Report from the SACGHS Task Force on Gene Patents and Licensing Practices
James P. Evans, M.D., Ph.D.

DR. TUCKSON: Thank you all very much. We will now turn our attention to the issue of gene patents and licensing practices. In March of 2004, the committee identified this as a high-priority issue because we had some concerns about adverse effects on access to genetic tests and services. At that time, however, the National Academy of Science had just begun a study on gene patents for the NIH, and we decided to postpone a decision on whether to undertake our own in-depth study until the National Academy's work was complete. That report, which was titled "Reaping the Benefits of Genomic and Proteomic Research," was published in the fall of 2005. In March of this year Debra Leonard, Jim Evans and Emily Winn-Deen, the team appointed to review that study, reported that its recommendations sufficiently addressed intellectual property concerns in the research realm but did not fully examine the impact of patents and licensing practices on patient access; very different.

In June we gathered more information on this topic before reaching a very clear conclusion that we needed to embark on an in-depth study of the effects of gene patents and licensing practices on patient access. We roughed out a scope for the study, discussed several investigational approaches, established a task force to guide our work on this issue, and tapped/drafted/hijacked Jim Evans to serve as task force chair.

Jim will now present on the work of the task force and fine-tune the study scope in developing the detailed work plan. We have two hours for this session. Our task is to discuss the task force recommended approach and give Jim and the committee some clear direction and marching orders so that he can lead the group forward.

So, Jim, as we turn it to you, again, I want you to be real clear about what it is you want from us. I mean, we can give you marching orders to lead forward, but we can give you marching orders that lead you up Mt. Everest and you'll never get there. So how specific do you want from us, and what do you want to achieve by the end of this two-hour session?

DR. EVANS: Thanks. This is obviously an extraordinarily complex topic, and it's a topic that really, I think more so than any other item that the committee has taken on, with the exception of genetic discrimination, really elicits passions in people, and I think that what we're after today is really three things. We would like folks to weigh in on the scope, which we spent a lot of time trying to determine what the scope of our investigation is going to be, we would like input on the study questions that we have defined, and we would like input from everyone about how we have proposed to go about this. None of these things are written in stone. So this is an opportunity early on for people to really change what we're doing. I certainly don't hold myself out as an expert on gene patenting, so we need lots of input from people.

This is the membership of the task force as it currently exists. Let me introduce a couple of people. One is not here, and that's Mara Aspinall, president of Genzyme, who has a role in the committee. But in addition, Brian Stanton, who is sitting right over to my right, is with the NIH Office of Technology Transfer.

Brian, if you'd raise your hand?

I think that most people know the other members of the committee.

The activities to date, to summarize very briefly because Reed has really already done it, in March of '04 it was really defined as one of the priority issues. In October of '05, Debra Leonard convened a small group to look at these issues, and then in March '06 many of you remember that at that point we were able to evaluate the National Academy report. It was thought before that report came out that perhaps it would really have done our work for us. That really is not the case. The National Academy report was quite heavy in looking at the research implications of gene patents. They were extraordinarily light on the issue that we feel is most important in the Secretary's committee, and that is ultimately patient access. So because patient access we see as our salient interest, we felt that more work needed to be done and that there was a role for this committee to take up issues of patenting that were not addressed by the National Academy report.

In June '06, we decided to move ahead with an in-depth study, discussed the scope and work plan, and established the task force that is reporting to you now. The first task force meeting was, as you can see, quite recently. We have come up with the scope and study proposals, and the goal of today's session is to try to reach consensus on that scope, on the study questions, and on the way forward.

Now, I'm going to go through a few things and then we'll have a chance to talk about these in detail, because I know people will want to weigh in on this. So I'm going to hold off for a moment on the proposed scope statement. We may want to modify it. One of our goals is obviously to be very balanced. I think everyone recognizes that gene patenting provides both benefits to this whole endeavor of genetics in medicine, but it also has certain downsides, and our ultimate goal is to try to guide things so that we can effect that balance to the favorable extent. You can follow the scope in the table folders that you got.

So we also wanted to define for you some of our terminology. I've referred a couple of times here to patient access. You will see the term "clinical access" used throughout our discussions, and just so everybody knows what we mean by that, patient access is pretty self-explanatory. We want patients to have full access to emerging technologies and things that will benefit them. When we say clinical access, we are also trying to capture the idea of the development of tests and the integration of genetic testing, for example, into patient care. This also subsumes issues that relate to reimbursement and cost. In other words, patient access hinges on a lot of upstream types of things, and we want to try to capture that flavor.

I would also keep in mind as we go through this that we are oftentimes looking at proxies for patient access when we look at the effects of patents. For example, we heard a lot of information from Debra, from Mildred Cho about, for example, the ability of clinical laboratories to roll out new tests and to offer genetic testing. Our charge as a committee is not really to look out for the welfare of molecular biology laboratories, right? Our charge is to look out for patient access, but that may be the best proxy we can get for those things.

So keep in mind the fact that we're oftentimes going to be looking at perhaps imperfect proxies to judge patient access.

So the study questions are the following, and again, we'll have a chance momentarily to go through these in detail. I'm just going to give you the 30,000-foot overview here.

What are the overall effects of patenting on clinical access? What are the quantitative and qualitative data for the positive and negative effects of gene patenting and licensing practices -- that's an extremely important part of this -- on clinical access? If there are problems, where do

those problems occur? Are they in the development stage? Are they in the reimbursement stage? Are they in the integration stage?

I think we need to think seriously about current licensing practices for two reasons. One is they're obviously very important in patient access, in the ability to roll out predictive tests, et cetera. They also may represent an area where we can have some influence because, of course, patents policy is based in the U.S. Constitution, so we're probably not going to recommend amending the Constitution. On the other hand, licensing is something that may prove a more tractable tool. If we identify problems, we want to think about the solutions.

The effects on cost is extremely important. That gets directly to patient access. When tests are prohibitively expensive, that's a problem. What we would like to assess is are there data that address the effect of patents on the ultimate cost of genetic tests, for example, and are there economic data that analyze the contributions of patents to these things?

We'd like to perhaps look at the effects on development of tests. Do patents and licensing practices as currently seen create barriers to the development and implementation of clinical tests?

This is one that I think is up for some discussion as to whether it even belongs on our plate in this task force, and that is the issue of quality of testing. It's been argued, of course, that when there's a patent on a particular test, it hampers the ability to engage in independent verification of test results and therefore has a deleterious impact on the quality of testing. That may not fall within our purview, but it's something to discuss.

We want to quickly go through the study approaches. What are the types of things that can be employed to assess the direct effect of gene patents and licensing practices on patient access? So if those studies don't exist, what are they? What are alternative models that are practical? Again, we're not interested here in going off on a tangent, and as Reed alluded to, trying to climb Mt. Everest. We're interested in practical models that might relieve any problems that are found without harming the good things, the beneficial effects of current patent and licensing practices.

So with that preamble, we can now get to the discussion, and the first thing to discuss before we get to study questions is the scope. Now, we came up with this scope, and I'll read it to you. I've already heard some very legitimate criticisms that we might be able to improve it by incorporating.

"While recognizing the benefits and importance of patenting in innovation and technology development, SACGHS will explore whether current gene patenting and licensing practices are having adverse effects on patient access to genetic technologies and ultimately on the public's health."

So I'll throw it open and let people make comments about that scope.

Brian?

DR. STANTON: Thank you, everybody. I appreciate the opportunity to be part of this.

When the emails were going back and forth about how to define a fairly substantial problem, my concern was that the scope of the study question can influence the way people approach the pursuit of the answers to the questions. So my thought was that my preference would be that we

not use the word "adverse" right in the scoping document of the scoping question, that rather we leave it a little more open-ended and use the study questions themselves. So rather than say "adverse effects," that the working group explore the effect or what effects gene patenting and licensing practices are having on patients access to genetic technologies, thereby leaving it open to both looking at positive and negative.

The reason I suggest that is because I think that as we explore this what we're going to find, from my own experience, is two things. One, on the gene patenting side what we're going to find is that sometimes patents get in the way, and sometimes it's the quality of the patents that gets in the way. So it's not necessarily the patenting and the IP, per se. The second thing is, when it comes to licensing practices, similarly that's something we have in our controls. If we look at what the effect is, where it's good and where it's bad, because there are both, and what factors push the balance in one direction or another. Then we can look at very operative outcomes to see where the system needs to be tweaked without changing the Constitution, which I don't know if we necessarily need to pull off the table but it's probably a little more cumbersome.

DR. EVANS: We probably need three hours for that.

DR. STANTON: Yes, we probably need three hours for that one.

So thank you very much.

DR. EVANS: So we could, for example, amend this to say "SACGHS will explore the positive and negative balance which exists in the current gene patenting and licensing practices, with an eye towards identifying how best to enhance that balance," something along those lines.

Other people's suggestions or comments?

Emily?

DR. WINN-DEEN: I mean, I think if you just want to keep it really neutral, you can just keep the first part of it and then say "SACGHS will explore whether current gene patenting and licensing practices are having an effect on patient access," et cetera.

DR. EVANS: I'm sure they're having an effect, right? I guess what we would want to do is follow that up and say are there things that we can suggest, practical issues that we can suggest that would enhance that balance or something, right?

Other suggestions?

(No response.)

DR. EVANS: I think if we start with "while recognizing," starting with the "while" means there's something coming, right? There's something negative coming. So would people be comfortable with a statement that really starts in with that second clause, that we'll explore current gene patenting and licensing practices in order to determine the balance of positive and negative effects on patient access, with an eye towards suggestions that could further enhance or enhance the positive side of that balance? Brian?

DR. STANTON: That would address my issue.

DR. FITZGERALD: Jim?

DR. EVANS: Yes.

DR. FITZGERALD: So your positive balance is the public's health?

DR. EVANS: Yes, right, and I think we should continue to emphasize that our role, that we see our mandate as ultimately coming down to patient access or the public's health, and you may notice the apostrophe there, that we aren't just talking about public health, we're talking about the public's health, which is different. It may sound nit-picky, but I think it's an important distinction.

DR. RANDHAWA: Just a question.

DR. EVANS: Gurvaneet?

DR. RANDHAWA: In the current phrasing here, the way I understand this, if you're focusing on patient access and ultimately on public health, and we losing the effect on patient outcomes?

DR. EVANS: No. Well, I would think that when you're talking about the public's health, that inherent in that would be outcomes, would be the kind of outcomes we desire. I'd maintain that that is inherent to any idea of a patient's health.

DR. RANDHAWA: Well, just to make my comment more clear, the reason I'm bringing this up is if we are assuming that because of patenting that there is proprietary information that cannot be shared, and knowing that is useful to determine how good the test is, then inherently there would be something about what are the outcomes of the testing and not just access to the test. I don't know if that concept has been clarified in the scope here.

DR. EVANS: I don't think it's within our purview to really decide on a case by case basis what tests are of benefit to people, et cetera. I think it's fair for us to assume going into this that there will be technology that is subject to patent law and licensing type practices that does indeed have a beneficial effect on outcomes, et cetera. So my own bias is that we need to assume that we are talking about tests that are found to be legitimate, that that's not our charge here, to look at how you determine what tests have a good outcome, et cetera. We're going to assume, I think, for purposes of this that those tests exist and that they are subject to patent law. Am I answering your question?

DR. RANDHAWA: I'm just trying to clarify the scope, that's all. You answered my question.

DR. EVANS: Yes, and that actually gets to a discussion in a minute about ensuring the quality of tests, which I'm not sure even belongs in our scope. But when we get to that, maybe we should discuss it.

Now, I can go back to the study questions one by one, and I should probably go ahead and do that. To remind you, the first study question is the overall effects, then the effects on development of tests, the location of possibly problems, impact of licensing, effects on cost, on quality, and then further study and alternative models. So I think that what I'm going to do now is I'm just going to zip back here to those study questions and we can take those one by one.

DR. STANTON: Jim?

DR. EVANS: Yes.

DR. STANTON: Before we get into the detailed questions, I do have a question. As I've looked internationally at the question of access in relation to genetic testing, the context of the national system in which the question is being asked sometimes can bring different answers. So I have a question as to whether or not we need to either put it in the beginning of the document as part of the purpose or whether we need to contextualize each individual question to say within a given national system, because there are different constraints within different systems. It's a thought to put on the table for this group whether or not we want to specifically limit it to within the U.S. system and its reimbursement or whether we want to globalize it.

DR. EVANS: Certainly I think the assumption of the task force has been that we're dealing with U.S. practices and the effect within our system. That's not to say that we don't feel like we might be able to get very useful information by talking to folks from other countries in different systems. But I think it's implicit in all this that we know who the Secretary works for, right? It's not another country.

So the first one is really the overarching issue of the overall effects of patenting on clinical access. "What is the quantitative and qualitative evidence for positive or negative effects of gene patents and licensing practices on clinical access?" That's kind of the lead-off study question that in a way summarizes in the broadest terms what we're looking at.

Comments? Suggestions?

DR. AMOS: Are you looking at economic quantitative and qualitative evidence?

DR. EVANS: Well, not necessarily.

DR. AMOS: You may want to spell that out a little bit more and define what exactly specific benefits you were actually --

DR. EVANS: Right. So, for example, what we're getting at is are there data out there that directly or indirectly assess the impact of current practices on patient access? Can you show, by whatever means, and that could be economic but it could be the inability, for example, of laboratories to develop tests, et cetera, are there data? What are the data out there for determining the current impact of patent and license practice? Do you find it too broad?

DR. AMOS: I guess I just want to know what you mean by "impact."

DR. EVANS: Well, okay. Is it things that are enhancing or limiting patient access? Our ultimate goal is to look at patient access. So when we're talking about having an impact on patient access, we're talking about are patients able to reap the benefits of these technologies?

DR. AMOS: So we'd be looking at the benefits of having a patent for a company as far as the acceleration of that technology, as well as --

DR. EVANS: That could certainly fall into are there data that show because patents are in place, because of licensing practices, this test was able to be accelerated, was able to get out there, whereas it wouldn't have happened without current patent practices. So that would certainly fall into that.

DR. TUCKSON: I think it is fairly broad. I think we need to sort of drill in. First of all, I think you should split the two between what are the positive issues, what are the negative issues, because it's so broad. But then I think if you start defining in clear terms at the beginning of the report what you mean by "access," since the question that Mike is raising is the premise of the entire activity, I think you've got to be really, really clear about what does access mean, and then I think what this question becomes is what would be the level of evidence that you would require for being significant, for saying that there is an issue. I think what you're asking is things like would it be the numbers of people, would it be the price of the drug, would it be the price of the licensing. I think that's what really people are asking, giving examples of what that quantitative and qualitative would mean.

DR. EVANS: All right. So we could have some sub-points there. We could split it into positive and negative and have some sub-points, examples of the kinds of things that we're talking about with impact on patient access.

So the location of possible problems, where within the health care system are barriers, if those exist, present? For example, in the development of tests, in the reimbursement of testing. So trying to in this sense drill down and figure out where those problems exist, if they are found. So in the first study question, what are the data for positives and negatives, and then where in the health care system do those exist? Some of these things have already been addressed by the National Academy report. But again, that focused primarily on extremely upstream kinds of stuff, and we again want to keep this focused on patient access.

DR. TUCKSON: So I think here what would be useful would be if this question could be accompanied by the chain of evidence, as it were, sort of saying let's start here, and by laying it out you're saying this is the menu of possibilities. But it would really, I think, advance everybody if we could see A, then B to C, to D to E.

DR. EVANS: That's a great idea. Yes, we could kind of show the flow from initial basic research, which again might not fall within our purview, and we can mention that, all the way to the patient being able to get reimbursed for this test.

DR. RANDHAWA: Just following up on that chain of evidence thought, usually we also have some comparator in that chain of evidence. So are we thinking that in this case the comparison would be to non-patented diagnostics? Would it be to patented therapeutics? What are we comparing it to?

DR. EVANS: You get to one of the difficult problems in here, which is what's your control group? If you're going to say what's the effect on patient access of having a patent, what you'd like to do is be able to compare that with no patent. That's very difficult to do with gene patents now because the way to do that, one way you could envision, would be seeing what happens when things go off patent. Well, there hasn't been enough time for that, right? That really raises one of the things that we struggled with as we talked about it, which is how do you quantitate these effects?

So I don't have an easy answer for you. I don't think there is an easy answer. There might be in 20 years when things have gone off patent and you can see. One example would be, one way of getting to this would be perhaps in looking at other systems where the patents aren't or the licensing isn't as restrictive. But your question I think is a really good one. It's one that we don't have a good answer for, and that's kind of one of the things we struggle with as we get to our methods for trying to carry this out.

DR. LEONARD: But I think you can go beyond patented or not patented, because there are a variety of licensing procedures that are used. So there's broad licensing at a reasonable royalty rate versus exclusive licensing versus proprietary testing, and you could look at the relative effects of those, although they are comparing one test to another test, and so you're also comparing apples and oranges in that the tests are not the same across all the different licensing practices. But you could look at the different licensing practices.

DR. STANTON: What I would suggest is that this question and three forward, the effect on development of tests, loci of possible problems, this question is focusing on the health care system, and to refine that and address some of these issues we might say where within the health care system and what elements of the IP spectrum are affecting the effective provision of clinical --

DR. EVANS: And elements of the IP --

DR. STANTON: In other words, in the research phase we'd say there might be preclinical aspects, there's IP development, there's patents. Once you get the patent delivered and you're going to deliver the test, maybe licensing issues. So you have this convergence between where in the IP spectrum, from the patent application process all the way down to licensing and delivery, or not, because there's the MTA issue as well, and then the different components of the health care system.

So that looks at which problem or solution may be present at which component of the delivery system, and then three questions down we ask, okay, now that we've identified which component of the IP system affects which part of the health care system, I guess, or spectrum, then we can go ahead and find out, okay, now that we know the convergence between which part of IP and which part of the health care delivery stream, now we go in and say, okay, is there a solution. So trying to find the convergence of those two components might clarify this question and bring it into the third one forward.

DR. EVANS: Okay. So moving on, I think that something that has been mentioned a lot here is worth emphasizing on its own, and that is the impact of licensing practices. Are licensing practices affecting the ability of industry and academia to develop accessible genetic technologies? What role do technology transfer programs play in influencing clinical access to genetic technologies? And then what are the downstream affects of licensing practices on clinical access?

I think that licensing issues probably deserve a lot of attention because of the possibility that these are things that can be more readily changed than some other aspects of patenting practice.

Comments?

DR. TUCKSON: So this is very much like the earlier one around what are the data sets. So what would be the criteria to determine that licensing practices had an effect? How would you segregate out that piece of the puzzle? I have no idea what I'm saying. I'm just trying to play around with ideas. Would it be that the relative proportion of expense of an ultimate test divided by the licensing fee was less than 30 percent?

DR. EVANS: Or do you factor in the reimbursement, that a percentage of plans that reimburse for this test or that test, what the cost is, et cetera?

DR. TUCKSON: Then the flip side of that is, again playing this out, of 100 manufacturers interviewed or developers interviewed, 3 percent said without a licensing fee I wouldn't do this, it's not worth my time. Therefore, there would be no test. This is where I think the real work -- actually, I'm kind of warming to this task now. This is pretty exciting. It would be to try to figure those things out.

DR. EVANS: Right.

DR. TUCKSON: So what would be the metrics?

DR. EVANS: And we get in a moment to some of those ways of trying to address those.

The effect on cost is obviously integrally related to patient access. Some of these tests are extraordinarily expensive, and there's all kinds of debate about just how expensive should they be. What we would like to try to figure out is the quantitative -- and I suspect we'll also have to deal with qualitative data -- on licensing practices, gene patents, ultimately on the pricing of genetic tests, and some of these types of data may come from the economic world that analyze the contribution of gene patents to their ultimate cost, and then again ultimately how does that affect patient access, because that's what we're most interested in.

Comments? Questions?

(No response.)

DR. EVANS: Okay. The effect on development of tests. Again, this is a very --

DR. LEONARD: Sorry. The way this is worded is it's a yes/no question. I don't mean to wordsmith, but we probably want to write it as does any quantitative or qualitative evidence indicate adverse effects?

DR. EVANS: Address the magnitude, for example.

DR. LEONARD: Right.

DR. EVANS: Because I think we probably all agree that --

DR. LEONARD: And again, Brian, I don't know if you want "adverse" out of there.

DR. STANTON: I was probably going to do that offline, but yes, because again the question is going to prejudice the answer. So let's make it neutral and see. I had a conversation with the Patent Office last week and I said if you would do -- I was there until two years ago, so I can say this. If we, when I was there, would have done a better job, then maybe we wouldn't have so many issues. So where the break points are and where the trigger points are is really important to find in a neutral manner.

DR. EVANS: Yes. I think that our role should be to look at these things and then let the chips fall, right? There's no reason we need to go into it with preconceptions just because there are popular preconceptions.

DR. AMOS: James?

DR. EVANS: Yes?

DR. AMOS: I think the only fair way to look at this is if you really take all of the genetic tests, the world of genetic testing and you look at the value that has been created by the ability of a company to patent and get protection in order to be able to afford to develop the test, and identify specific examples of how limited licensing practice or having a patent has specifically kept a product or a test from getting to the clinic.

DR. EVANS: Or once it's in the clinic, it's kept from patients being able to get access to it, which exists now. These are very complex --

DR. AMOS: I'm talking about actually in clinical practice.

DR. EVANS: So am I. There are lots of tests out there that many of our patients can't get because, for example, they're so expensive. So I think you have to look at the whole gamut, right? Does that make sense?

DR. AMOS: Sure, and that gets back to insurance issues as well.

DR. EVANS: Right.

DR. AMOS: But I think it's critical to be fair.

DR. EVANS: I couldn't agree more, and believe me, I understand there's a certain default kind of feeling among many people that gene patents are bad, and we don't want to, I think, come across as saying gene patents are bad. I think we need to take a very balanced approach because you're right, we all recognize that there are incentives that I'm sure are very good in bringing tests to fruition that might never have come to fruition, but I think that we also can't shy away from when they do limit patient access and do cause problems. That's one of the reasons we're here to look at it.

DR. McGRATH: I just would agree with keeping it balanced and neutral but not try to neutralize the language too much, because we are representing the patient side of it. There are other bodies around that are looking for the positive effects of patents. We don't need to do that here. So my recommendation would be to keep the words "positive" and "negative" in there and not to just get rid of both of them, not to just have it neutral but keep both.

DR. EVANS: Yes, I think that's good to constantly keep in mind that we're looking at both the positive and negative effects, because I don't think that we certainly want to come at this from the idea that everything is rosy or that everything is evil about patents and licensing practices. Fair enough? Okay.

So the effect of development on tests. This is, again, one of these upstream issues, and we should probably say to gene patents and/or licensing practices enhance or create barriers to the development and implementation of clinical tests, because one could certainly argue that perhaps they enhance as well, and we could probably be more balanced in this.

DR. WINN-DEEN: You don't want something that's just going to give you a yes or no answer, right? So you want to somehow get into the details of in what ways does it --

DR. EVANS: How do gene patents -- there you go. Right, right. "In what ways" or "how do gene patents."

This one, I'm not sure if this belongs within our purview, so let me read it. "Is the quality of genetic testing affected by gene patenting and licensing practices? Are current patent and licensing practices having an adverse effect on the independent verification of test results?"

The genesis of this concern really stemmed from Recommendation 13 of the National Academy report, which said, okay, there could certainly arise situations in which only a single laboratory is doing a test, and that therefore there wouldn't be any quality control, right? I'm not sure this really falls within our purview. Perhaps this falls better in CMS or somebody who is more concerned with quality of testing. Again, our concern is with patient access, and I'm kind of presuming, getting to Gurvaneet's previous question, I'm kind of presuming that we're concerned about the tests that make a difference and the quality tests, and that it really isn't within our bailiwick to be deciding about quality.

But what do people think? Is this within our purview?

DR. HANS: Jim, could I ask a clarifying question? I know that this question came out of really the second part of that compound question; that is, no independent verification of tests. But in that first statement about quality, is the following hypothesis included or not in quality? That is, there are seven different genetic changes that are responsible for a certain condition. One lab owns three and another lab owns four. The lab that owns three has decided not to pursue them but is not giving anybody else access to being able to use those. I would say that that is not a very high-quality test, then, if you can only look at four of seven. Is that included or excluded from this definition?

DR. EVANS: That's a very good point, and I hadn't really thought about that particular spin on the idea of quality. In a way, I think that is subsumed under patient access to genetic testing. If people, because of a patent, are not able to get tests for three of the seven genes that can be responsible for it, that would be an access issue, not so much a quality issue, but I see how it could be spun that way.

DR. COLLINS: I hear why you're questioning whether this fits in here, but I don't know how you can really separate the idea of patient access to tests from the idea of those tests actually being meaningful. I do think there's a serious issue here, and the National Academy, while highlighting it and making sort of a suggestion, it's not clear to me that anything is going to happen with that. So to leave this untouched I think would be unfortunate. I think there is a real issue when you have tests that have been exclusively licensed to a single provider, that there is therefore no natural way, through an objective outside evaluation, assess that quality outside of what perhaps ultimately will get done by other government oversight but which right now is a bit unclear. So I think it belongs on your list.

DR. EVANS: I'm certainly fine with keeping it in there. I think you both make good points.

DR. LEONARD: Well, also, if you look at the broader charge to SACGHS, quality of genetic tests is what got this whole committee started to begin with.

DR. EVANS: Before it was SACGHS.

DR. LEONARD: Right. So I think this is smack in the middle of what SACGHS is supposed to be doing.

DR. EVANS: Okay. Great.

DR. STANTON: Hi, Francis. How are you doing?

(Laughter.)

DR. STANTON: Francis and I have had a number of discussions over the years.

I agree 100 percent with the quality as an issue. The only reason I would suggest that maybe it's not for this particular task force is the following reason. I think Jim said it very well. If we look at the broader question of where is the convergence of intellectual property and licensing on the ability to even have the test in the first place, then the derivative question is how does that affect the quality of that product? But if we can't even get to the first base of I can't get the genes together for the gene trip to do the test, or I can't get the five genes to do a prostate -- I was looking at a prostate test the other day where it needed seven genes to do it, and they only had access to six.

So there's a qualitative question, which is fairly subjective from a medical perspective, and there's the -- I hate to say objective in IP, because nothing's objective, but there's a question of how does IP get there, and then once we're there, if we can have all the genes, do you need them or not? And I wonder if that's a separate question that's for this committee but not for this study.

That would be my point, that the quality of the test itself isn't the charge here, although it's an important question. The question is can you get to the genes in the first place so that doctors can determine how to put the test together.

DR. LEONARD: But it goes beyond that, because sometimes you can't even do the test. So you end up with a sole provider of a test because they're exclusively enforcing their right to do that test, they decide the national standards of how that test will be done, the testing method, and so you aren't getting the broad medical community doing the test and developing a consensus standard. So it affects the quality of testing beyond just whether you can get the license to use all the genes necessary for a particular test, because this is single-gene tests that you can't even do.

DR. COLLINS: Yes, I would submit that this is one of those that could fall through the cracks. I hear what you're saying, Brian, in terms of this being slightly on the periphery of the main sort of focus of this particular study, but at the same time this would also be on the periphery of a study that looked at quality of genetic testing. They would probably not pay that much attention to this particular issue.

DR. EVANS: And they'd say that --

DR. COLLINS: That's patenting and licensing. So if it's going to be captured, why not capture it now?

DR. EVANS: I tend to agree with that, and I think that I'm going to argue against what I said before, just to show how open-minded I am. As somebody who orders genetic tests all the time, I do lament the fact that there are certain tests that I can only get from, say, a particular laboratory

that I have been far from impressed by, and that is an impact on patient access to good genetic testing. So I think there's a reasonable consensus to keep this in.

DR. FERREIRA-GONZALEZ: I would like to add to the issue of the quality of the testing, not just only if you can access the test but something that was mentioned earlier. If you only get access to three mutations and not seven mutations that you're supposed to, then we are obligated or allowed only to offer an assay that might be 70 percent sensitive, versus if we can get to the other patents or licenses of those particular patents, we can improve the sensitivity of the assay that we can provide, not only for the reference laboratory but also for the manufacturers, too.

DR. EVANS: Yes, and I think that the issue is very persuasive to me that this could fall through the cracks in another committee. Since it could be seen as peripheral to others, we might as well tackle it.

Study approaches. What quantitative and qualitative approaches can be employed? So on the one hand we're asking what are the data out there for the effective patents and licensing practices on these issues? Here we're asking what are the approaches that could be employed to assess the direct impact of gene patents and licensing practices on patient access to genetic technology if those do not currently exist in the literature? We're going to talk a bit more about this. It's a bit of a departure from what the SACGHS has done in the past. So I would suggest that perhaps, unless there are driving questions, we hold this for a second discussion until we get to that aspect of our study plan.

DR. LEONARD: But could we just say what additional quantitative and qualitative approaches not identified by the above?

DR. EVANS: Okay, that sounds good.

Are there feasible alternative models and innovations that could be applied to the patent and licensing system to preserve its inherent incentives? I think feasible is an extraordinarily important part of this statement. This is such a thorny issue. There are so many stakeholders, and there are a lot of constraints on what we can do and on what the Secretary can do that I think we have to focus on feasible.

DR. FITZGERALD: Just on this one, Jim, I understand the reasons behind focusing on the U.S. situation, but in this one might we want to look more broadly just to see if there's something out there globally that might be more useful?

DR. EVANS: Yes, and I think that we could add something to the effect that we'd like to cast a wide net, continue to keep it feasible but cast a wide net in alternative models.

DR. AMOS: So when you're trying to do the study, will you actually provide a list of the constraints? I mean, there are going to be things that we just can't get by.

DR. EVANS: Right.

DR. AMOS: So you have to build your story within that context.

DR. EVANS: Yes, and I think that what we envision, as you'll see in a minute here, is that we would like to convene a roundtable in order to start to approach some of these models, and that will have to take into account, again getting it feasible, what those constraints are.

DR. AMOS: So, for instance, I think the Secretary of HHS can do a lot with regard to proposing new licensing procedures for NIH, but I think it's going to be more difficult for industry, and that would require laws. Also, it kind of flies in the face of administration policies to promote industry, not limit things like that.

DR. EVANS: Correct me if I'm wrong, Reed, but certainly the committee has not been shy necessarily where we see a need about encouraging the Secretary to promote certain types of legislation with Congress, et cetera. Look at the genetic discrimination issues, right? We know that the Secretary can't mandate genetic discrimination. That has to ultimately be done through Congress. But I think it's not unreasonable if we identify alternative models, things that could be done, even if they aren't in the direct abilities of the Secretary, that the Secretary, she or he, can still have an influence on that.

DR. LEONARD: So while we've taken out "adverse" in all the other things and made it positive and negative, can we do the same thing to this to say "could be applied to the patent and licensing system to mitigate any negative effects while preserving its inherent incentives"?

DR. EVANS: Sounds good to me.

DR. LEONARD: Because we want the balance.

DR. EVANS: Right.

So we've gone through the study question topics, and we come now to the proposed study plan, which has four components. We feel that an in-depth study is in order to figure out what are the data that are out there now that address these questions, that address the issues that ultimately get to patient access in the current environment, both from a positive and negative standpoint. We feel that a public consultation process is especially important with this topic, and we can talk about that more in just a minute as we go through each of these things.

Again, I think that I'm continually amazed at how both little knowledge is out there among even the fairly knowledgeable members of the public about gene patents and the fact that they exist, and I think that's in combination with the fact that one gets very strong feelings from people when they learn about these things. I think it's very important that we have an extremely open process that elicits public perceptions, feelings, and ultimately the public's goals in this. So that, I think, is an important part of this and I think can be compared with the process we pursued when discussing genetic discrimination. That was something the public had strong feelings about and a strong stake in.

DR. TUCKSON: Yes. However, I want to be careful, at least that in my mind, that I remain open. If you say -- and you didn't mean this, so I'm being deliberately provocative -- dear public, do you realize that people make money on licensing these things and it elevates your cost of access to these things? Grrr, looking for somebody to kill. On the other hand, phrased a different way --

DR. EVANS: Right.

DR. TUCKSON: So I think it's going to be extremely important that the public consultation process be engaged once there is a clear set of facts, information, reasonable methodological data, derived facts, and then sort of saying there are some choices and some issues that need to be addressed. But I think the work is really on the front end to define if there is a problem, the

magnitude of the problem, the elements of that problem, before the public really gets brought into this.

DR. LEONARD: But part of what this public consultation process is to define is, is there a patient access problem that is happening individual patient by individual patient that we don't know about and would never find out about by any studies that have been done to date? Kind of like the genetic non-discrimination public comment. Is anyone experiencing this?

DR. TUCKSON: Let me take advantage of your experience and ask do we now know enough to know how much of that is because of licensing independent of any other factor?

DR. LEONARD: I don't think we know. But, for example, the Canavan families brought a lawsuit against the holder of the patent. So there is an effect on an individual patent level, at least for that one. There may be others that we're not aware of where disease organizations haven't brought a lawsuit, and I think that's the qualitative evidence that we may be able to get to that others can't if we do ask this question of the public.

DR. TUCKSON: So the way in which you would ask -- excuse me, Jim. I'm breaking every rule that I've established here. It would then, I think, Debra, mean that you have enough ability to phrase the question to the public that would say do you believe that you have been denied access because of patenting or licensing issues, and here are criteria that you can use to determine whether it was simply not affordability but in fact was patenting and licensing, given that so much of the patenting and licensing is below the water. The patient may not perceive it, so they may just interpret some things as, yes, I think it's probably in there, I think I've been denied it because things cost a lot.

DR. EVANS: The same is very true of, for example, genetic discrimination. People's anecdotal experiences weren't necessarily what really happened, and yet it seemed like an important thing to pursue.

DR. FITZGERALD: Just one thing on this. It might be critical to decide in this process, as Reed's questions have sort of elucidated, who are experts and who is the public, in the sense that I would consider some of the people that Debra is thinking about, like patient advocacy group people and all that, to be expert in some sense. They're expert exactly in that type of information. Are there people who are being blocked because of patents and licenses and that kind of thing, or are there people who are engaged in lawsuits or something like that? If those are the people who we're thinking about in the public comment process, absolutely, we've got to hear from them even before we can establish the language we're going to use to do perhaps a more broad public inquiry.

DR. LEONARD: And when we did the genetic non-discrimination public comment, we heard from patients, genetic counselors, physicians. I mean, it was at a number of levels, and I think you could do that process similarly with this.

DR. TUCKSON: Well, I'll back off on this and just say that the thing I'm going to be attentive to in looking at this is going to be the language that is used to describe whether or not you feel that you have been harmed in this regard.

DR. LEONARD: But that would have to be reviewed by this committee.

DR. TUCKSON: I'm just saying I can withdraw because I think that's where the art of it is, in the description.

DR. McGRATH: I'm going back to the earlier ones where I was really happy to see the emphasis on qualitative and quantitative research. When I read that, I was thinking that it would address issues just like this. So I'm wondering is it really consultation or is it rigorous qualitative research trying to get at these questions? Are you really trying to consult with individuals or you're trying to gather that data in the research phase? In my mind I could see it more as the research phase rather than as a separate consultative phase.

DR. EVANS: Yes, I think that's a good point. I think that one of the things that drove us to consider this whole issue of a more formal and a more elaborate public consultation, as opposed to what happens every time a report goes out, which is the public sees it after it's been drafted, one of the things that drove that is how difficult we all realize the task is of figuring out the impact of gene patents, et cetera, on patient access, and we are not probably going to have pristine quantitative research that demonstrates in a controlled fashion the effects, and we are going to have to rely to some extent on qualitative research, qualitative experiences and comments of various stakeholders.

DR. FERREIRA-GONZALEZ: Jim, going back also to in-depth public research studies and the public consultation process, maybe we need to propose the research that is being performed in a systematic way. When you go back to in-depth research study, if you're going to do a review of the literature on the ability of laboratories to bring new testing and the constraints because of current patent practices, I think you'll find a very different environment five years ago versus what you see today. You'll see, for example, if you asked me five years ago, in my laboratory did I have any problems with this, I would have said no. But if you ask me today, I would say in the last four months I was not able to bring six different tests in our laboratory. So it's a very different environment.

So maybe what we need to do is not just an in-depth research of the literature but also maybe to charge some of these.

DR. EVANS: Exactly, and that's actually something we get to in just a minute.

DR. TUCKSON: So what you have, then, if you go back to the points that I heard from all three now, is the public consultation process includes consulting with advocacy organizations, the public at large, and people like you, so we get all three of these constituencies coming forward.

DR. LEONARD: Maybe it could be called a public data gathering process, or information gathering process.

DR. EVANS: Sure.

DR. LEONARD: Because we're using the literature, number one, getting what information we can from published studies, the literature that's out there. The second is experiences of different groups who might have been affected to indicate whether there's a problem, and then the international perspective. These are just three ways. I didn't mean to jump ahead to the international perspectives. Those three would lead into the development of a comprehensive report to the Secretary where we could provide what information we found, but we could also say where the problems are and whether studies are needed, whether certain things need to be addressed by policies, these kinds of things.

DR. EVANS: So going ahead to the international perspectives, I think that as we deliberated, as we put this together, we all realized that perhaps we could learn something from the models in other countries. Obviously, we're going to have to be very careful to keep such comparisons germane and feasible. We exist in very different political and governmental situations, so we're not going to be able to transplant practices from another country into the U.S. However, we might be able to learn something that has been implemented in other countries that have dealt with these things. It would be kind of crazy, I think, to ignore the world experience with this if it could inform us, and then the development of a comprehensive report.

Now, going in-depth into these things, the in-depth research, we want to refine the study topics for literature review in the relatively near future and start a contract for that literature review. We'll commission that and then see what types of gaps, by the spring of '07, exist. At that point, then, what we have envisioned is a roundtable that would identify what gaps exist that are quite amenable to further data in a fairly near-term type of perspective, and what we have envisioned is if there are discrete types of questions that don't have an answer simply because the data isn't out there, the study hasn't been done and it's relatively straightforward, at that point we could actually commission limited studies in order to address those gaps.

If we find on review of the literature that all the questions are answered, we don't need that. If we find that, well, the questions aren't answered but there really doesn't seem to be anything very feasible, then we wouldn't go on to this. But if there are practical types of things that could be commissioned that would help fill those gaps, we'd have an opportunity to do that through this committee.

DR. AMOS: What sort of things do you envision finding in the literature? I mean, it seems to me that people are not going to talk a lot in the literature about their failures.

DR. EVANS: Well, in the literature or not, you look at Mildred Cho and Debra Leonard's work looking at the ability to develop certain clinical tests, those data are already a little bit old, and it could be, for example, what Andrea said a minute ago, that the landscape is changing quickly. Would it be wise to commission some kind of update to look at how is the field changing, how is the landscape changing? So I think that most of these things will be proxies. Most of these will be proxies for patient access that hinge on the ability to develop a test, the ability to offer a test, cost issues. I could imagine that there may well be a body of economic literature that has used modeling to look at aspects of the ultimate effects of access that gene patents and licensing affect.

DR. AMOS: What about a parallel study, like a questionnaire or something like that, some sort of survey that could be administered, maybe through the College of American Pathologists, that would actually -- I think the people who are actually using the tests and running the tests would have a pretty good handle on, like you said, Andrea, about what really the limits are and what they haven't been able to do.

DR. EVANS: Right. So if those things are either too old or they aren't out there, I think that's exactly the kind of thing that we could commission that would be affordable, because we can't commission a -- it has to be affordable and it has to be doable in a relatively short period of time, right? And that kind of thing could be.

DR. STANTON: Jim, as I listen to this, I think I'm finding one gap here, and that is the benchmark against which we're going to measure our results. When I hear that somebody can't deliver a genetic test, my ears prick up because I'm a big supporter of IP. But the other question is what's the standard of care and where are we going to gather the data or gather the opinion as to

what should be the standard of care so we have a benchmark against which to measure what should be provided? What's the ultimate goal to provide and what's feasible to provide given economics, given our tangible situation? So if we don't have that somewhere, and maybe it's when we consult with the experts that we have to get some input somewhere about what an appropriate standard is --

DR. EVANS: Kind of what an appropriate level of access is or something like that?

DR. STANTON: Yes.

DR. LEONARD: Are you talking about access or are you talking about whether that test is medically necessary for patient management?

DR. STANTON: Well, I guess I'm going to have to leave it to you, to the other side of the table to figure out the answer to that. What I'm saying is that in the abstract to say that the patient doesn't have access, the question that just came to mind as I was going through the methodology is should they have access to X versus Y, and when in the spectrum of medical care does that come into play? If, as we're going through our consultative process, we don't ask that question as to where it fits into the care process, then we're going to have this study in isolation.

DR. EVANS: Right. I think that could be addressed by -- well, you're talking about a survey. A survey could not just be administered to laboratory directors but to genetic counselors, to geneticists who have had experiences in which there was limitation because of the current licensing practices. This really gets to this issue of commissioned studies.

This, I think, we actually did not word very well. We are not interested here in expanding the literature per se. That is not our intent, and I think we should edit this a little bit. What I think this should be taken to mean is we don't want to reinvent the wheel. We want to look at where there are fillable gaps that we can commission a study in order to address. In that sense, it would make a contribution to the literature. But our real goal is not to make a contribution to the literature, it's to answer specific questions that we raise and recommendations that we can then make.

Emily?

DR. WINN-DEEN: I have two concerns. One is that if you don't go out in a very neutral way and do what I would call market research, you're likely to get a biased outcome here, because I think that some of the previous studies had a hypothesis in mind.

DR. EVANS: An axe to grind?

DR. WINN-DEEN: And they did a study that supported their hypothesis, good or bad. That's what science is all about in the general term. But I think in this case what we're trying to understand is what really is the scope of the problem.

The other thing is that I think if you only talk to lab directors, you'll never know why companies made a decision to do or not do. So I think you should make sure that you're looking at that side as well. This is the job I do at my company. I do in and out licensing, and depending on how somebody asks me questions, I could tell you just the horror stories or I could tell you the whole story of how 90 percent of the time it's okay, 5 percent of the time it's a pain in the ass but I get it

done, and 5 percent of the time I can't get the license that I want. So I think it's really important that whoever we commission to do this has a script that is not biased by the way it's written.

DR. EVANS: There's a refrain here, because Reed was saying much the same thing, I think appropriately, about the public consultation process. We don't want to bias the results by asking questions in the wrong way, and I think that's something we definitely need to keep in mind.

DR. FERREIRA-GONZALEZ: Jim?

DR. EVANS: Yes?

DR. FERREIRA-GONZALEZ: I also would like to see that we get not only an unbiased process in this, but looking from the two different perspectives of academia or laboratories, independent laboratories and industry, what has been the issues in licensing from different individuals and how that impacts on the overall cost, but not only in the overall cost or even access, but has it delayed access to the testing. Sometimes you have to wait a year to get reagents available because there's some litigation or some patents already. So access is not only being able to offer the test today but also have you been delayed in offering the test because of these issues, a year or six months.

DR. EVANS: Yes, I think that's an appropriate caution about who we address and how we ask them these questions. That's critical.

DR. AMOS: So will there be a prospective aspect to this report as well, or are you just looking at what's happened in the past that has blocked things?

DR. EVANS: Yes.

DR. AMOS: Because I think what I would like to see personally for the future of health care in the United States is some sort of plan or some sort of vision for what we could do to help get around some of these barriers as we move forward if there are any changes in the patent laws or anything like that, but also within the constraints of what the laws are now and what we have to live with now, what specific things we can do to help get around some of these things and make these things more accessible to the patient.

DR. EVANS: Yes, and what I would see is that as far as the specific studies that we commission, they're going to have to be very modest in terms of time and scope. But I could certainly envision in our final report really encouraging exactly that type of thing on a prospective basis that would look to the future.

The public consultation process. I think we have --

DR. HANS: Jim, just on the last point, I realize that Dr. Zerhouni and the Office of the Director can weigh in at any time, whether we ask them or not, but I realize that they're currently cogitating about what NIH can do on patenting and licensing. I'm not sure in what context, whether it's just in response to the IOM report or whether these issues are also in their minds at the moment. I wondered whether the committee had officially asked the NIH director whether there were particular perspectives or questions that they wanted to ensure were in the development of the scope.

DR. EVANS: No, I don't think so.

Sarah?

MS. CARR: Brian, do you want to speak to it, or Phyllis? Both of you are serving, aren't you, on the working group?

DR. STANTON: Well, we can come back to it. We're meeting again. We're not finalizing the study yet, so we haven't gotten to that stage yet as to the analysis of the Academy report.

MS. CARR: Well, I think it's safe to say that the working group has been paying close attention to Recommendation 13 in addition to the others in the report, and they're aware of SACGHS' interest in this issue and the patient access part of it, and they may speak to that, or I guess there are a variety of options on the table that may be presented to Dr. Zerhouni, one of which might support the work this committee is doing, and I think they just haven't finished cogitating completely.

DR. STANTON: Actually, I'd add this to Reed. I would say in some of the discussions it's okay that this committee is doing some of the work so we don't have to do it. So I guess the question is maybe there needs to be a conversation at some point between the two committee chairs and simply say how are we going to split up some of the questions, because we're looking at each other and sort of waiting for the other one to finish something.

DR. TUCKSON: We think you should do all the hard work and we get all the credit.

DR. EVANS: There you go. I like that.

(Laughter.)

DR. EVANS: We really, I think, have covered this ground. The take-home message, I think, from the discussion about the public consultation process is that we have to be very careful how we word these issues, and we have to try to target the appropriate public, some of whom will be experts in their own right because of their own experiences with these diseases, some of whom will have other interests. So we were thinking that we would solicit public comments over a two-month period and that that would be in early next year. We would invite key stakeholders to an SACGHS meeting next summer and then ultimately develop a final product that documented these public comments.

With regard to the international perspectives, we will identify and invite international experts that have written on these topics or have some position in which they deal with these things as part of their bread and butter, and then develop questions for an international roundtable session that I think, again, needs to keep as a primary focus the whole time the practical types of things that we can learn and not just kind of pie in the sky types of issues, and then next fall have the roundtable session.

As far as developing a comprehensive report, we hope that by late spring of '07 and ongoing to develop a first draft, then solicit public comments on the report by late summer, and by sometime in mid '08 have an actual report that we could submit to the Secretary. What we would like to get feedback from today is do you feel that the components of this approach will achieve the study goals? What do you think about the timetable, specifics about the methods that should be used to solicit perspectives from the interested stakeholders, and how can patients and consumers who have been affected by gene patent issues be identified? Again, that's a very difficult situation

because, just like in the discrimination sense, who knows whether I was denied this because of patent issues or whether I was really discriminated against?

That said, I think, again, involving the public is an important aspect of this because it is something that people feel strongly about.

Comments? Questions? Advice?

Emily?

DR. WINN-DEEN: Well, much as I don't like to say the timetable is too short, I think the timetable would be fine if you're not going to go out and try to get new information. But unless you're going to do that in parallel with the literature, I think it's probably a little ambitious.

DR. EVANS: Yes, I actually agree with you. As I was going through it just now, I was thinking, God, are we nuts?

(Laughter.)

DR. WINN-DEEN: Yes.

DR. EVANS: Yes, exactly. Now, it is true that we can pursue some of these aims in parallel, right? But I agree with you that we might have to revise this to be a bit more realistic since we're doing two things that are, in and of themselves, time-consuming. One is the public consultation period, and the other being, gosh, that we're really looking to generate some new data, if that's needed.

DR. HANS: Just thinking a little bit about what's gone back and forth on getting input from the public and the experts that work in the area, and yet we know that it's very difficult to determine exactly the reasons why access was denied, if I was writing a scope of work for a contract, I might include an option in the contract to do some case studies following the consultation period so that you could further explore what you got out of it, to go back to the companies, to go back to people and say we heard about this and we would like to find out more what that is about and all the reasons for the access. So you might have the option later if you found there were some issues that you wanted to explore more, that you had the flexibility in the contracting to be able to go back and do some case studies.

DR. EVANS: Yes, I like that, so you aren't just left hanging if you get interesting things you'd like to follow up. Okay.

Finally, as far as next steps, we'll revise the scope, we'll revise the study proposal, we'll revise the timetable and move forward and come back to you with our progress.

DR. TUCKSON: Jim, since you're really at the end of this, first of all, this is terrific. I really think that the methodology here is going to push this thing forward in a way that I hadn't thought of, and just the way you get at it, the way you try to answer the question of the significance of, the criteria, is I think going to be very interesting. I'm just starting to wonder whether or not there is some expertise or consultative advice that is different from what would normally be in this sort of domain that you may have to draw on, ways of trying to crack a problem like this. I'm trying to use examples that I'm not trying to stick by, but what percent of licensing fee versus total cost is a

significant number. I mean, how do you think about that? Are there health economists -- excuse me, regular economists, not even health economists, that this is how they make their living?

DR. EVANS: Right. What you bring up is exactly right. This is a really difficult issue. Trying to quantitate and characterize the impact of patents and licensing on something as downstream as patient access is immensely difficult, because we know that you can come up with all kinds of theoretical pluses and minuses to the whole thing. So not to be too much of a pessimist, I think it's entirely possible that we'll come through this and say we don't know, that we don't come up with definitive types of data that address this, but I think we have to try. It's clearly important, and we have to be creative in the people we ask and in the methods we use to try to get at those things, because we're not going to get direct answers. A lot of it is going to be by proxy, and I agree with you that the economists may have things to offer, et cetera, but it is very tough.

DR. TUCKSON: So we're going to all have to help them. The committee is bright and we've got a lot of smart people on it to sort of reach out and think of it in other ways. This reminds me of an IOM committee that I was involved with, the consequences of uninsureds, and it's interesting once you start to try to calculate the economic cost of uninsurance on a community. It's not traditional health stuff, and you start getting into a whole variety of downstream things, which almost brought in the need to invent a methodology for thinking about something like that.

So anyway, this is terrific.

Are there any other closeouts? Jim has still got the steering wheel for the closing.

DR. EVANS: Just basically other questions on the work plan? Other suggestions?

DR. PAREKH: Jim, a quick question. Is there any hypothesis that we have here, or given that it's a research study we're obviously not trying to couch it in one way or another? That's the first question.

DR. EVANS: Well, I think that the hypotheses will probably have to wait until we see what the gaps are, right? If we identify gaps that are fillable, once we look closely at the literature I guess we could formulate hypotheses. But actually, I feel like it's important to try to maintain a large degree of neutrality about these things and say, okay, here's a question that isn't answered, and let's see if there's an answer. So this really isn't, in my mind, really hypothesis generated or hypothesis driven.

DR. PAREKH: Whenever this concludes, in 2008 or 2009, the end product, do you see this being more of a report or potentially recommendations?

DR. EVANS: What I really hope for, and I don't know if we're going to be able to accomplish this, would be actual recommendations. I mean, the real dream here would be we identify some things that are good and some things that are bad and we say, look, here are three or four discrete things that the Secretary could work towards that would enhance that ultimate positive/negative ratio of the pluses and minuses to gene patents on patient access. So I would hope that we would have some tangible recommendations. I don't know if we're going to because I don't know if we're going to be able to get the kind of concrete data that would allow for discrete recommendations, but I certainly think that's what we should shoot for.

DR. PAREKH: Thanks.

DR. RANDHAWA: I should have asked this earlier, but just a clarifying question about the scope. How are we defining the test? Is it strictly a genetic test in the context of a genetic counselor/geneticist, or is it a more broad-based definition?

DR. EVANS: Well, I think in a way what we're talking about here doesn't matter so much on the modality of testing as it does on whether gene patents affect that, right? So if people are doing -- as we all know, you can do genetic tests without ever looking at a gene, right? But if gene patenting doesn't have an impact, then I think it's definitely outside our purview. So I would just try to keep in focus the fact that we're interested in how gene patents affect testing. Usually I think that will rely on looking at either the gene or its expression in a fairly proximal sense, but I think that would be the answer.

DR. RANDHAWA: The only reason I'm asking that is I don't know to what extent is patenting common in testing platforms and methodologies, as opposed to specific genes. Are we going to be exploring that or not?

DR. EVANS: Say that again. Looking at --

DR. RANDHAWA: Again, I'm no expert here, but, for example, say microarray technology or proteomic technologies which are not looking at specific genes but a platform or a methodology is being patented.

DR. EVANS: Right. Let me think, because I hadn't really thought about it in those terms. I don't think we're talking here about the patenting of technologies and platforms, and please weigh in if this isn't what you all perceive. I think we're interested in, again, how the taking out of patents on genes, on specific genes have an impact on all this. That's different from, say, patenting a technique for sequencing, or patenting a technique for analyzing expression. Would you agree with me on that?

DR. STANTON: You said something earlier that I agreed with, and then you phrased it a little differently, so maybe clarification is useful. When I think of a gene patent, you said gene patents and closely allied or first derivatives technologies, the gene expression product or the gene. The gene: what does that encompass? Maybe one of the things we're going to have to do as we start down this road is define what we mean by that patent family.

I will share the experience that two years ago my office tried to ask the question of the effectiveness of NIH's licensing and said what are the metrics we should use, and we found that you can't use a single metric. So in the same way, if we were to look at the entire family of patents, I think we wouldn't be able to get any answers. So maybe the first thing we should do is sit down as a group and say what do we mean by a gene patent, and then that will lead us into our case studies so that we can -- I think Sherrie's suggestion is fantastic, to use that so we formulate our questions with very concrete algorithms in that way.

DR. EVANS: I agree. So I think your question is a good one.

DR. STANTON: It's right on point.

DR. EVANS: Right. We obviously do need to define that, and the trick really comes in at how far downstream from the gene do you go. I think we would all agree that a new sequencing technology would not be something that is within our purview, but I think we have to decide whether it goes beyond the patenting of a specific sequence or, say, alleles, SNPs.

DR. AMOS: I'll give you a specific example of how a gene patent can affect other testing. When you own the rights to a gene sequence, you own all the rights to use, to make, to have used, to have made, et cetera. So in any case where somebody wants to develop a protein test and they have to express that protein recombinantly, they can't use your patent unless you license it. So it's pretty broad.

DR. EVANS: But that would be people who own the patent on the sequence of that gene, right?

DR. AMOS: That's the whole point.

DR. EVANS: And that would be important for us to analyze, what the impact is.

DR. AMOS: It goes beyond just a test to see if somebody has a specific SNP.

DR. EVANS: Absolutely. Exactly. So when somebody owns the patent on a sequence, they own the whole shebang, right.

DR. FITZGERALD: Jim, just one other wrinkle to that, though. I mean, I think you also have to take into consideration the fact, certainly in some of the cancer tests that might be developed, that you could have gene expression changes that aren't due to any somatic or germ line mutation but just an epigenetic change, a methylation difference or something. So you probably wouldn't want to be quite so narrow to demand that it would have to be --

DR. EVANS: Well, the question again is would those types of things be covered by somebody who owned a patent on the sequence of that gene and its alleles?

DR. FITZGERALD: No, not necessarily, but they could presumably patent the information involved in the methylation testing. Therefore, you'd still have something that would be acting like a genetic test the way you're defining it.

DR. FERREIRA-GONZALEZ: I think what we were thinking about here is not just going to inherited disorders. Don't focus just on inherited germ line mutations or changes. Expand that to allelic variances and also somatic changes that cause cancer, which is a genetic disease.

DR. EVANS: Well, again, I think what this gets back to is if somebody owns the patent on a gene sequence and its allelic derivatives, if that is used in their assay or in somebody else's assay, research, diagnostic test, it's covered by that patent.

DR. AMOS: Yes, if it can be used to block somebody else from doing something that's going to help a patient.

DR. RANDHAWA: Help me out here, because I'm still not sure I understand how this would apply to proteomic tests, which are looking at profiles of proteins or peptides.

DR. EVANS: I don't think it would, unless they used in their technology the sequence, just like you described. If they need to create a peptide from the gene that you have patented, then it would have an impact on it. But as far as a technique that uses NMR to look at proteomic degradation products in the serum to diagnose something, that would not be related. That wouldn't fall under the issue. There's a lot of confusion and gray areas about what's a genetic test and what isn't, and that's very legitimate. But as far as what's a gene patent, I think we can

probably come to a pretty concrete definition for that, and it's the patenting of the sequence and its allelic variants.

DR. HANS: Jim, just to remind everybody, it's in the statement that you have in your scope of work, but the charter for the committee actually covers both sides; that is, gene patents and access to genetic technologies. So you still have to define genetic technologies.

DR. EVANS: But I see us as linking that, gene patents and the impact on access to technologies.

DR. HANS: Genetic technologies. It says "genetic."

DR. EVANS: Exactly, but starting with gene patents.

DR. HANS: But I see it as overlapping circles, and you're only doing that which is colored in the center.

DR. EVANS: Right, which I think is, in and of itself, a huge bite to chew off. I think we need to focus on the impact of patenting gene sequences and alleles. That would make sense to me.

DR. LEONARD: However, everything that's gone on with gene patents is likely to occur further down the road with proteins and proteomics, since proteomics is more nascent than genomics. So whatever recommendations are made relevant to gene patents could easily be translated and applied at an earlier phase and hopefully prevent less of the exclusivity in clinical practice on the proteomic side.

DR. EVANS: That's a good point.

I think we're actually a little ahead of schedule.

DR. TUCKSON: For which you get an extra cookie.

(Laughter.)

DR. TUCKSON: Didn't he do a good job? Thank you. Good job. You get some applause, too, by the way.

(Applause.)

DR. TUCKSON: This is going to be a fun one. This is really going to be fun.

Public testimony. No, you're not getting a break yet. This is the public testimony.

DR. LEONARD: There isn't a break scheduled. So can't we have one?

DR. TUCKSON: There wasn't a break scheduled? Why don't we take five?