Patents and Licensing Session
Full Roundtable Panel and Full Committee Discussion and Next Steps
Facilitator: Debra Leonard, M.D., Ph.D.

FULL PANEL ROUNDTABLE DISCUSSION

DR. LEONARD: Mildred, Mark and I are going to sit down there and I'm going to be a panel member for this next panel discussion and Reed is going to head up the discussion. I'm going to take my nametag and go down there.

DR. TUCKSON: I want to thank her for that and I want to make sure it's very clear. I'm really urging Debra to have the freedom to present her thoughts and ideas not constrained under the role of panelist but in her role as expert on this topic. So she is clearing changing roles and I want her to do that.

Julio was first from a way long time ago and then after that Francis, and then we'll do Cindy and then Kevin.

DR. LICINIO: I had my initial question followed by another one, which is that the use of the testing is very important and the three of you gave wonderful presentations. One thing that I think is even more of a problem than what has been discussed is the technology has evolved and will continue to evolve very fast so let's say some of the things that Francis was doing in the lab like 30 years ago nobody would be doing today. We are doing things much more efficiently. So this idea of doing like one genetic test and one by one for each disease separately and charging for them as individual tests is technically in the process of becoming obsolete. So let's say you could put all of the tests on a chip or let's say at least all tests for a whole—like for all neurological—neuropsychiatric disease or for all heart, metabolic, endocrine diseases in one chip, and that would be much easier to do and much cheaper to do.

But I see that what you guys presented as roadblocks in terms of the patent holding is not only a problem for the present but it's going to be a major roadblock for kind of technology development and making these things available in the same way that you would have for other types of genetic testing for research. How can the technology evolve with this roadblock in the middle?

I understand that the company is going to like invest so many million to develop something but what you said towards the end, Mark, let's say that you come up with these five markers for one disease or for one condition. It's kind of—now the Amplichip is like testing for two genes. It's kind of almost stupid to put like an Affymetrix chip testing for two things so you could put 200—2,000 tests there.

So if everybody is charging then I think it's going to become completely prohibitive and how do you handle—what's going to happen in the future?

DR. MCCAMISH: Thank you.

(Laughter.)

It's a great question, Julio. Yes, multiplexing is obviously the future. One way right now we're looking at 160 million tests so it will be unlimited in terms of what things can do as the technology advances. I think as we move forward you have to provide some flexibility in both

areas. How do you provide incentives for research to move forward and how do you provide for adequate health care and the use of the diagnostic?
Right now the big issue is showing these polygenic associations with the disease. Those are hard to do in finding sufficient SNPs that give you enough clinical utility. I mean for us to find a single gene associated with one of the phenotypes we've been talking about is pretty straight forward. To find enough genes and a polygenic trait to be useful is difficult but all of those would be for one particular.

So let's say that you then had a predictor of diabetes and a predictor of let's say cardiovascular disease and you wanted to use that on a single patient, your question is, well, if two people own that patent, how do you deal with it. It's just something that we'll have to evolve with and if there's adequate use of the test and the cost of the test can be lower so that anyone who spends money on research can allow that to happen, and to me this is not real new.

I mean being as part of the industry and part of research the whole time—I've never been in a marketing or sales position—it always drove me nuts when you would finish this 14 year program in developing a drug and you hand it over to marketing, and the pricing is not based on the most people you can treat. The pricing is based on what the market will bear. What's the most money you can make with the drug? I'm not here to say that's right. I'm just saying that's what's done.

There's a balance and how do you make that balance of doing the research, getting treatment out there but then expanding it to the most patients is a question beyond that.

DR. TUCKSON: Let me just make sure that we—right now the order is Francis, Cindy, Kevin, James and Emily but I want to make sure, also, that Debra and Mildred have an opportunity also to dialogue with each other. So would you please feel free to interrupt each other if you have a comment that's relevant to the comments that are made. Please do that without permission.

DR. LEONARD: Well, I would like to respond to Julio's comment/question. It's one thing if a company has genetic information and makes an in vitro diagnostic test kit and sells that to laboratories to be able to do testing. I don't know what your plans are, Mark, for these five to ten markers that you find, whether you're planning on being a reference laboratory or making in vitro diagnostic test kits that will go through the FDA and then be sold to laboratories to be performed.

We don't really have a problem as laboratorians with that approach to the diagnostic testing and probably then that information will be proprietary. We'd have a black box test which doesn't always make us comfortable because we're used to be able to know how it works and that kind of thing. But then that test can be broadly provided by a number of laboratories. There can be competition for pricing and you would set the price or a company would set the price of that testing but that's much more palatable than a single provider of a laboratory service.

We have test kits that are provided for our chemistry tests, for our hematology tests, and we—there's competition for pricing, et cetera, and we use those test kits.

So I would imagine that much of the genetic testing like Julio was imagining would be in the form of in vitro diagnostic test kits developed by companies and sold broadly to laboratories which doesn't raise as much concern in my mind, although I wonder if the companies would have the problem with the cross licensing issues and whether it puts limits on a company's ability to do more broad diagnostics than the single gene or whatever they can get the patent rights to use.

DR. MCCAMISH: Let me just respond in terms of that. For our plan what we've determined, bad or good, is that it's hard to make money with a diagnostic. With all the investment we're putting in—

DR. LEONARD: We have the same problem.

DR. MCCAMISH: --it's—

(Laughter.)

DR. MCCAMISH: --I mean I feel for diagnostic companies in this term. The only way that we think we can make a profit is to, in fact, support the use of the—pay for the diagnostic so that more patients are screened and more could theoretically be exposed to the drug. So the revenue we would get would theoretically be through the sales of the drug and not through the diagnostic itself. We'd be supporting the diagnostic.

But let me get to one point and you brought this up a couple of times, and that is price competition for you and other labs doing a different test that may be patented and that you could do it cheaper and, therefore, it's better. I mean, to me, that's almost like if you take Lipitor—I mean there are a lot of companies that can make Lipitor cheaper and there are pharmacies that can compound it and there are people that can tablet it but that's inherently against, I think, having that proprietary position with that exclusivity.

So providing it cheaper with various labs to me does not necessarily suggest that we should change patent law for that issue because you can take a drug like Lipitor and make it cheaper and make it available through various generic houses but that's not allowed simply from a price perspective.

DR. TUCKSON: Francis?

DR. LEONARD: In other parts of my talks—I give a lot of gene patent talks, you might have assumed that—I talk about the difference between diagnostics and drugs, and I know that patent protection is needed for drug development because it's—but you don't need the patent protections and incentives, as Mildred showed, with the HFE gene patent and hemochromatosis testing. That incentive is not needed for the diagnostic development in clinical laboratories.

So to talk about drugs, yes, I agree that patent protections are needed and I've never argued that you should get rid of patent protections. It's really the licensing and enforcement that needs to be changed.

DR. COLLINS: So I want to thank Debra for organizing this session and all three speakers for very thoughtful contributions to what has been a discussion that has been going on for a couple of decades.

I think we are at a critical juncture. I agree that the National Academy panel, while they came up with some very useful recommendations for research, they did not get into this territory as deeply as we are this morning. Obviously it is a thorny set of issues.

Certainly from my perspective having been here now for 13 years, this issue of intellectual property and genomic discovery is practically never off the table. It's always there either explicitly or implicitly. I think the strategy that NIH has tried to take from the beginning is

to always ask the question what is going to give rise to the maximum public benefit. It really seems like that is the question one ought to consider in making a decision about what kind of patenting and licensing policies ought to be followed for genomic discoveries.

That led, of course, in the sequencing of the human genome to this fairly dramatic and unprecedented decision to release all of the data every 24 hours without filing any intellectual property claims on any of that sequence beginning in 1996 and continuing right up to the present moment, a strategy that we will continue to follow. That same strategy which was formalized in the so-called Bermuda principles and later on somewhat expanded to other types of genomic data--we had a meeting in Fort Lauderdale—has guided our efforts in other projects like HAPMAP, which also placed all of the information about human genetic variation in the public domain where it could be maximally utilized by anybody who was interested.

But, of course, now what we're talking about is moving one step closer towards a utility which is connecting that genetic variation with phenotypes and particularly with disease phenotypes.

I think traditionally that has been an area where such discoveries generally have led to patent applications, whether the discoveries were made in academia or in the private sector. Certainly I don't think too many people would question, just in terms of the grounds of novelty, utility and non-obviousness, that the patent office is probably not likely to change their perspective that a discovery of a gene variant that's connected to a disease risk phenotype is probably going to meet their standard and they would probably consider that a patentable discovery, whether or not we like it or not. I think that's probably the case just based upon the way the patent law is interpreted.

So unless one wants to try to change the law, I think it will be difficult to try to lobby the patent office to get them to stop allowing such issuances. That probably is not a viable solution if your goal is to try to make these more broadly accessible.

Instead it seems the solution really has to be the actions of those who are doing the science. In that regard I think everybody is aware that way back almost 10 years ago the NIH Guidelines on Research Tools made it fairly explicit that this goal of public benefit ought to guide what happens if you're getting NIH funds, and that has been implemented fairly explicitly for intramural research.

One consequence of that is that gene discoveries of this sort we advocate ought to be licensed non-exclusively for diagnostics, although potentially exclusively for therapeutics if you can make the argument that that's necessary for the investment to occur that would be required to bring a therapeutic to market, which as we all know can be a very large expenditure and for which I think one can in many instances make the case that patenting really has benefited the public by allowing that kind of investment to be made by an organization that then will enjoy a limited monopoly to recoup their investment.

For diagnostics I have to agree with the conclusions that Mildred's study documented and that Debra has also mentioned but I don't think the data is really there to suggest that in most instances, maybe in all instances, that you require that kind of exclusive licensing capability in order to inspire the development of a diagnostic because developing diagnostics these days, while it's not trivial, it is not a heavy investment requiring kind of activity. There are all kinds of wonderful platforms that will allow you to do genotyping for incredibly low cost and most of those are fairly generalizable so it's not as if you have to come up with a new technology for each gene that you discover a variant in. It's the same technology.

So more recently NIH issued a document which I think has been well received, although there were some objections raised to it, called Best Practices for Licensing of Genomic Tools, again getting into territory where we don't have legal authority to enforce actions but we do have the bully pulpit and this was an effort to use it basically to say to NIH grantee institutions that when it comes to licensing if you have now gotten a patent on a genomic tool, and this specifically included this kind of discovery of variants in genes that are associated with disease risk, we would urge fairly strongly that that not be licensed exclusively in order to, therefore, avoid the kind of outcomes that Debra outlined for us where a monopoly situation appears to both keep prices high and potentially limit access and maybe even do some damage ultimately to quality because there's no incentive for competition and, therefore, to drive the new platforms into perhaps even higher efficiency and better quality kinds of territory.

But we are now in an interesting time. As Mark outlined, the real exciting research agenda right now, and it's one that's coming to pass very quickly, I think more quickly than most of us really had quite expected, is the use of the HAPMAP approach to enable us to discover gene variants that are associated not with rare diseases but with common diseases, with hypertension, with heart disease, with schizophrenia and bipolar illness, with asthma, with diabetes, with obesity. You can go right down that list of the diseases that are most common and that fill up our hospitals and our clinics, and we are going to discover, folks, in the next two or three years the major genetic contributions to those conditions.

Now I say "major" in that we all know there are hereditary factors but no single gene variant that gets discovered for any of those diseases is going to be definitive, of course. There are going to be a long list of gene variants to contribute to something like diabetes and each individual variant maybe will only increase your risk by 20 or 30 percent but you put them all together and you have a pretty interesting circumstance where perhaps in two or three or four years the ability to make predictions about who is at highest risk for what disease or what reaction to what drug will start to get pretty reasonable and then get better as more and more of these discoveries come along.

So how do we want that to play out in terms of the availability of those kinds of diagnostics? I have to say if we end up in a circumstance where what you really want to do is offer a multiplex test that covers the possibility of more than one disorder and lots of variants for each disorder, it's going to be a really colossal mess if in order for any provider of laboratory services to be able to put together such a multiplex testing panel they have to do two years worth of legal work and pay all kinds of royalties on each one of these individual discoveries that is owned separately. If some of them are exclusively licensed to one entity then we're even in a bigger mess.

So if there was ever a time, it seems to me, to try to have these sorts of discoveries not constrained in that way, this is it.

So what are we doing about that? Mark described to you some of the work that's going on in Perlegen, which is a remarkably effective platform that they've developed and it was a major contributor to HAPMAP in terms of putting together the catalogue of human genetic variation. And, of course, they are now a major player in applying that for discovering variations associated with drug response or disease risk.

But there are lots of players and, in fact, NIH intends to support a lot of this research in they course of the next couple of years.

Now, interestingly, when you go and talk to big pharma about this issue of how should we handle intellectual property for discovery of gene variants that are associated with common disease, my conversations with quite a number of those companies is they would really much prefer for that information to be considered pre-competitive and placed in the public domain. They're not worried for the therapeutic consequences of these discoveries about having intellectual property protection.

They think this is a great way to identify attractive targets but they're confident enough that their ability to actually capitalize on that will depend upon their ability to find a small molecule that goes after that target, and they don't think the target itself needs to be claimed or owned by anybody.

Now that may sound surprising but it's backed up in a specific instance by Pfizer deciding to make a major donation of funds, actually genotypes, for this project called GAIN, which we have talked about around this table before, the Genetic Association Information Network, which is a public-private partnership between NIH and the private sector, notably Pfizer contributing the genotypes, which are being done by Perlegen, and also additional funds from Abbott and Affymetrix also contributing chips to enable this to go further.

So out of that project which is now under review, applications received as of May 9th, seven studies of common diseases will get underway come this fall and the first data from this should come out in early 2007. The intellectual property policy which you can read about on the website for GAIN, which is run by the Foundation for NIH—they are the organizer of this partnership—explicitly states that the intention is that all of the data from this association effort will be placed into a database where anybody with a valid sort of interest in the data can see it and they'll see it at the same time as the investigators who submitted the DNA samples in the first place and there will be pre-computed associations of which SNPs showed association with which phenotypes.

There will be also an explicit statement, there is already, in that set of policies that in the view of this public-private partnership it would be better for these associations to be donated to the public domain and not constricted in terms of intellectual property claims.

The pre-computed associations are an explicit intention to try to make that obvious and to put that data in the public domain as prior art so that third parties will not be tempted to jump in and try to claim such associations. They will be publicly disclosed from the very first moment.

That's a very concrete example of how a major company, a couple of biotechs, and the NIH an the Foundation for NIH are all trying to influence the circumstance to inhibit the likelihood of large numbers of patents being filed on individual variants that are going to be associated with disease risk or drug response.

The NIH has at this very moment a very intense discussion going on led by Betsy Nabel, the Director of NHLBI, about how we should handle other examples of whole genome association studies for common disease that NIH is going to be funding because GAIN is just covering seven studies. There's a whole new initiative which, if the congress approves it, will kick in FY07 called the Genes and Environment Initiative, which you've heard about before and David Schwartz mentioned yesterday, which will fund additional studies of this sort. I think there's a strong sense so far in that discussion that in those instances as well we should strive for public disclosure at the earliest moment to try to discourage constraints on the use of that data in terms of further downstream applications for diagnostics.

So that's a bit of a long statement and I'm sorry it's not really a question. It's really a little bit of a speech but I thought for this discussion it would be very relevant to hear what the context is here at NIH where we're likely to be funding very large numbers of these studies even though they are expensive over the course of the next two or three years, and we do see this as really a historic moment and one where if we do it right we should achieve really remarkable public benefit but if we do it wrong it will be tangled up in all kinds of constraints for a much longer period of time than it should be.

DR. TUCKSON: Well, first of all, thank you, Francis. I think that kind of perspective is exceedingly important and useful.

What we're going to do then is, as we take the rest of these questions, there's a two step process that the committee has to engage. With that very important background and the other presentations, you should now be asking the questions that you need answers to, to be able to participate more effectively in a discussion after the question and answer period with just the committee among ourselves to try to determine what, if any, next steps you think you want to proceed.

So just understand where we're at. So right now you have a chance to query the speakers to get information that you need to better participate in a discussion around what, if any, actions you want to take as a committee.

Cindy, you're next.

MS. BERRY: I agree completely with what Francis, of course, was saying about the realities of the patent and trademark office and what they deem patentable and what not but, just suspending reality for a moment, how useful would it be or could it be to make a distinction between a gene, discovery of a gene, and a genetic variant versus development of a test to locate that or identify it? I mean would that—

DR. LEONARD: It would solve the problem.

MS. BERRY: Would that—

DR. LEONARD: It would basically solve the problem. If you consider that the gene-disease association is a natural phenomenon, we're just identify that it exists like gravity, then that's in the public domain. We use test kits all the time that are patented but we have the ability to also use that basic information if there isn't a test kit available. It's not controlled by one person. That distinction is exactly what's needed in my mind.

DR. TUCKSON: Thank you.

Kevin?

DR. FITZGERALD: Two quick questions, one perhaps for Debra specifically and the other one for all three.

The specific one is what—do you know what the basis was for the writ being dismissed as improvidently granted in the metabolite case? You had the other—the minority opinion was interesting.

DR. LEONARD: Well, that's all that was written but—

DR. FITZGERALD: That's all that was said?

DR. LEONARD: --it's my understanding that the product of nature argument was not fully argued in the lower courts.

DR. FITZGERALD: Right.

DR. LEONARD: And that's the major point of the presentation to the Supreme Court.

DR. FITZGERALD: Right.

DR. LEONARD: So the Supreme Court basically sent it back down.

DR. FITZGERALD: So that they would reargue product of nature in the lower courts.

DR. LEONARD: If it gets there.

DR. FITZGERALD: Got it.

DR. LEONARD: I mean if that's done.

DR. FITZGERALD: Right.

DR. LEONARD: It's not clear that that will be done--

DR. FITZGERALD: Okay.

DR. LEONARD: --and that it will go back up to the Supreme Court.

DR. FITZGERALD: Okay. The other question I have for the three of you, if you have any input on this, again I understand the U.S. situation is somewhat unique. We have our own patenting questions but I always like to know a little compare and contrast what's going on elsewhere and what their experiences are, particularly in Europe where they have a different sort of patenting arena.

So what are the experiences of the diagnostic labs there with this patenting issue since it's a much different sort of landscape?

DR. LEONARD: They don't have this problem as far as I know. There is—in talking to David Korn there was a group from NAS that went to Europe and explored the European experience. It was only half of the NAS committee, though, that went. They were very—I don't know what it is but it's something that we—that you, as a committee, could explore in future deliberations to see what the differences are between the European patent system. But there is some basic difference that allows these things either not to be patented or not to be enforced for medical use and I don't know the details of that but it is something that could be explored.

DR. TUCKSON: Thank you.

James?

DR. EVANS: I'll save my comments for the discussion.

DR. TUCKSON: Emily?

DR. WINN-DEEN: I guess I wanted to go back a little bit to your comments about kits being okay. Do you have concerns about a situation where a gene is exclusively licensed to one manufacturer and manufacturers have problems. What happens if even if they make a good kit and you're happy with it if they go on back order in the case of the HFE, an earthquake hits California and there's no production for some months? I mean what's your opinion about sole source even for a kit?

DR. LEONARD: It's bad. I have two examples. One is when Biorad was selling the HFE kit and enforcing that against laboratories, there were two major mutations that it is detecting but just adjacent to one of them, H63D, there is another S65C. So 63 versus 65 is not very far away. In fact, the S65C was not taken into account in the original design of the kit and it created problems for incorrect results for H63D. Yet that could be the kit that everyone is forced to use.

Also with Invivoscribe, there were technical problems with some of the Invivoscribe kits such that you would get false peaks where you weren't supposed to get them and they could be interpreted as false positives. This wasn't occurring with laboratory developed methods or other reagents that were being used and yet we're being forced to use this kit.

So I was a little bit trying to give a shorter answer. Given a sole provider of a test where you send the test to a reference laboratory that's the sole provider of that test versus having a test kit that's sold broadly that's better versus being able to choose the way you want to do the test that's the best quality test that you can provide to the patient either using that kit that's available or your own methods or tweaking that kit.

So not to go on and on but Invivoscribe, also as part of their license agreement, you had to use their kit as they specified it with the reagent concentration that they specified. If you used half the reagents because you could do the 25 microliter reaction volume instead of 50 microliter reaction volume and get the same answer, they charged you more.

So there are complications with even having <u>in vitro</u> diagnostic test kits but on a scale of things it's all relative.

DR. MCCAMISH: It would be really interesting maybe to get Joe Hackett's response in here. I was thinking more again in the polygenic and predictors of drug response. So let's say—and from our perspective you've asked how we're going to do it. I really don't care how the diagnostic gets out there from my perspective. I'd like as much broad coverage as possible in terms of doing it. But from an FDA perspective, if a company proceeds and develops a co-product so it's a diagnostic predictive of an adverse event to a specific drug, and the label comes out that says you need to test patients and exclude them if they're at high risk for this adverse event.

Joe, how would FDA handle that? I mean, let's say if we discovered that and then we just broadly made that available. As Francis mentioned, the work we've done—we've put all of our SNPs in a public database so that has not been an issue. So let's say we make that broadly available. How would FDA handle that because it is being used as a diagnostic test for use of a drug? Would you allow labs to generate their own tests or would it be required that it would be handled by a sponsor or manufacturer?

DR. HACKETT: The answer is yes and no. If the drug manufacturer says you have to use the test to eliminate adverse reactions then they'd have to use the test. Preferably a diagnostic test but it could be a home brew. On the other hand, if you use a test exclusively to develop the drug itself, you could use that just about any way you wanted to. It would not have to be FDA approved. So there's two uses. You develop a drug and you use the test once the drug is marketed. Once it's marketed it could be a licensed—approved diagnostic test or it could be a home brew. Our preference, of course, would be approved test.

DR. TUCKSON: Very good.

DR. MCCAMISH: So your preference was an approved test versus a—

DR. TUCKSON: One of the things, by the way, we're going to do on—Francis, you wanted to comment on a particular point?

DR. COLLINS: I just want to clarify. So you would not, therefore, expect that it had to be a test that was exclusively licensed and contributed by a single laboratory as long as it was a test that was validated. I'm trying to understand what you're saying about the specific situation where the test is attached to a drug and basically the test needs to be done according to the labeling before the drug can be prescribed. Does it matter to FDA whether that test, once the data has been generated to show its value, is conducted by a single laboratory source or whether it's non-exclusively licensed and is available from multiple sources?

DR. HACKETT: Probably would not matter whether it was exclusively licensed or not because the labeling could say that you should test where there is a test available for such and such without identifying whether it's licensed or not.

DR. TUCKSON: Julio?

DR. LICINIO: I had a question on the point about the testing that's not for diseases. So let's say if you have a gene for all the tests that Deb described so well before for canavan disease, for the other ones, for cystic fibrosis, et cetera. If you have the gene or the breast cancer genes, if you have those you have a certain likelihood of having disease, they are like a disease causing gene. For the complex diseases and for pharmacogenomics to some degree it can be a susceptibility gene. In other words, in some cases, let's say if you have the CYP2D gene duplicated, and you have ten copies, you are going to metabolize a drug faster than if you have only one copy.

But in terms of drug response, sometimes what you see is that there is more contribution by one gene in the end to have the full response of the drug and these drugs—some of them are kind of dirty and act at multiple targets. You have to have a certain number of variants at a certain number of genes. Different populations even can have different variations in that so that we frequently see as we edit papers and our review of them that sometimes what's published in one population is not replicated in the other. It's not because the result of the first one were like false or the science was bad but because the genetic contributions for the other one may be different.

So when you're talking about genes that have like a 5-10 percent or even less, 2-3 percent effect in terms of causing a susceptibility to a disease that's also aggravated by environmental factors, you can have all the genes and if you have a different type of environment you may not even have the disease to begin with.

So how do you deal with that kind of testing because you're not testing for—usually when we talk about the diagnostic testing for like a diagnosis you're telling someone like something that's likely to happen. But if you have a two percent susceptibility of something because of a variant, how do you deal with that in a certain population, maybe not even in the other?

DR. CHO: Can I respond to that? It depends on how the patent claims are framed in the patents that are actually issued, which varies widely. So it depends on what is specified in the actual patent. The way the patent language goes is not—does not really track with the way scientists think about how the—how effective the tests are or whether they are diagnostic or not.

So, for example, some kinds of these patents claim the association between gene or a certain variant of the gene and maybe particular variants that are specified where the actual sequences of the variants are given in a particular disease. Some of them claim the gene in general and don't provide a lot of detail on the variants. Some of them actually claim the act of analyzing the gene, meaning sequencing it and looking for haplotype in a very vague way not specified.

So whether it's the predictive value or the diagnostic value is irrelevant to the way the patent law works.

To the issue of multiplex testing, I think the response that we have seen from laboratories so far is that the laboratories that are moving towards multiplex testing and even some of the tests that may have 800 or more genetic markers on them, on chips, have basically been ignoring the patents at this point. Partly because you can't even keep track of how many—and the specific language of each particular patent for each particular genetic variant or gene or whatever, and there has not been a lot of enforcement on the multiplex tests for these massive numbers of kits.

But having said that, I think you probably are familiar with the situation with triple tests where a patent was enforced on one of—on that and there was sort of a revolt from the medical community about that enforcement and so that may be sort of an indicator if patents are enforced on high volume tests what will happen.

DR. TUCKSON: Okay. Let me do a process check. We have seven to eight minutes of more time for questions and we have three people in the queue so we're going to do Sherrie, Andrea and then Barbara.

DR. HANS: Thanks. I just have a quick clarification to make sure that I've understood the implications of some of the discussion this morning.

Dr. Leonard has suggested one mechanism to fix some of the issues that she has raised, which is to exempt medical personnel who perform genetic tests from patent infringement actions, specifically for clinical purposes.

Would that have any impact, Dr. McCamish, on your business model, particularly as you've said you don't believe you can make money from the diagnostic tests alone if that suggestion from Dr. Leonard were put into effect?

DR. MCCAMISH: Again I'm not here as a diagnostic manufacturer. I think as we have looked at the business models it's difficult to justify the investment necessary in to a genetic diagnostic predictive of disease, for example. It doesn't make a lot of sense as you go forward.

Now Francis mentioned that it's not very costly to do some of the testing but to gather the information and get the phenotyping and the samples necessary for the things that we do is quite costly in that situation. So I would say by exempting medical practitioners and labs from patent enforcement would be problematic in terms of developing diagnostics of clinical utility as we go forward particularly in the polygenic area.

In the monogenic area that's a difficult thing to deal with. I would say, from my opinion, yes, that would be difficult.

DR. HANS: Yes. We probably don't have time but I have to say that I don't entirely understand the argument.

DR. MCCAMISH: You don't understand the argument of research—

DR. LEONARD: If you're not going to make money on the diagnostic, why is it a problem if we can do the diagnostic for you and you make the money off the drug?

DR. MCCAMISH: Well, from my perspective, I think that's fine. All I'm trying to do is represent adequately a diagnostic company that's purely investing in the diagnostic itself and they've been doing it for years. When you look at this again—when you do an SMA20, for example, and you come up with ways of doing 20 different tests and making money on those particular tests because they're used time and time again all the time, this is a genetic test and even BRCA1 and BRCA2—I mean the cost for these are like two or three grand for doing the test. And that's because again I'm trying to get some return on investment for the development.

If it's in the public domain and you have this information that comes from an academic community and it's out there in the public domain and anyone can use it that's fine. All I'm suggesting is when it gets into the complex polygenic markers of disease there's fairly substantial investments involved with that. And if you can't recoup that then individuals aren't necessarily going to be investing in it.

DR. HANS: I think the actual cost of a laboratory like Dr. Leonard's doing such a panel of 200 genes is going to be prohibitive on an individual basis. Then you really are talking about developing a kit. I mean it seems like the economics are completely different when you're talking about a small handful versus a very large—

DR. MCCAMISH: No, I think in my example it was between SNPs or something of that nature. It would not be difficult for a lab to set up a test for 20 SNPs. The research process of screening for 1.5 million SNPs is very costly. The lab itself is not that costly.

DR. TUCKSON: Mildred, do you have a quick comment?

DR. CHO: Yes. Just on that point about recouping the investment. To the extent that many of the tests that have been—the research to find the associations were government funded so there wasn't really a lot of private investment. Now on certain specific examples like the HFE example, I think from Mercator's point of view, they basically lost their investment but the patents didn't save Mercator in that case anyway.

So I think what Francis said is every important. The more—as we move towards multiplex testing the more that the associations are in the public domain, the more the investments won't be needed. And then, as you saw from the data, the post invention resources are sometimes minimal.

DR. TUCKSON: This is a key point, I think. I think it's a very important point to underscore what's in the public domain and clearly how much the nation has invested in this, and then who takes benefit, and I think we need to be clear about that.

Very quickly, Andrea.

DR. FERREIRA-GONZALEZ: A comment on being in the public domain but also when you have a company that has a patent on a limited number of SNPs for a specific application and you have a different manufacturer, a different company working and adding two different SNPs that will add value to the testing, how do you come up to working together or you have to start licensing these increasing the cost of the other one or not having that benefit to the public domain. So there are other issues also to consider.

DR. MCCAMISH: It gets into patent law on that issue and again I'm not a lawyer but if you add something to it, it's really different. So if you can add additional value by doing two additional SNPs that could be additional intellectual property that's there.

DR. TUCKSON: Barbara?

DR. McGRATH: This is just a question of information. Mildred, your research that you reported on, you've mentioned a couple of times that it was two to four years old or something. I'm just wondering if you can update us whether anything has changed in the environment now that we're getting more towards complex diseases? A lot of the examples were single gene diseases. Has anything changed that we should know about?

DR. TUCKSON: Do you want to comment on that specifically?

DR. FERREIRA-GONZALEZ: When Mildred did the study we only—on the period that she did the study, we decided not to offer hemochromatosis. That was the only test that we were looking in my laboratory to look at introducing. In the last six months we have decided not to introduce four different tests due to being informed of different patents that are being in the process of being formed. So I think an update of this study may be something that we want the—

DR. TUCKSON: Yes.

DR. FERREIRA-GONZALEZ: --because things have changed and there's a lot more things that are being patent even that we are not aware.

DR. TUCKSON: Good.

DR. FERREIRA-GONZALEZ: For example, for the—

DR. TUCKSON: Why don't we save that for the discussion?

DR. FERREIRA-GONZALEZ: Okay.

DR. TUCKSON: But I think you've made the point and I think you may be moving into the area of what might be recommendations.

Barbara?

DR. McGRATH: That was the question.

DR. TUCKSON: Joe?

DR. EVANS: I'll wait until the discussion.

DR. TUCKSON: All right. Let me just ask a couple of dumb questions at the end here, just a really fundamental basic dumb question. Debra, can you take us through again—I'm trying to come back to the licensing thing with what FDA licenses in the diagnostic tests and so forth. When you do a diagnostic test that does not require the use of somebody's kit, so you're not using anybody else's deal, you're doing it on your own, you are using the knowledge that allows you to do that, the ability to do that test comes from—where do you get the knowledge to be able to do that test?

DR. LEONARD: So, for example, with hemochromatosis?

DR. TUCKSON: Right.

DR. LEONARD: So, first of all, my knowledge comes from being an M.D., having a Ph.D. in molecular biology and having done Ph.D. and post-doc, and I know how to do molecular biology methods. And then I know how to use those molecular biology methods in a clinical setting meeting all the regulatory and quality standards because of my M.D. training and pathology training. So that when a paper is published like the Mercator paper, and it says that there is a mutation at this point in the gene, I can design primers or use their primers that were published to be able to amplify that region, cut it with a restriction enzyme, run it on a gel and say that that variant is there or not there. That's basically exactly what was done.

So we take samples. We basically took samples from patients who were being—with consent—who were being phlebotomized because of hemochromatosis, and took some random blood samples from just blood donors, and were able to validate that this mutation was correlated with the presence of hemochromatosis, and then start offering it as a clinical diagnostic test.

DR. TUCKSON: Now the knowledge that is—the ownership of this intellectually, what you've just described—it sounds like ultimately the fundamental thing that you benefited from was a paper produced in the literature that said here is how you do this thing.

DR. LEONARD: No. This is the genetic variant. This is the genetic variant. I would have the ability—I mean, you use—in fact, most laboratories used the published Mercator primers and it was a problem that eventually came out because one of the primers was sitting on a site that had a polymorphism. And so—I mean sometimes using the published primers aren't even the way to go and I have the ability to design PCR primers for any variant region. You have to have enough molecular biology and genetic knowledge that you know that there may be pseudogenes, that there may be—I mean, you have to have all the molecular biology knowledge to be able to make sure that what you're doing is producing what you think you're producing.

DR. TUCKSON: So at the end of the day again the thing—I just want to keep coming down to can you just be really explicit then about what it is that somebody who has this license—this patent says if it were not for me, my company, what we did, you could not have done what you did and it's because of my genius or my something that you are now able to do it.

DR. LEONARD: Well, actually in the case of Mercator it was genius because they were able to discover a gene in a region that does not have much recombination and makes it very hard to find that mutation and the variants.

DR. TUCKSON: Okay.

DR. LEONARD: But the question is it's probably also hard to figure out $e=mc^2$ or figure out gravity.

DR. TUCKSON: Right.

DR. LEONARD: And so the question is when there's a disease variant that's in people with a disease and you make that discovery of what that specific disease variant is and it's associated with the disease—I mean should that be patentable? Well, that—then you get into USPTO and everything that Francis was talking about.

DR. TUCKSON: Right.

DR. LEONARD: And you probably don't want to go there. I would love to go there because I don't think it's really reasonable. Basically that's what Francis Collins is saying. I won't get excited about this but, I mean, that's exactly what Francis Collins and the NIH are trying to prevent.

DR. TUCKSON: Right.

DR. LEONARD: They think that that basic information should be in the public domain. So why not go at what the USPTO is doing?

DR. TUCKSON: Right.

DR. LEONARD: So that genetic variant disease-association is the remarkable thing. Once you know that information using what is called prior art you can make a test to discover—to test for that genetic variant in any patient you want for that purpose of diagnosing the disease.

DR. TUCKSON: Joe, do you in FDA with that—I mean so you—again, you've got one company who has like a real fancy kit and they get—they go through processes. You can have Debra who is doing the same work. She doesn't have a fancy brand name associated with her activity. She's brilliant Debra doing the work in the academy. She comes—

(Simultaneous discussion.)

DR. TUCKSON: No, we're not using that word. Now she is coming to an answer, a conclusion, using the same methodology. Now which one is regulated? Which one do you sort of say we pass the seal of FDA-ness over this—what's happening?

DR. HACKETT: If she boxes up her test and sells it to another laboratory, we exert control.

DR. TUCKSON: Right.

DR. HACKETT: If she doesn't, we don't.

DR. TUCKSON: Okay.

DR. HACKETT: So if she offered a service, we don't.

DR. LEONARD: But I'm regulated by CLIA.

DR. TUCKSON: That comes back—I just wanted to make that explicit link back to the earlier discussion yesterday. So it's back to CLIA and that regulation. That's where these two connect. All right.

Lastly from—

(Simultaneous discussion.)

DR. MCCAMISH: FDA doesn't give you patent coverage or things of that nature so you're really talking about what they regulate, which is different from the patent trademark office.

DR. TUCKSON: Right. Now, we're going to go to this break and then come back and have this discussion but let me ask Mark—oh, I'm sorry.

DR. CHO: Can I just ask a question along those lines?

DR. TUCKSON: Please. Yes, please.

DR. CHO: Because I'd like to get clarification on sort of the FDA role here. Let's say that I am working in a company and I find—discover an association between red hair and melanoma. Can I box that and sell it as a kit? A little camera that measures red hairness or something?

DR. LEONARD: It determines whether it's dye or original?

DR. CHO: Right.

(Laughter.)

DR. TUCKSON: So that's the question.

DR. HACKETT: If you box that and sell it then we would control it. If you just offered a test from your facility, we would not.

DR. TUCKSON: Okay. Mildred, I think part of your question though is back to what Debra is saying about Francis' comment, I think. Let's say that you have the ability to know that variant and discover it based upon a bazillion dollars worth of public research that comes out of money that went from the NIH extramural program to academic center Z on a federal grant that allowed those people to figure that out. Then the question, I think, that's on the table, if I understand it, and not resolved, is do you now have the right to then take that knowledge, box it, patent it and then charge the nation back another fee that says look how smart I am and what I did on your money?

DR. LEONARD: Yes.

DR. MCCAMISH: Yes, you do.

DR. TUCKSON: Okay.

DR. MCCAMISH: And you'd be surprised that most—I mean not most but a lot of the patents that are obtained—

DR. TUCKSON: Okay. That's the way it works.

DR. MCCAMISH: --are funded eventually through NIH.

DR. TUCKSON: Mark, the last thing is you—I don't think you can answer this but I'm just going to ask you and see if you have any information on it. From the point of view of the industry—I mean you're not—you're one company, you can't speak for everybody and I don't know if there's a trade association that gets into this. Clearly this is a big issue and a fundamental social conundrum for the nation. This cannot be the first time that you and your colleagues have heard these discussions.

Is there some private sector activity that we should know about that is trying to find a solution to this such that the interests of commerce and the interests of health are addressed? Is this on the agenda somewhere or basically is it that it's left to organizations and committees like ours to try to figure out a way to move through this?

DR. MCCAMISH: I'm not aware of any private associations trying to resolve these issues. I think from my perspective what I'm trying to do is foster the use of this science to better patient care. What I'm seeing is that it's not being pursued by big pharma. It's not being pursued by the classic diagnostic companies because of the return on investment issue that's there.

DR. TUCKSON: But as you make that comment, are you making that comment on both the diagnostic side of the equation and the therapeutic side of the equation or are you segregating that comment?

DR. MCCAMISH: No. I'm making that primarily on the polygenic. This new pharmacogenomic technology arena that is—we're attempting to foster and pursue. The pharma companies are not necessarily pursuing this aggressively because they see it, as I mentioned, as a way of subsetting and getting less potential penetrance for the market. On the diagnostic side, diagnostic companies are always looking for this information. They are just not willing to sponsor the research to discover it.

Once you discover it—that's why the academicians are patenting as they go forward because once they discover it then the diagnostic companies are willing to come in.

DR. TUCKSON: All right. I want to really—Mildred, before we lose you because your comments are so important, Andrea sort of got to a question that was put out and that is the sense as a researcher in terms of do we need to resurvey. You've had a chance to look at it. You're proud of what you have done already. How—do you think there is another set of study survey analysis that needs to be done with more resources perhaps even than were available to you? Do you have a sense, if so, of what that exploration--how it might be defined?

DR. CHO: Yes. I think that there would be reason to re-analyze those kinds of—the sort of things that we did five years ago because things have changed a lot, especially in this multiplex testing arena. Again, what we and others have found indicating that there isn't much patent enforcement is probably partly because of the time window. So things will change and things

probably have changed. I think it would be useful to look in more depth although it's difficult at the actual sort of test by test impact as opposed to on laboratories and look at the economic impact on actual costs.

DR. TUCKSON: How much money did your—ball park. I mean how much—what is the resource expenditure necessary for you to have done this survey that you did, the study that you did?

DR. CHO: Yes. So we had a grant from NIH and I think the program officer is here, too, and she could probably give you the exact dollar figure but ball park was a three year NIH study probably in the ball park of—I don't know—a few hundred thousand dollars.

DR. TUCKSON: Okay. A few hundred thousand. Okay. Good. Just to get a sense of—just trying to get a sense of scale here.

Here's what we're going to do. We're going to take a break. It's 11:05. You need to really be sharp for this discussion so we're going to give you a full ten minutes.

(Laughter.)

But here's the deal: When we come back we are—I want you to be disciplined about this discussion. You really need to focus in. Do you want to do something in this area going forward? Is this something that you want to get involved in? And is it important enough to move forward?

Secondly, what is it that you want? What are the questions that you want to have addressed? The part of this that you want to get—you've got to phrase what you want to do and then you've got to define what it is you want to do. You've got to be very precise about that in this discussion. Otherwise this will go all over God's green earth and get nowhere. So you've really got to lock in on those three.

When you speak in the discussion you need to tell us where you're speaking to. What part of this you're speaking to. Do you want to do something? What parts of this thing do you want to do something in? And then what is it that you actually want us to do? And then the committee will be able to—the subcommittee will take that and they will run with it or they will disband depending on what you say.

All right. See you all in ten minutes.

(Whereupon, at 11:05 a.m., a break was taken.)

FULL COMMITTEE DISCUSSION AND NEXT STEPS

DR. TUCKSON: So like—where is Julio? Okay.

Well, like if you were on an airplane and you were like 4,000 miles in the sky and the pilot comes on and says, "Ladies and gentlemen, for those of you interested in the score of the game, it is one to nil, Brazil."

Laughter.)

"We expect to be landing appropriately."

All right. So here we go. You've got your marching orders. What I'm going to do is I'm going to—sometimes you will notice that I will disrespect the order whenever I see Debra's hand because I want to get Debra to be an active—to get her points in as a member of the committee before she has to segue into being the chair of the discussion. So she's free and unencumbered until like 10 of 12:00. So with that we've got Joe and then James in the queue and then we've got Emily, and then we've got Kevin, and then we have Sylvia.

Take it away, Joe.

DR. TELFAIR: My question is sort of—because you—of your marching orders, you'll probably laugh, which is what to do. I think what I would like to see is address the question related to more of a public health type of question on this in order to be able to—for this group because I think—and at least a part of what we can actually do is make recommendations but I think the arena to make recommendations in are really similar to what Francis was saying earlier.

So my question having to do with the real public health question of balance on the other end is when someone who is a provider needs one of the tests done and is real concerned mostly about the person on that—their person and who they need to serve to be able to help with this, what is it that we need to consider in terms of the benefit to public health because I heard—and then—and, please, both of you all correct me if I'm wrong on this, but that there's a benefit on both ends and there's an argument on both ends that there's the focus on public health.

One being that there is—by having some controls over that you can best streamline something or assure—actually assurance is a term that I actually heard—saying about work being done and making sure it gets done.

On the other hand, by having the opportunity to carry a number of the tests out without having the restrictions placed on it by the patents you can also benefit the person on the other end.

I heard both these arguments being made. So I guess for myself if, one, I can get clarity on sort of the balance here between the two and then, secondly, is it—can we be able to make some recommendations that would really push more the model that was being recommended here and of being able to come to some middle ground and can we make recommendation that whatever is done be done such that there is some way that we can look at both sides because both sides are very much in the real domain?

So that's what I'm asking a question about and that's where I'm at.

DR. TUCKSON: Debra, do you have an answer to that?

DR. LEONARD: Well, I don't mean to speak for Mark because Mark is still there but I think Mark made the point repeatedly that the diagnostic doesn't make money but you need the patent incentives for the whole discovery process.

DR. TELFAIR: Yes.

DR. LEONARD: However, Francis and now Tim—you can't read your papers, Tim, you have to pay attention.

(Laughter.)

--was shaking his head when Mark was making statements about this research will not be done unless you have the patent incentives because the research is being funded by the NIH. I think in the private sector that research might not be done because the basis may be the wanting to help patients but there's an underlying financial aspect to the private sector research that's being done because if the company doesn't make money they don't stay in business. So there is this financial incentive that's needed in the private sector but to say that the research won't be done without the patent incentives, I think, is incorrect. Will it be done as quickly? Will it be done in the private sector? Those are questions that we could look at and potentially address.

DR. TUCKSON: Good.

DR. TELFAIR: I guess me and my questions have to do more with if I was—not being an M.D. but coming at it from the perspective of receipt—those at the—who is the point of receipt of this effort.

DR. LEONARD: Well, that's the other point.

DR. TELFAIR: That's the other point I was trying to make.

DR. LEONARD: So the laboratory analysis that Mildred did is a proxy. It's a proxy for patient access. So all we know is that the tests are not as broadly performed. But Jim and Barbara and I were talking at the break and Jim at least has some evidence from his testing laboratory that being able to provide testing for free, which a company or a sole provider of a service may not be willing to do, gets more people having a test than when you have to pay a large sum of money, and that's something else that we could explore as a committee.

I don't think we have to have the answers now as to what will be our recommendations. I think there's a lot of exploratory process that this committee could do like you've done with large population, like with coverage and reimbursement, like with other issues that we've worked on to explore exactly these kinds of questions so that we do—we, you, come up with a measured response and recommendations that are balanced and don't do harm.

DR. TUCKSON: Thank you.

DR. TELFAIR: Thank you.

DR. TUCKSON: James?

DR. EVANS: Yes. I want to amplify something Debra just brought up. The studies that Mildred and Debra and all have done are landmark studies that are really important. They are a proxy though for what we all know is the most critical thing and that is what is the impact on patients. What we really want to know is, is the patent situation that exists today, is it having a deleterious impact on the access of patients to care?

I can speak to that to some extent because we have a unique relationship with Myriad in the sense that we are allowed to do BRCA1 and 2 testing for free if a patient can't afford it and if we don't charge them. Okay. So you can imagine it's a very expensive thing. BRCA1 and 2 testing right now is $3,150. Every year perhaps I have one or two people who whip out their American Express card but or almost everybody else that is a formidable barrier to testing.

We're writing up data now that shows that over the last six years in our experience just about 50 percent of individuals had to avail themselves of free testing or would not have had testing done.

As you can imagine, there's a statistically significant discrepancy between African Americans who needed to avail themselves of this service more frequently than did Caucasians. Physicians are used to giving people bad news but it makes you feel even worse when the bad news you're telling somebody is you can't have a medical service because you can't afford it because you don't have enough money.

I think that this committee needs to take up this issue. I think it's an absolutely crucial issue for the future. There are no easy fixes and I think that there's important—there is obviously very important aspects to the incentive that patents give.

But there are significant downsides that we're all going to have to grapple with so I think we should take it up. I think we need a number of things. We need updated information from, for example, Dr. Cho's study. The landscape is changing.

DR. LEONARD: Can I ask updated before we—

DR. EVANS: No, no, no. I think we should—

DR. LEONARD: Because that could take five years.

DR. EVANS: --move on. Absolutely. I think one of the things we should recommend to the Secretary is that this needs to be looked at in the changing context.

DR. LEONARD: Is that really going to be valuable we're going to find out any more that more laboratories can't—

DR. EVANS: Well—

DR. LEONARD: I think what needs to be done is the patient access--

DR. EVANS: Yes. Don't get me wrong.

DR. LEONARD: --piece of this.

DR. EVANS: I don't think that that should be necessary before we move on. I think it should be one part. I think what is most important—and it's a very hard issue to get to—is we do need to look at how this is all affecting patient access.

And then, finally, I think we need to, with the right information and guidance from all kinds of groups, try to come up with reasonable recommendations. I'm not interested in a quixotic pursuit here that puts forth things that are completely unfeasible.

On the other hand, I think that this is a really important issue and I think that our committee needs to take a stand on it and render some advice.

DR. TELFAIR: Just to the last part—I mean could I just add—

DR. TUCKSON: Mm-hum.

DR. TELFAIR: I appreciate this because this is the question that I had but in terms of the access issue I would just say that I would recommend that whatever the committee is coming about, if it can just—if the—if at the end there is the short and long term. There needs to be some way to—whatever decision is made, whatever or however we arrive to it, whether or not it is an absolute decision or is a decision that is in flux, that it still be something that can be maintained.

Because one of the—as I've heard—learned actually a lot from the discussion here, this is a—being that it's an ongoing discussion, being that it is an in flux changing the dynamic environment and because of that, whatever decision is made today, the level of relevance to that decision for years may change because of the flux here that there needs to be some idea of a balance but balance with a view that there may need to be—we may need to revisit this.

DR. EVANS: Well, sure, but I don't think we can let the changing—the rapidly changing landscape keep us from addressing it.

DR. TELFAIR: I'm not saying that. I'm just saying that when you go about this that you do it in a deliberate way such that you take into account that the—

DR. TUCKSON: So let me be clear as we get ready for Emily's comments that, James, I want to give you a chance to precisely state what your recommendation is. You said three things. One, we need to go forward in this domain. Number two, you're saying that there should be a recommendation of some sort and we don't need to be fine about it now.

DR. TELFAIR: We need to keep a focus.

DR. TUCKSON: But there should be something that starts to look at collecting or encouraging the collection of a database of surveying of what is going on out there similar to the—

DR. TELFAIR: At the level of the patient.

DR. TUCKSON: And then, third, was—

DR. TELFAIR: If possible.

DR. TUCKSON: And I think third you were saying let's really focus in on what it means in terms of the access for patients and being able to get a sense of is this having a chilly effect on access—for patient access.

DR. TELFAIR: And fourth I think that probably the major charge would be for us to try to come up with recommendations and solutions to this. It's not enough to say to the Secretary why this is a real mess.

DR. TUCKSON: Right.

DR. TELFAIR: We need to try to identify—

DR. TUCKSON: Recommendations and solutions.

DR. TELFAIR: --reasonable solutions.

DR. TUCKSON: All right. I want to make sure our crack staff team, who helps us so much, has got those four down on a piece of paper and feel good about it for the moment and that they capture that.

We now need to move to Emily.

DR. LEONARD: Reed, can I just make a suggestion?

DR. TUCKSON: Yes.

DR. LEONARD: Also, one of the ways to look at the access for patients would be in a public forum discussion like we did for genetic non-discrimination legislation and looking at genetic discrimination. One of the things this committee could do would be to put a question out there to the public, to genetic counselors, to physicians, and see what data we could collect. Could we make another phone book that says, "Yes, there really is an access problem or, no, there isn't."

DR. TUCKSON: All right. So taking the work obviously and the suggestion, and you'll come back and approve all this at some point, but the suggestion has been amended to include to define some of the people that—to include a public forum and we've even defined some of the people—the categories of people who would participate. Patients, clinicians—and you had another one?

DR. LEONARD: Genetic counselors.

DR. TUCKSON: Genetic counselors. Patients, clinicians, genetic counselors would be invited to that forum.

DR. MCGRATH: Nurses.

DR. TUCKSON: Genetic counselors/nurses—and nurses. I'm going to get nervous about the politics. All right.

So we've gotten very specific. People will have—people who don't like that suggestion or want to modify it should speak to it when their turn comes up because I think you can see that there's a consensus getting around that and if you don't like that consensus you're going to have to do something about it in a hurry.

Go.

DR. WINN-DEEN: Okay. So I want to just expand a little bit on the diagnostic company perspective on this. As someone who—every new test that we think about bringing out as a product, the first thing that we ask is do we have freedom to operate. So this is a barrier to commercialization for sure. From a kit manufacturer point of view, if a license is available at reasonable terms then you would consider going forward. If a license is not available then that's a killer right at the start.

My experience in dealing with—so the people I deal with are quite different. I deal with tech transfer offices at universities who don't seem to have any connection to this concept of patient care. I've had experience where I went in and tried to get a license on a non-exclusive basis and was told by the tech transfer office that it was easier to just do an exclusive and they had already selected their exclusive licensee.

I sent them a copy of the NIH Best Practices and said, "This was research funded by NIH and here is the NIH guidance." And they said, "Sorry. It's easier for us to just do an exclusive license."

So I think there's a major disconnect and we have to deal with the fact that the people who are controlling these licenses are not the physicians. They are not the researchers. They're the tech transfer officers and they are a very important stakeholder that I think have to be brought into this discussion.

DR. TUCKSON: Let me propose—

DR. WINN-DEEN: So that was my one point.

DR. TUCKSON: Let me propose on this point specifically that—and I want to see if there is a consensus on this or not—is that we need to hear legitimately an organized perspective from two groups. One is industry. The industry association. That's why I was trying to push whatchamajigger about that.

DR. LEONARD: You have to be careful about lumping industry together because there's a lot of different components of industry.

DR. TUCKSON: Good. So let me—

DR. LEONARD: There's the IVD industry. There's the drug industry. There's the reference laboratory industry.

DR. TUCKSON: Okay. Let me just—and we're going to pause for a minute. You've still got the floor in a moment but we're going to work this one out. So I was going to say with my limited knowledge industry and the university—

DR. WINN-DEEN: Tech transfer.

DR. TUCKSON: --tech transfer offices, which is what provoked me to put those two thoughts together.

Now Debra is becoming even more specific and let me just ask Debra for the sake of the people keeping notes so we've got—so again you've got a bunch of stuff now. We've got the conference, the public people. We've defined the public that's coming—going to be invited to the table. Now we're talking about a separate session as part of that—that public meeting that's going to have industry and the academy tech transfer offices.

Now Debra is going to detail a little bit more about what kind of people we may want to consider. We're not going to write the conference today but the kind of people that would be on the menu for consideration would be from industry.

DR. LEONARD: Emily, you can comment as well.

DR. TUCKSON: What sub-segments?

DR. LEONARD: But industry—there's the in vitro diagnostic test company industry.

DR. TUCKSON: Okay.

DR. LEONARD: There is the pharmaceutical industry.

DR. TUCKSON: Okay.

DR. LEONARD: And there is a reference laboratory industry. They are part of bio actually. The biotechnology industry organization has Athena Diagnostics at least as a member so bio in a sense.

DR. TUCKSON: Okay. Good.

DR. WINN-DEEN: Well, there is pharma and bio.

DR. LEONARD: Yes.

DR. TUCKSON: So I think I want to be careful that I don't try to micromanage a meeting inside of a meeting. So I think what we've kind of got is a sense of guidance for our subcommittee about what we mean by having industry at the table. They'll work through the right people and the right sub-divisions.

Emily, you can move to your next point.

DR. WINN-DEEN: Okay. So I think I just wanted to get that in that that's an important stakeholder but within that is the NIH guidance on best practices and potentially what we could recommend to the Secretary is some method of turning best practices into something with a little more teeth to it which basically says if you get a grant you must follow these practices, not you may or we'd like it if you would. So there's the possibility to give the NIH more teeth.

DR. LEONARD: You can say anything you want because you're going to be gone in three days.

(Laughter.)

DR. TUCKSON: Okay. Hold on. Discipline here for a second. What we're going to do—now don't forget, by the way, Kevin, Sylvia and Steve, don't get nervous—you're in the queue for your points. We're just going to nail down Emily's points real quick.

MR. LESHAN: Can I just—

DR. TUCKSON: Tim, you're going to comment on this point?

MR. LESHAN: Very quickly. One is that while that might be an interesting recommendation, there are some limitations on what the NIH can and can't do in terms of requiring grantees to follow certain practices. Not that you couldn't recommend it. I'm just saying that it's going to be—

DR. WINN-DEEN: But you do require them to put all sequence data in the public domain, for example.

MR. LESHAN: Right. No, I'm just telling you because of the Bayh-Dole Act it's going to be more tricky in this arena.

But the other point that I just want to get on the table is that given your discussion it might be a good idea to have the Office of Technology Transfer here at the NIH at this discussion.

DR. TUCKSON: Good for you.

MR. LESHAN: Okay.

DR. TUCKSON: Let me just sort of say, though, Emily, I think what you may—and let me just ask if this would be useful—is that either—through some mechanism from the subcommittee that we would be able to pull together at least a definitive definition of a description of what science is being put into the public domain so we understand at least what those efforts are and what they're trying to achieve.

And then, secondly, that we at least describe for everyone in an accurate way the meaning—the functional import of science being put in the public domain and what relevance, if any, that will have on this issue. I think we just need to be clear about the efforts to put it in the public domain and what the significance of putting it in the public domain mean. It may not mean anything.

DR. LEONARD: No. It means that that information then cannot be patented and controlled.

DR. TUCKSON: Right.

DR. LEONARD: Once it's in the public domain it can't then be patented.

DR. WINN-DEEN: Well, it can be patented and then put in the public domain.

DR. LEONARD: Right, but if it's put in the public domain before it's patented then that putting it in the public domain basically precludes it being patented.

DR. TUCKSON: Right. So unless there is violent opposition, I think I'd like to sort of put that as part of the task of the committee to consider whether we can put something like that together so we describe this because I think people need to understand this issue pretty clearly going forward. What's going on and what is the meaning of what's going on and whether or not that—of course, then the third step from that is whether or not that—we will have to assess it once we learn—whether or not that becomes part of the solution as it were to the conundrum.

DR. WINN-DEEN: Okay. So I just had one other comment that I wanted to make which is really to echo what we heard this morning about common complex disease and the role of genetics in those diseases. There will be significant royalty stacking issues that will prevent commercialization either at the reference laboratory or the commercial kit manufacturer level. If we don't—I mean I would urge us to consider whether there is some way to bring together stakeholders and to have—to encourage a patent pooling strategy so all patents related to cardiovascular risk get pooled and then all the different stakeholders that want to license can go to a single entity for licensing interaction but without having to go to 20 different companies, each of which hold one gene or one SNP in one gene. It's just going to—it's going to provide a huge hurdle at every level of laboratory testing. I think that's going to affect academic laboratory developed tests as well as kits.

So somehow we're going to have to, I think, bring that issue forward that as panels speak—realistic diagnostic panels that have meaning for an individual's patient care, as those panels get

larger, this issue is going to have to be dealt with in a different way than going and getting individual licenses to individual genes.

DR. TUCKSON: Is this a—is what you're calling for a part of the definition of the problem analysis or are you calling for something that—I mean is this more definitional or is it more action for us?

DR. WINN-DEEN: Well, I think for me it's—I think the group—if this committee elects to work on patents that it should broaden its scope beyond monogenic disorders to thinking about the polygenic issue and to consider trying to make some recommendations about mechanisms, potential mechanisms that could be put in place to overcome this issue of multiple patent holders and multiple licenses being required.

DR. TUCKSON: Great. So I would urge then as we think about this—I think this is a—I think she is advancing important thoughts on the definition of what it is that we consider that we are looking at, what the issue is. The statement of the problem.

DR. LEONARD: But, Reed, one thing to consider is that recommendation 11 from the NAS report is exactly NIH should undertake a study of potential university, government, industry arrangements for the pooling and cross licensing of genomic and proteomic patents as well as research tools.

So that at least—it's not targeted at the clinical diagnostics but it would be easy to take that recommendation and broaden it to—I mean so—

DR. TUCKSON: Right.

DR. LEONARD: _--there is already this recommendation out there.

DR. TUCKSON: Right. But I think the key thing here is that I think—I want to make sure, Debra—is that you could if you wanted perhaps look at this through the narrow prism of single genes as opposed to looking at combinations. If you did it, depending on your assumptions of how you walk down the road, it could lead you in different directions, more or less thoroughness, more or less completeness in terms of the problem, more or less definition of some of the conundrums.

So I think we're just simply being encouraged to look at it in its more complexity than opposed to just more simplicity. I think that's a challenge that we would give to the subcommittee to take through. So I think that's a legitimate issue for the subcommittee to grapple with.

Kevin?

DR. FITZGERALD: Just to get on the bandwagon before there's no more room—

(Laughter.)

--I would also very much recommend exploring this issue and leading to the possibility of specific recommendations for the Secretary.

A couple other people I'd like to see or groups I would like to see involved in our data gathering: I'd like to get more on the legal on this. I'm not—I mean, we've had enough presentations on

patenting and Debra did another good one on just basic patenting but maybe someone from the USPTO for a Q&A session on some of these specific issues.

Now I know often times we say no change is possible there. However, I believe that there is the possibility of change. There is progress or development going on internally.

DR. TUCKSON: Right.

DR. FITZGERALD: They are looking at these issues so it would be good to know what they're thinking.

DR. TUCKSON: Let me push you a little bit on that.

DR. FITZGERALD: Sure.

DR. TUCKSON: And just sort of say—ask you in terms of the legal analysis—I mean legal regarding the answer to—I mean I'm trying to get why—what you want.

DR. FITZGERALD: That's one. The PTO. And then the second would be—

DR. TUCKSON: On the PTO?

DR. FITZGERALD: Right. That's one. And then the second would be somebody—and the person who comes to mind just because I know her is Laurie Andrews, who I know argued in front of the Supreme Court the metabolite case and then some of the other cases.

DR. LEONARD: She did the canavan case.

DR. FITZGERALD: Yes. She also did the canavan case.

DR. LEONARD: Right.

DR. FITZGERALD: But she also did the metabolite case and so she could give us some insight into some of the legal wranglings that are going on particularly in the courts and some of the discrepancies there on some of the ruling on these issues.

DR. TUCKSON: All right. So I think—that's what I was trying to get to, Kevin.

DR. FITZGERALD: Yes.

DR. TUCKSON: I think what you're—I want to make sure that I'm not putting words in your mouth. What you want is to make sure that we understand more thoroughly the legal certainties and uncertainties that govern this field.

DR. FITZGERALD: Right.

DR. TUCKSON: That's what I think you're saying.

DR. FITZGERALD: Certainly the ambiguities at this point or even the—

DR. TUCKSON: Because you're asking those things because it may be that there is a role and obviously you can't predict it until you study it a little bit more but a role for recommendations from us that may attempt to try to deal with that reality. So I think that's what you're getting.

DR. FITZGERALD: Right.

DR. LEONARD: One of the things to think about with the USPTO if they do come is a history of how we got to this point of patenting because everybody always refers to Chaklobardy (ph) but Chaklobardy was patenting a bacterium that was actually created by man because the genetic make up of that bacterium was altered by man.

DR. TUCKSON: Right.

DR. LEONARD: It wasn't discovered in nature. So how did we get from that to patenting—allowing patents on human genetic variation disease associations?

DR. TUCKSON: So again we are—just again to keep—I'm just trying to make sure that we—because you can tell my anxiety is not to have the subcommittee having to go off into 18,000 different directions. I want to make sure that—because we could chew up a lot of time. So what I think we're doing simultaneously, and this is not right so you're going to keep thinking about it as you make your suggestions, is we're sort of saying do we have a problem. Why do we have a problem and what are—what may be the available tools to help resolve the problem? One of which Kevin is saying are legal issues.

So what we're sort of saying is if we determine we have a problem, are there—what is the certainty or uncertainty or the status of the legality of how we got here and what's possible and then maybe that might lead us to some recommendation that is appropriate for us to recommend? We don't know that but you're putting that in the differential.

DR. FITZGERALD: And then one last group I would like to hear from--not necessarily the raw data on the patient access and things but the patient advocacy groups. Some of which are actually actively pursuing patents for control of how the disease is researched and how the treatments are developed. That would be a really interesting perspective to get, too.

DR. LEONARD: In fact, one of the ways that disease organizations are fighting back against the patents is to—

DR. FITZGERALD: Yes, exactly.

DR. LEONARD: --if they are going to have their members participate in research then that organization has to be named as part one of the patent holders so they help control—

DR. FITZGERALD: Right.

DR. LEONARD: --the patent and you could ask why and what had been the nexus.

DR. FITZGERALD: Or the directors actually get their names on the patent like Sharon and Patrick Terry. Sharon is here this afternoon, isn't she--from my understanding?

DR. TUCKSON: Right.

DR. LEONARD: Yes. And I don't mean to put words in your mouth, Kevin, but at the earlier discussion you had also suggested hearing from the European and maybe Canadian perspective—

DR. FITZGERALD: Yes, that was my—

DR. LEONARD: --so—

DR. FITZGERALD: I had that on my list.

DR. LEONARD: Oh, sorry.

(Laughter.)

DR. FITZGERALD: That's okay.

DR. TUCKSON: Now time out for one second. Debra, the clock has run out on Debra's advocacy role and now she's objective chairperson of the thing to figure out how we're going to all proceed.

So, Debra, I pass the baton to you. You've got Sylvia, Steve, Cindy and Martin in the queue, and then Tim. So those are the people that are lined up in that order and I will try to represent this team well in front of our illustrious director, Dr. Zerhouni, and report back to you this afternoon on whether he thinks you're wonderful or not.

(Laughter.)

DR. LEONARD: Everybody understands my conflict of interest so I mean I made that clear this morning.

One of the things that we do have to consider is we have until 12:10. Reed is not gone yet but could—does everyone feel comfortable making a decision at this point? This doesn't end the discussion but can we table—can we have a decision as to whether this is something that the committee thinks we should work on?

DR. TUCKSON: Thank you for that. Let me just—

DR. LEONARD: Okay.

(Laughter.)

DR. TUCKSON: I vote that we do something.

DR. LEONARD: We're not going to do this individually. We're going to do hand raising, Reed.

DR. TUCKSON: I just want you to know I'm definitely in the group of doing this and feel strongly about that so I just wanted to be on record.

DR. LEONARD: Okay. So is that okay that we move ahead? Okay. So everyone in favor of voting, raise your hand. I mean in favor of working on this.

(A show of hands.)

And everyone opposed to working on this?

(No response.)

Wait. Let me do it this way. Anyone opposed to working on this?

(No response.)

Okay. So it's unanimous for working on this. Okay.

So now I think we've created a very long list of things that's going to be very interesting to see how we do this but I think that's what we need to focus on or the last two of the questions that Reed posed to us is what things do we want to hear about. What discussions do we want to have? And then I don't know that we can pre-assign what recommendations we might want to make. I forget what the third point of the question was. But anyway—so paths forward. Let's focus on discussing that.

Sylvia?

MS. AU: I just wanted to make sure that we weren't being kind of territorial. There's lots of health care providers that order genetic tests besides geneticists so we want to make sure that health care provider is the category and not just genetics professionals.

DR. LEONARD: I think we had clinicians so we can do health care provider.

MS. AU: And then also another group is public health programs. Having personal experience at having to halt a program to implement genetics into a chronic disease program because of a patent, I probably think that some public health problems might have similar experiences as my public health program and that would probably be important.

DR. LEONARD: Thank you.

Steve?

DR. TEUTSCH: I just want to put a couple thoughts on the table I think we touched on. One is the whole concept of a clearing house for this kind of information so it can be gotten and I think the other concept I've heard here is we need to find a fair and reasonable way to make that available and that might be done through something such as a clearing house which sets those kinds of standards.

The other thing I'd like to just build on beyond just access to these tests, clearly there needs to be access but it's also access to tests that actually matter to patients that make a difference. There's a lot of stuff out here and I think we need to keep focused on the things that are actually going to make a clinically important difference in the management of these folks. Going forward, hopefully, there will be a lot of that but at the moment there's only a modest amount of that given the therapeutic alternatives that are available.

DR. LEONARD: Okay.

Cindy?

MS. BERRY: Perhaps this would be taken care of by industry representatives but maybe we would benefit by having some outside economists that could help us with the other end of the access question just so that we're fair and balanced, not to paraphrase a certain cable news network.

(Laughter.)

Because I think we're all leaning in one direction assuming that there are access problems because of this patent issue but if you take away or if we issue recommendations without carefully considering potential access problems of stripping some intellectual property protections then I would rather our recommendations be informed by getting all sides of it and I don't have anybody in particular to recommend but somebody could help us.

DR. LEONARD: It's interesting that you bring this up because we did search. I don't know where Sarah is but we searched for someone who could bring an economic perspective and it was very hard to find someone. I'm not sure that this kind of research has been done.

Tim, do you have any idea whether ELSI has funded—

MR. LESHAN: There haven't been—we've done a very little bit of research in this area but not so much specifically related to patents. More economic analysis as it relates to integration of genetics and genomics into health care practice. Scott Ramsey is someone who comes to mind from UW who wouldn't specifically talk about patents but he's at least someone you could talk to about economic analysis in this area. If not him, he would know the others in the field.

DR. TEUTSCH: Or Richard Gold.

DR. : Yes, he's done work on this.

MS. BERRY: I know there are a lot in the area of pharmaceuticals but I don't know about this particular area.

DR. EVANS: I know Gold has worked on the genetics patent and he's an economist.

DR. TEUTSCH: And Pat has worked on pharmacogenomics.

MS. BERRY: Pat?

DR. TEUTSCH: Danson.

DR. LEONARD: Pat Danson. Okay.

Martin?

MR. DANNENFELSER: I am just following up on Kevin's point. I thought when the Genetic Nondiscrimination Act—some of the more interesting forums we had were with people from Capitol Hill and we at different times had someone from the House and the Senate. So on that legal question in particular I think an appropriate person from House and/or Senate committee would be very informative in this area, and perhaps doing a search to see if there's already some legislation that's pending in congress that addresses this issue.

DR. LEONARD: I know there isn't any pending but Lynn Rivers had introduced legislation that could be reintroduced. I think the College of American Pathologists may be able to address that because they had worked with Lynn Rivers and they are looking for a forum to get that reintroduced.

MR. DANNENFELSER: Okay.

DR. : But there is legislation relating to patent reform in general that is on the table in the House and the Senate so there are people in the various committees that could potentially address the broader issue of patents but they may not have considered genetics in those discussions.

DR. LEONARD: Okay.

MR. DANNENFELSER: I think our particular focus should also be on where there's government funds involved. I think that's the strongest hook where particularly NIH is funding research and to the extent that people then go patent things that they develop based largely on the NIH funding.

DR. LEONARD: Okay. Since one of the ways to approach this in addition to—was congress, congress and USPTO or courts. I would like to hear from Breyer, frankly, but I don't know whether we could get him to come in here since—no. Okay. Well, I just—I was reading that in my office like cheering and I was sad that it was the dissenting decision.

Anyway, let's see. We have Tim.

DR. : Just one quick point. Given that the National Academy has done this study that focuses on the research side, I think it's important for the committee to make sure you stay focused more on the clinical side of this issue so that you're not rehashing old business.

DR. LEONARD: Right.

DR. HANS: Just a quick comment on several points that while the tech transfer folks may be good, it may be even better to have the deans and the university presidents who control what the tech transfer offices do.

DR. LEONARD: Do they really?

(Laughter.)

DR. HANS: Well, they have interests on both sides of the table when we're talking about NIH funded research and what kinds of things NIH may choose to do or not do, and trying to get money out of their tech transfer offices. They have interests on both sides of that equation.

DR. LEONARD: Right.

Barbara?

DR. MCGRATH: I'm sort of struggling with this issue that, Kevin, you brought up about the legal and that was my idea, too, but I'm going back to what Dr. Cho was sort of saying that in the last couple of years a lot of the patents haven't been--regulations haven't been enforced. Usually when society doesn't enforce a law it means that there's a sea change going on in society. I was

trying to figure out the best way to capture that and maybe it's like Laurie Andrews. We're trying to pick up what that is about rather than just the laws that exist but what's the societal implications of this. It's a more amorphous sort of thing but it would be nice to somehow capture that perspective as well.

DR. LEONARD: Could that be done through someone like Laurie Andrews, the societal implications? I mean legal societal implications. What type of person are you thinking about--

DR. MCGRATH: Well, that's the—

DR. LEONARD: --to do this?

DR. MCGRATH: Maybe she would be one to ask about that if she would address that issue. That's what I'm struggling with but I don't have an exact person to capture that but something is going on. If the laws aren't—the regulations aren't being enforced and there's something going on other than what—than the regulations as written.

DR. LEONARD: But which laws are not being enforced?

DR. MCGRATH: Well, the regulations—the patent regulations, right?

DR. LEONARD: The patent—

DR. MCGRATH: That was one of your comments that you were saying the changes in the last couple of years since your research was done was that they haven't been enforced on the—

DR. LEONARD: Oh, Mildred did mention that. I think what she meant was there has been a window—so most of my examples were from '99-2000 was the latest. And there has been like this window of three or four years but now there is EGFR, Gleevek. There are now—it is all like emerging again.

DR. MCGRATH: Okay.

DR. LEONARD: So I think there—for some reason, and it's not clear why, there was this like little window where the patent enforcements had—

DR. MCGRATH: It's not a trend. It was just a window.

DR. LEONARD: I don't think so.

DR. MCGRATH: Okay.

DR. FERREIRA-GONZALEZ: I think what is happening, too, is that we knew about these targets. There was a lot of research that was done. Now we have new targets that research is being done and now that we have research to make that CLIA association the patent holders are coming back to enforce that.

DR. MCGRATH: I see.

DR. FERREIRA-GONZALEZ: There is something to enforce.

DR. LEONARD: Right.

DR. FERREIRA-GONZALEZ: And we might see that there are a lot more patents out there for like beta 2 adrenergic receptor that might be waiting for more people, even the federal government, to pay for all these types of research to come and enforce.

DR. LEONARD: Right.

DR. MCGRATH: Got it.

DR. LEONARD: Like number 3 on the opportunities list of the FDA's critical pathways document is asthma and its beta adrenergic receptor variant correlations with response to treatment in asthma and they want that researched. However, that is patented.

Any other comments?

Joseph?

DR. TELFAIR: Yes. Just going back to the—just in the tasks for specific groups. Since the practitioner group is going to be a broad group, I would just recommend that they—if we're going to ask them about what was recommended, a balanced view of access, that we be very specific about what elements of access we're talking about in terms of that. Is it the receiving end? Is it the actual receiving of the benefits? Is it the asking of a particular question? Is it the screening issues? What is it that the access problems may be or not and then whether it's being helped or not? It just seems to me that if we have such a broad group, given the multidisciplinary nature of the group, it would be better if we just were very specific about what we asked them.

DR. LEONARD: Well, I think if we are going to—if the group feels that having a public discussion forum would be useful with different constituencies—we have to write a document basically that says what do we want them to address. What is the question for public discussion? So that's part of where that would be defined, I think, in the writing of that document that would be sent out to the patient groups, the patient advocacy, genetic counselors, health care providers, all the different groups that we think could contribute to this public discussion.

MR. DANNENFELSER: The most high profile issue that has the Secretary's attention right now is pandemic flu. NIH is doing a great deal of research on vaccines and I believe working with the private sector. I don't know if there's any connection here at all. Maybe Tim could speak to this. In terms of if patent issues rear up in that—in there, is there any exceptions that are—in terms of this research where they can't go out and patent it because of the public interest and the massive ramifications?

DR. : All I know is there are patent issues but I don't know the details. I think there are other people in the room who—other people from NIH who probably would know better but it's something we can definitely address in another meeting.

DR. LEONARD: One of the things to consider is this committee, SACGHS, has a broader mandate than SACGT had. So SACGT was really focused on genetic testing and that limited somewhat as to what they could consider. We have a mandate that includes bioterrorism organisms and there are patents on hepatitis C virus. There are patents in other areas and I don't know if we want to think about this more broadly or we really want to keep to the genetics but it is a question to think about.

Emily?

DR. WINN-DEEN: Yes. So if you broaden the view to genetic-based tests there's quite actually a long list of viruses whose entire genomic sequence is patented. So if you want to make a test for this virus that targets any place in the genome you must take a license. Some of these licensees are widely available. Some of them like Hep C are very closely guarded and very limited licensing available.

So it does open up a whole other list of things that one might explore in terms of public health and the benefits to society of having widely available testing.

DR. LEONARD: In a sense it's genetic sequences in general and, in fact, the Invivoscribe patent that I was talking about is a somatic variation that you're looking at, not inheritable. But genomics—we've had this discussion as to what's genetics, what's genomics, and I think this committee has taken a much broader look or perspective on genetics than just inheritable change. So it's something to think about.

Any other—I think if we give the staff any more suggestions as to what we could do we're going to be looking at this for the next three years or you are. This is my last meeting by the way.

(Laughter.)

MR. LESHAN: Debra, just one other small thing.

DR. LEONARD: Yes, Tim.

MR. LESHAN: I think what—

DR. LEONARD: Is this the thin mint?

(Laughter.)

MR. LESHAN: I think one of the things that Dr. Collins was trying to say is that there is a lot of work being done here at the NIH on some of these issues and some of that will clearly inform your deliberations, the committee's deliberations, as it goes forward. I'm sure we, the NIH, will be happy to provide that information as we go through with that.

DR. LEONARD: Can you just expound a little on how much teeth can the NIH have in this realm or not?

MR. LESHAN: I don't think I know all the details on that but I think that there are limits on how much teeth the NIH can provide in this area but I think there's an interest on the part of the NIH to sort of push that envelop as far as possible without breaking the law and without going too far without harming that balance that Joseph was talking about in any way but wanting to make sure that enough of this information is publicly available to the research community primarily.

DR. LEONARD: Well, I think NIH is setting a bar, a standard if you will, like with the GAIN project and putting the information in the public domain, and that's nice but even though you teach kids to play nice in the playground they are still going to fight and they're still going to do the wrong things or what you don't want them to be doing. So setting a good example is nice but it doesn't prevent anyone from doing the opposite or something that's not as noble, if you will, as

what the NIH is trying to do, both with the Human Genome Sequence, with the HAPMAP and with the GAIN project but we still have patents and patent enforcements and it's not solving the problem.

MR. LESHAN: No, I don't think it's solving the problem. I think NIH is just hoping that it will benefit—make some headway in terms of trying to solve it.

DR. LEONARD: And how much do you—so one of the things that I think this committee has to grapple with is—and I've heard this said by people at NIH also—is that for genetics and genomics the horse is out of the barn. Basically there is so much genetic sequence already patented that why bother. So one of the questions is there are a lot of patents that exist and do we do something that just fixes things going forward or is there something that can be done to protect against the enforcements that already exist because I think Mildred showed a list of the number of patents that exist and they are enormous. So I think that's something the committee is going to have to grapple with as well.

Any other questions or comments? I think we're right on time for finishing and I wish you all the best of luck.

(Laughter.)

So let's see. I now have to do my other job here, which I've lost my commentary. Where's my script? Thank you.