouraging in regards to that issue is if you look at the three major sectors - not sectors but countries or jurisdictions, the United States, the European Commission and Japan, they've all issued guidelines on patent pools, on standardization, standard-setting and how to deal with them. They're very general, but they're very optimistic in another way. The FTC and the DOJ have actually been really, really positive if you look at the more recent formations of the patent pools in terms of actually working with the developers, the initiators of the pools and making sure that the pools actually meet competition law, anti-trust issues.

DR. EVANS: Thank you very much.

Emily, I think you're next.

DR. WINN-DEEN: Yes. So I guess my basic problem with the philosophical approach that we've been taking today is that I think there is probably unanimous agreement that there's a set of best practices out there that everyone should follow, but the problem guys are the ones who don't follow them. So we need something more than just best practices, because best practices would not have kept Myriad from doing what they did. It wouldn't have kept the Canavan story from ending up where it did. I've encountered one or two incidents in my life as an end-licensing person where despite sending a technology transfer office the NIH guidelines and saying, by the way, there are at least three or four of us out here who are interested in a non-exclusive license, the incentive for a tech transfer office is to make a big-money, exclusive license, and that incentive is completely at odds with all of these guidances.

So if you're the poor schmuck working in the tech transfer office, who are you going to follow? Are you going to follow the guidance that's depending on what your raise is going to be that year, or are you going to follow some theoretical thing that emanates from NIH or one of these other organizations?

So I think we need something that has more power to it than just guidance, but we also need to recognize that there is a really big disconnect between tech transfer goals and all the things that we've been talking about today, and I don't know how to reconcile those except by just saying it is NIH policy, if this was developed under NIH with Bayh-Dole money, you will not be allowed to do an exclusive license, rather than saying we think it's best if you consider non-exclusive.

So I think there are a lot of companies, a lot of universities, a lot of people who are doing the morally right thing and trying to disburse things in the right way for patient health, but there are always some bad actors who are just not going to do what they should unless they're forced to, and I don't

know how to deal with that. That is, I think, what we really have to struggle with.

DR. EVANS: Yes, I think that's one of the biggest things we have to grapple with, is that issue. You essentially have to force people sometimes to do the right thing. You have to incentivize people with tangible incentives. You can't just expect -

DR. WINN-DEEN: But in the end we have laws and cops because we recognize that not everyone is going to do the right thing.

DR. EVANS: Right.

MS. SAMPOGNA: Thank you, Mr. Chairman. That's an excellent point. In fact, I was going to actually raise that point but I didn't want to go into it this late in the afternoon. I think you're absolutely right. I think there's a sort of disjunction between how we incentivize TTOs versus these goals that we're trying to achieve, and you're absolutely right. For most of the TTOs, there's a lot of work that's been done in terms of they're interested in the short-term, high-return, get the money in and think about long term at another point in time, and that's a real challenge. But the utility of the guidelines isn't just for them, first of all; and then second of all, I don't think that just because that isn't working, that they're not useful.

Why do I say that? Well, because when we were developing them, we did this public consultation with hundreds of stakeholders from every sector around the world and we got a lot of feedback that even the entities who are trying to be good corporate citizens, sometimes they're a little unsure of what it actually means, and to have the document say, well, here is some guidance, here's how you can do it or not do it, is useful for them. That was one of the recurring themes that came through in terms of, again, saying thank you for doing this, this is great and we're looking forward to the final product and what-not.

So that's one element. Then the other element is - you're absolutely right, there's going to be bad corporate behavior, and it's always going to be there, and so the aim is to try and minimize that. So you can have guidelines, but you can also have the guidelines, as you mentioned, in a very enforceable way. You don't necessarily just need to have them as soft law. There can actually be an enforcement element added to them.

DR. WINN-DEEN: Yes, and I didn't meant to denigrate the work of coming to consensus on what guidelines should be. I think that's very important work, to reach a point where all the voices have been heard and there is some sort of common ground that's emerging, but I still am worried that all the bad stories we heard wouldn't have been dealt with by any of the guidelines that are out there.

DR. EVANS: Kevin is next on the list, and then what we need to do is we'll get everybody up here, go through the last few slides of just general questions and discussion. So if we could get - we've got Dr. Straus and Ms. Sampogna. Excuse me. Dr. Straus, if we could get you up here, and Dr. Parthasarathy, and Mr. Barton.

Kevin, you go ahead.

DR. FITZGERALD: This is for Professor Barton. I'm intrigued by your interpretation of the consequences of Metabolite and the idea that, in a sense, because of what happened, we may end up where the Nuffield Council sort of wanted to go anyway. So speculating, if that had not occurred, if the decision had gone one way or the other on the Supreme Court, would either decision had gotten us to a place where we didn't want to go?

MR. BARTON: Well, I think that's a very fair question, and I think it depends on who the we is. That is, I think if you're Myriad, a decision definitively upholding this kind of patent would have gotten them where they wanted to go. I think if you're a health administrator, a decision striking down this kind of patent would have gotten you where you wanted to go. Where we are is obviously somewhere in-between.

DR. EVANS: Okay. Now, the way we're going to structure this is we've got a few slides, and I hope they won't blind you all. As we discuss these, when there are pertinent questions for our panelists, go ahead and I'll put you on the queue.

This first question I think has its answer just below it. How should pending U.S. patent reform initiatives be addressed as we develop recommendations? In other words, this is a rapidly changing field. There's legislation going on, there are court decisions going on, and I think the only obvious way to me is that we should probably have an update at the next session as to the status of such legislation and any court decisions that have been issued. Do people agree with that or are there other mechanisms by which you envision us keeping track of things?

Marc?

DR. WILLIAMS: Just an operational question. How important is it to present this to this entire group at that point in the timeframe of what you're actually doing, as opposed to just making sure that your group is up to speed?

DR. EVANS: That's actually a very good point. I mean, I think it would probably be reasonable to the task force to get an update from the appropriate people. If there are major developments, then we can report back to you people. I think that's a great idea.

DR. LEONARD: Well, going through all the initiatives that Judge Newman went through, there doesn't seem to be much that's directly relevant to patient access issues that we're looking at. So I would say that the update, we need to monitor it and see if there's anything relevant, and if there is, bring it to the entire group, but if not, then we just monitor.

DR. EVANS: That makes sense to me. Okay.

So this gets more to the meat of what we were trying to accomplish today. Are there approaches utilized by other countries or international advisory groups that could be adapted to the U.S. system? Which approaches should be used as models to apply to the U.S. system? That's about an eight-hour discussion, but does anybody want to weigh in with any specific comments or observations?

DR. WILLIAMS: Can you help me with a scope question here? As I understand our abilities, we can really work only through advice to the Secretary. So it seems to me that these questions have to be framed in the context of within all the realm of things that could be done, what can actually be done under the purview of the Secretary?

DR. EVANS: Right, and I think that we can certainly suggest things to the Secretary that are not necessarily exclusively the domain of the executive branch, right? Look at GINA and us weighing in on non-discrimination. So I think that, again, is kind of an operational question that as we begin to define where we're at and what types of recommendations we want to come down on, we have to think hard about how those would be implemented through the Secretary, what kind of advice we can give that is within the Secretary's purview.

DR. WINN-DEEN: Certainly there are things like NIH policy, what you put on a grant award, should there be something formally attached that says "I agree in accepting this money to follow the guidelines," period.

DR. EVANS: Right. So there are actually some very definitive kinds of things that can be done by the executive branch in that sense.

Debra, is this a good time?

DR. LEONARD: Could I ask Alan for clarification? The NIH develops policies, and it's like you're playing nice in the sandbox, but you actually have powers to march in and take rights over patents, I believe. Could you clarify what it would take, if that's true? And secondly -

DR. EVANS: Alan personally.

(Laughter.)

DR. LEONARD: And when you do, can I watch?

(Laughter.)

DR. LEONARD: But what it would take and what the inhibitions are to doing an action like that for a specific patent such as the ones held by Myriad, Athena Diagnostics, the ones that are of concern and have basically generated this whole discussion? As Claire Driscoll demonstrated, most of the patents held or exclusively licensed by Athena Diagnostics come from academic institutions. Therefore, NIH should have some ability to influence at least those patents.

DR. GUTTMACHER: So let me answer Jim's question first. It will be easier. No, you cannot watch, because if we did this, it would be in the dead of night, obviously.

(Laughter.)

DR. GUTTMACHER: To be honest, I don't know all the ins and outs of this, but you can imagine that it would be quite complicated and would have repercussions beyond NIH per se, and would be something that would have to be, even to the degree that it's doable, that would have to be legal counsel and other advice, because this is not a clear-cut, slam dunk that of course the NIH can just do whatever it wants to do in this area kind of thing. But I think in terms of recommendations to the Secretary, it would be feasible certainly to call the Secretary to ask the NIH and other federal agencies to look at their abilities to do this and to consider doing so under certain criteria, et cetera, et cetera.

DR. LEONARD: Well, it's kind of in stark contrast to look at what the U.K. did with Myriad and how the U.S. just kind of laid down and - I'll be polite - took it.

DR. GUTTMACHER: I don't think that's a dysfunction of the difference between the NIH and U.K. funding institutions.

DR. LEONARD: No, no, no. It's not, and I didn't mean to imply that. But looking at the system, why did we as the U.S., why do we allow Myriad to be the sole provider of a medical service that's important to a large percentage of the population of the United States when we've had statements made by multiple people that testing should be done locally, that that's in the best interest of patients and patient access, and I'm not targeting you.

DR. GUTTMACHER: I would think that the answer to that question comes from beyond the NIH.

DR. LEONARD: Right, right.

DR. GUTTMACHER: But I certainly share the view that it's an interesting question.

(Laughter.)

DR. EVANS: I think Michael Amos is next.

DR. AMOS: I think the answer to your question, Debra, is that we operate under a free enterprise system, and we have rights under the Constitution to do that. One of the things I'm a little concerned about is that we're operating in a little bit of isolation here, because we really haven't heard from industry. I think in order to be fair, in order to be balanced, we need to hear from folks other than - I mean, I have the greatest social concern myself, but at the same time I think that there are certainly important economic issues that need to be taken into account when you start talking about changing policy to control industry.

DR. EVANS: Yes, we did actually have a representative from Perlagen who came to speak. We have tried. I think your point is really important, that we have to be very balanced here and we have to take into account industry, and we did have somebody from industry come and present, but we could certainly work on bolstering that.

DR. LEONARD: But one of the problems is there are all these polar opinions, and how do you get an opinion that can balance everything? So there are economic implications of patented health care testing for health care economics. So how do you put all this together? I guess that's what

we're trying to do. So you get an industry rep coming, you get a health care rep coming, you get a patient advocate group coming, but how do you put it all together into something that's reasonable and isn't going to hurt one group and yet protect those who need protecting?

DR. AMOS: I think, actually, the FDA is really good at doing that.

(Laughter.)

DR. AMOS: Steve? We haven't heard from Steve at all.

PARTICIPANT: It would be a SACGHS meeting without Steve.

DR. GUTMAN: We'll develop a guidance document to take care of this.

(Laughter.)

DR. EVANS: I would also point out that on our task force, Emily Winn-Deen is from industry, and Marla Aspinal is from Genzyme. So it's very important to us to have the industry perspective because there are many facets to this.

So again, part of this is just to kind of pique people's interests, and appetites will be struggling with these same questions in the task force and maybe calling on some of you all again for further advice.

Finally, did the international roundtable session provide sufficient information regarding approaches of other countries, international organizations, and what other information, more importantly, what other information might be critical for our information gathering process?

Gurvaneet?

DR. RANDHAWA: In response to that second point there on that question, I'm not sure - and this speaks to just my (inaudible) of this field. I'm not sure I've been totally clear as to the utility of patents in promoting innovation. I don't know that the case has been strongly made. Certainly I don't sense a decrease in the number of biomarkers of the diagnostic tests that are coming into the market, be it for predicting cardiovascular disease or other diseases. Again, folks here in this roundtable might know this better, but I don't think most of these are actually patented, or licensed for that matter, but maybe they are.

So it would be useful for me at least to understand how many of the diagnostic tests actually need patenting, are patented, so I can understand the business case for innovation. To what extent does patenting actually get to that? I don't know that that connection has been made.

DR. EVANS: Actually, that's really a focus of Bob Cook-Deegan's group and the types of case studies they're going to be doing and the data that they're collecting. So that is actually a major goal, to try to figure out what data exists. Now, much of the data is simply temporal associations. Here was the Bayh-Dole Act, and then we see an increase in patent applications by universities. Certainly one can infer causation, and in that case probably very reasonably. But one of the ongoing efforts of this committee and of the task force, and by commissioning the folks at Duke, is to really address exactly that, what data can we get that really shows causation.

MS. SAMPOGNA: Just a really short comment, Mr. Chairman. In fact, at Duke there's also Wesley Cohen and John Walsh who actually are doing quite a lot of study in this field in terms of innovation and the role, and it's actually very interesting because they tried to do it from a higher level than Bob Cook-Deegan and his group do in the sense of Bob looks more at case studies and Myriad and HER and those types of things, and Wesley and John try to look at it in a more systematic way, a more high-level way. So it may be useful for this committee to actually look at that body of knowledge in a coherent manner because they might actually bring up different elements that might be of interest.

DR. EVANS: That's very valuable and I think we should, as a task force, look into their work and maybe even get them to come and discuss things.

I would ask, too, what other speakers, what other organizations that the committee as

a whole might think they would benefit from.

DR. FITZGERALD: I would just like to ask our panel, we heard today a bit about TRIPS and things like that, but my wonder is do we need to hear more about the role of the WTO certainly from an international perspective? I mean, I don't know. I just don't know how influential you think they're going to be in how all of this works out in an international forum. So I'm just curious.

MR. BARTON: Let me start an answer to that one. I think 10 years ago it was the WTO you needed to hear. I think now it's WIPO. There are currently patent harmonization discussions going on in WIPO. They have broken down, broken down primarily on differences between the U.S. and the developing countries, but that is one of the contexts where law is potentially made, and in that context it will be made by essentially patent office representatives plus senior executive committees who, on the whole, will be more pro-patent than the rest of the society. Certainly within this country, the key decisionmaking centers include the Patent Office, the CIFC, the Supreme Court, the Congress, and the U.S. Trade Representative, and they all have different policies and different goals. As I go international, I think at this point it's going to be less the USTR and the WTO than it is the Patent Office at WIPO, although there will be coordination and the WTO will draw some lines and there will be plenty of politics between them.

DR. EVANS: Okay. I think, Mike, did you have something? No?

One more comment. Steve?

DR. TEUTSCH: We all know that innovation is obviously important. Patents not only protect that but stimulate that, but we also know that these innovations are driving a lot of the increases in health care costs. I don't know whether it's here in this international forum or another forum where we're going to be looking at some of the tradeoffs in terms of the broader health care system. I think some of the things that Deb was getting at is because we don't have good social decisionmaking for these kinds of things, like we heard in the NHS and how they handled the situation. It's really a matter of the nature of the social contract.

The patent system clearly stimulates the private sector approach to this. I'm part of the private sector. My employer appreciates that because I get a lot of advantages out of patenting drugs. But I think there is something within this innovation that we then need to strike that balance that we heard about, and I don't know where we have that dialogue that sounds like we probably need to have, and I'm not sure who we bring in here to talk about that.

DR. LEONARD: One of the issues that needs clarification, and there's a study out there showing that you don't need patent incentives for diagnostic development innovation, because once a sequence is known and a mutation is identified as related to a disease, and if that's a prevalent enough disease, laboratories will start doing that testing using prior art with no patent incentives whatsoever. So I think that the diagnostic testing - and I say diagnostic but genetic testing in general is what we're supposed to be looking at, and we have to come up with ways of allowing that to happen in the innovative way that it does at academic medical centers across the United States and wherever it happens, the large reference laboratories and everything else, without inhibiting the things that do need to be protected, like pharma development or gene therapy and things like that.

DR. TEUTSCH: Right, and can I just follow up really quickly, because what you then have is multiple places where tests are available and can be done, and you create a different kind of marketplace than you do under a patent protected kind of a marketplace, and that has different financial as well as access and other kinds of consequences.

DR. EVANS: Yes, that's probably a great place to sum up. I would sum up with the theme that I want the committee as a whole to think about.

Dr. Straus, did you have a comment?

DR. STRAUS: Before you summarize, the last occasion, if I may.

Number one, I've heard the intervention about the NIH and how NIH should act and how should it use its power in, let's say, influencing the form of licensing. I would strongly urge you to really think about the entire complexity of this issue. If there is something like the Cohen-Boyer technology or monoclonal antibodies and similar things, you will easily get licensees taking a non-exclusive license, and everybody who is reasonable will only offer a non-exclusive license. But then you have other cases where the risk is such that you cannot license without an exclusive license. It's not a question that you just like to have a chunk of money from the very beginning. Things are much more complex. And don't forget that Bayh-Dole had some very deep roots and reasons for that. There were 40,000 U.S. patents held by publicly funded organizations, not used, and that has changed. It's not only the increase in patent applications from publicly funded institutions, but it was before very similar.

I have been quoted a couple of times because I said that in the National Academy of Sciences some 10 years ago there was not such a big difference between the Soviet Union and this country. In both countries you had the opinion that what was publicly funded had to be available for everybody, and that doesn't work. So that's number one. Please don't take any rigid, non-flexible decision because that is not an advantage.

Number two, the TRIPS. I a little bit disagree with my distinguished colleague from Stanford. At WIPO, I do not believe that there will be any substantial development progress because even the developing countries now have detected that WTO is probably the more powerful organization because there they can pressure Americans, Europeans and Japanese. But because that point has been made this morning, the TRIPS and GATT, which means the new world economic order, works much better for the developing countries, including India, China and many others. If you take statistics, there is no doubt there is a lot of technology transfer, a lot of foreign direct investment, a lot of move which you would not have without TRIPS and GATT, and I'm just trying to make this point here because also in your country, in certain circles you may have the feeling that this is something working against the developing countries. It does not. It is overall to the benefit, even in the case of Africa. If you take the statistics, that's quite clear.

The last point, of course, is that it's most complicated how to balance the economic interests of two equally important systems, in your country for instance, meaning the health care system with enough innovation in the area of pharmaceuticals. I think there is no clear recipe for that, but it is quite clear that at present internationally, health care systems like in your country, like in all countries, are subsidizing the Australians, maybe even some neighbors here to the north, because yes, it's very simple to say everybody has to have access to the drugs, and who is financing that, subsidizing that? You, us, the Japanese. I mean, that has to be taken into account.

To the extent, as Myriad is at hand, I don't know what John Barton would say to that. I would say that an eBay decision would be very well imaginable, that if Myriad would not give licenses, would not get an injunction, will get some reasonable royalties, and that's probably something that you would also imagine as a balance.

Thank you, and sorry for interrupting the intra-U.S. discussion.

DR. EVANS: That's great, very valuable comments. If you want to finish, Dr. Barton -

MR. BARTON: Am I allowed a response?

(Laughter.)

MR. BARTON: First of all, I think your point about who pays for innovation is absolutely crucial. I mean, one of the clear things that's happening is the United States first, and then to a significantly lesser extent Europe and the other developed nations are paying for the cost of

pharmaceutical innovation. I don't know what the numbers are in genomic diagnostic innovation, but nevertheless the rest of the world is free riding on us in pharmaceuticals. You're absolutely right.

But I'm not at all convinced that TRIPS is that good for the developing countries. I mean, the standard argument -

DR. STRAUS: Together with GATT.

MR. BARTON: GATT is good, no question.

DR. STRAUS: You cannot separate them.

MR. BARTON: Well, the question is whether or not the whole balance came out. The extent of royalty in the United States has increased significantly, particularly from Canada, and the extent to which foreign direct investment was encouraged is, at the very least shall we say, a matter of doubt. It's no question that it was one of the key issues at the time of the debate, but it is not at all clear to me that the nations which have actually received the foreign direct investment have strengthened their IP systems that much.

But with GATT, with the rest of the system, I'm happy to agree. Then there's no question there's a balance. We'll stop at that.

DR. EVANS: So I just want to sum up here. I think one of the most valuable things to come out of this, at least for me personally today, was further confirmation of something that's been emerging as the task force deliberates, as the full committee deliberates, and I think that again, as I mentioned earlier, is the need for nuance and the need for distinction between, for example, diagnostic testing and how that's contrasted with pharmaceuticals, drug development products. Really, I think that Dr. Barton's comment in his sixth slide in the Nuffield report is the explicit theme that to the extent possible, distinguish the sequence as information, kept unpatentable, from the embodied sequence as a chemical, which would be patentable. Now, whether that's patentable, non-patentable or licensed exclusively or non-exclusively, et cetera, is a matter for some deliberation.

But I would just ask the committee as a whole to think along those lines because I think we're all in agreement that our major goal is to look at issues with regard to DNA diagnostics, and as Debra brought out, they're different from issues regarding DNA as drug development.

That really is the end of our discussion. We do have a timeline here that I don't think we need to spend much time with the whole committee going through. Suffice to say that we do have a timeframe, we're trying to adhere to it, and I'm shooting ultimately for a draft report to be presented to SACGHS in the fall of '08.

I want to give a hand again to our speakers, who were fantastic.

(Applause.)

DR. TUCKSON: And can we get a hand for Jim and Yvette?

(Applause.)

DR. TUCKSON: Outstanding. Thank you all very much.

We have one important presentation left, and we will turn to that right away. We have a presentation from the CDC about the public's awareness and the use of direct-to-consumer genetic testing. We have been concerned for some time about DTC marketing of genetic tests and its impact on public health. I remember Francis Collins many meetings ago bringing that Nutriceuticals for the Millennium deal forward, a slide that I use regularly in talking about this issue. Several years ago we recommended that further efforts be made to gather data on the issue. We have been encouraged by CDC's responsiveness and are pleased that Dr. Katrina Goddard is here today. We're glad that Katrina is here to tell us more about what CDC has learned in the past year.

Katrina is a geneticist from Case Western University. She's currently serving in a fellowship at the National Office of Public Health Genomics at CDC.

Dr. G., we are so thankful that you joined us.

(Laughter.)

DR. GODDARD: Well, thank you very much, and thank you to everyone for staying until the very end for my talk.

Direct-to-consumer genetic tests have recently exploded onto the market. In 2003, Golost and co-workers reported that there were 14 companies that offered direct-to-consumer health-related genetic tests. Through our work, we have identified 27 companies that are currently offering these tests, between 1 and 16 tests from each company. Although there are non-health-related direct-to-consumer genetic tests such as paternity testing or ancestry testing, our work is really focused on the health-related tests such as nutrigenetics, predictions of fetal gender and tests that we're more familiar with, from clinical testing such as BRCA1 and 2 testing, hereditary hemachromatosis and CF carrier testing. The Internet gives nearly everyone immediate access to these tests.

Concerns have been raised in a variety of contexts surrounding these tests, including a GAO report last summer on nutrigenetic testing, and one of the main concerns that is raised is that the test may be misleading, unsubstantiated, and may make ambiguous predictions.

I'm not going to go through this because Marc Williams already gave a very nice talk this morning on the regulatory and oversight issues of genetic testing in general, which would apply to direct-to-consumer genetic testing as well.

So the CDC has undertaken a variety of tasks in the last year to look at surveillance about direct-to-consumer tests, and our main goal was to provide some baseline information on public demand and interest in nutrigenomic tests, and also to assess provider knowledge and experience with direct-to-consumer genetic tests. As this information is collected over time, we could be able to assess the impact of changes in policies and any public or provider education programs that occur and how that impacts awareness and use of these tests. We can also look at the evolution of the availability of the tests and how that might change the demand for these tests.

So there have been two national surveys that were conducted in the past year. The first is called the HealthStyles Survey, and that included 5,250 consumers from around the nation, and then the DocStyles Survey was an online survey of physicians that included 1,250 respondents.

There are also several state programs in public health genomics, including Oregon, Michigan and Utah that added questions about direct-to-consumer genetic testing on the Behavioral Risk Factors Surveillance System, or BRFSS surveys the past year. These surveys are considered to be more representative of the population because they use random digit dialing to recruit the participants in the studies.

So I just wanted to go through this quickly so you can see that although the different sites discussed the questions ahead of time, the final content of the questions was different for most of the surveys. So in red, you can see that Oregon and Utah and the national surveys specifically mention the words "genetic" and "DNA," whereas the Michigan survey used simpler language and said "a sample from the inside of your cheek," which could also be a little bit more restricting and not include types of genetic tests that are not from a cheek swab. In green, you can see that all the surveys mentioned that the test could be ordered directly, but the national survey did not mention that health care providers were not involved in the testing. In blue, you can see that the Michigan survey restricted the time period only to the past 12 months, whereas the other surveys were more general. In yellow, you can see the differences in what the intended benefits were of the tests.

So quickly going through the results of the different surveys, there was variation in the awareness of direct-to-consumer genetic tests, with the highest rate in Oregon of 24.4 percent and the lowest rate in Michigan of 7.6 percent. The Michigan survey may have a lower rate because of some of

those differences in how the questions were worded.

Another issue that we need to address is that the characteristics of the populations may be different in these different sites, and using U.S. Census data the Oregon, Michigan and national distributions for important characteristics are actually very similar, but the Utah population tends to be younger, more affluent and more educated than the other populations. So that could have led to a higher rate for that state than for the others.

In terms of the use of direct-to-consumer tests, they all had reported a very low rate, less than 1 percent, and that was similar across the surveys.

All of the surveys identified the same characteristics of age, household income and education level as being important predictors of awareness of direct-to-consumer genetic tests. For age, you can see that the rate of awareness increases as the age increases, except for the oldest age category, where you see a drop in awareness for that group. Those with the highest household income and the highest level of education were also more likely to be aware of the genetic tests.

In terms of where consumers hear or read about these tests, they're most likely to find out about these tests through the media such as television, magazines and newspapers, but we found it very interesting that for the 29 respondents of this survey who had used a direct-to-consumer genetic tests, over 60 percent of them had heard about it from a health professional, and we did not distinguish between physicians or other types of health professionals. So that would be a question that would be interesting to address in the future.

Looking at the results for the survey of physicians, slightly less than half of the physicians were aware of direct-to-consumer genetic tests, and none of the factors or characteristics that we looked at were very different between those who were aware and those who were not aware of these tests, except that males were more likely to be aware of the direct-to-consumer genetic tests.

Only looking at those physicians who were aware of direct-to-consumer genetic tests, about 75 percent of physicians had less than 1 percent of their patients ask them questions about these tests, and over 90 percent of physicians had fewer than 1 percent of their patients discuss results of a direct-to-consumer test with them. So these tests, if patients are taking the tests, it's not really coming back into a practice with a physician.

Then turning towards physician sources of information, we asked several questions about this topic. On the Y axis of this graph you can see the results from the first question where we asked physicians to identify up to five of their most trusted sources of information on patient health-related topics. So journal articles was the most trusted source, government agencies, et cetera. So they're ranked from most trusted to less trusted. In Panel A you can see that physicians reported that they used the more trusted sources more frequently. However, for direct-to-consumer genetic testing in Panel B, you can see that the media was the most likely source for physicians on this topic, which was one of the least trusted sources.

So overall, we found that only a small percentage of the U.S. population is aware of or has used direct-to-consumer genetic tests, and that the media is the most frequent source of information for both consumers and physicians, suggesting that other venues for learning about these tests such as through professional organizations or government agencies might be useful, and that there are several limitations of the existing surveys, including the small number of respondents who used a direct-to-consumer genetic test, so we weren't really able to characterize that population very well. Also, there may have been some confusion over wording of the questions and the differences in the questions between the surveys, and we did not assess any health outcomes as a result of having the testing done. So we weren't able to assess what happened to people once they had taken a test.

Then I'd just like to acknowledge all the co-workers from the CDC and also from the

Oregon, Michigan and Utah state health departments who contributed to this work. Thanks.

(Applause.)

DR. TUCKSON: Can we have a round of applause for the speaker? Oh, we already did that part.

Are you going to keep doing this? Is this one shot and out, or is CDC in this for the long run?

DR. GODDARD: We have questions on next year's survey at the national level, and I don't think it's entirely up to the CDC whether it will be put on the BRFSS surveys.

DR. TUCKSON: The CDC doesn't have any juice to get it on there? Muin, is it a powerless organization?

(Laughter.)

DR. KHOURY: It's too late in the day to respond to you.

(Laughter.)

DR. TUCKSON: One quick question, rushing for time. Slide number 11, what do I take on the proportion, like 0.6? Does that mean basically almost nobody has seen anything?

DR. GODDARD: Sixty percent of the people who had used a direct-to-consumer genetic test heard about it from a health professional.

DR. TUCKSON: So that's just only the people who have seen it.

DR. GODDARD: No.

DR. TUCKSON: Who have done it, who have gotten it, have sorted through that. So there's no survey that says how many people actually have received these things.

DR. GODDARD: The black bars refer to people who say that they have used a direct-to-consumer genetic test, and the green bars are for people who have heard about them.

DR. TUCKSON: Okay, so that is a significant penetration. So these are common. Okay, thank you.

Questions?

DR. McLEAN: With that slide right there, do you have any sense of what kind of genetic tests were being mentioned by the physicians but allowed to be sort of negotiated entirely by the patients themselves? Was it BRCA or paternity testing?

DR. GODDARD: Well, the way that the question was worded, we were asking about tests that analyze DNA, diet and lifestyle for potential health risks. So that was a very generic question and we weren't able to ask about specific tests, but we're hoping that that is referring to health-related tests versus the non-health-related tests such as paternity testing.

DR. TUCKSON: Thank you very much.

DR. GODDARD: All right. You're welcome.

DR. TUCKSON: So we'll look forward to seeing other results of that.

Now, here's the deal. It's 5 o'clock. We only have to summarize. So the summary is that the next meeting, I need to ask a question of Jim.

Jim, your work plan says basically that I don't think you intended to come back to us with anything definitive at the next meeting, but it's the meeting after that. Can we have a brief update on where you are and so forth and so on?

DR. EVANS: Sure.

DR. TUCKSON: All right. So the next meeting will be focused exclusively on pharmacogenomics and oversight, right? Those two. Coverage and reimbursement will have some analysis of the CMS letter

DR. WILLIAMS: Are we restricted to wait until that meeting? I mean, if we develop

a response -

DR. TUCKSON: Send it forward, and then we'll look at it. But we'll have it formally on the agenda for just a brief update. Okay, sir? Okay, so those three.

Committee, is there anything that you feel that you want to bring up that you have not had a chance? Ex officios? Anybody? The quiet ones, anyone?

DR. LEONARD: Given that Cindy Berry was the head of the coverage and reimbursement, wasn't she? So does somebody need to be named to carry that baton forward?

DR. TUCKSON: Marc.

DR. LEONARD: Oh, good.

Hi, Marc.

DR. TUCKSON: And finally, there's no more public stuff? Everybody is cool back there? I want to thank the public people for staying.

I want to thank all the technical support, and I don't know why you all talk so loud and fast, but you're incredible. So thank you, sir. You're very wonderful.

Give him a round of applause.

(Applause.)

DR. TUCKSON: And the webcast people who struggled with apparently all kinds of technical things in this building and persevered, and then our miracle workers who somehow created the Canada telephone line when the Canadian system didn't work, and it's clearly the Canadians' fault and not ours -

(Laughter.)

DR. TUCKSON: Let the record be clear.

Thank you all very much. See you next time.

(Whereupon, at 5:05 p.m., the meeting was adjourned.)