

**Continued Discussion of Public Consultation Draft Report and  
Range of Potential Policy Options for Public Consideration**

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DR. TEUTSCH: If folks could take their seats. I hope Paul is on the phone. His flight got canceled from the West Coast last night. He will be joining us, hopefully, later, but he has to be on the phone, and so will be heard if not seen.

Jim, please lead us through.

DR. EVANS: Let's keep plowing through this. We have this session prior to lunch and then we have two hours after lunch. I would like to devote that entire two hours to going over the range of policy options one by one.

We are finishing up the case studies with two interesting cases. One is cystic fibrosis, the other is Long QT syndrome. Now, CF is a recessive disorder that affects about 30,000 Americans. About one in 20 of us is a carrier for a cystic fibrosis mutation. When we inherit two of those, we have the disease. What it means is there is an overwhelming likelihood that somebody in this room carries, for example, a heterozygous mutation for CF.

Delta-F508 is the name of a particular mutation in the CFTR gene which is present in about 70 percent of cases and at least one copy. The early detection and screening for CF does, arguably, allow for better disease management, although there is no cure for CF.

DNA-based carrier testing and newborn screening is available and is endorsed by medical professional societies. I think 35 or 37 states, at last count, engage in CF testing as one of the newborn screening panels.

Patents for the CFTR gene mutation and methods for detecting those mutations are held by three entities: University of Michigan, the Hospital for Sick Children in Toronto, and Johns Hopkins, again reflecting the big role of universities in this landscape.

All of these patents are non-exclusively licensed. So this case study gives us a way to look at the landscape of, in biogenetic terms, a relatively common disease for which there are patents held but no exclusive licenses involved.

The testing price varies over the 64 laboratories that offer some type of CF testing. The full gene sequencing offered by a subset of those laboratories ranges from \$1,200 to \$2,500. Targeted mutational analysis -- for example, looking for the Delta-F508 gene, which in half the cases will be there in two copies, and one can employ targeted analysis -- costs between \$84 and \$595.

That price range, however, is influenced by the fact that there are a number of different panels that one can order. One can order a panel of seven or nine mutations that are fairly common, all the way up to a panel of several dozen. Then the most exhaustive type of analysis would be full-gene sequencing.

With regard to whether the prospect of patents encouraged the search for gene-disease associations, it does not appear that gene patents were an important incentive for CFTR gene discovery.

The parties involved in commercialization, both researchers and funders, agreed to pursue patent protection so that broad access to CF genetic diagnostics could be encouraged through non-

exclusive licensing strategies. In a way, my understanding is that the history of the CF patent issue is that these were, in a way, preemptive patents that were taken out by the discoverers so that they could control matters and make sure that broad access was available.

There is no evidence that patent process affected the speed of genetic test development. There were, however, interference proceedings that weren't resolved until 2002, fairly recently in the big scheme of things considering when it was cloned.

How do patents and licensing practices affect price. Lab-to-lab comparisons are difficult because of this range in services. You can get whole gene sequencing. You can get a variety of different panels that look at different mutations. You could, for example, if you wanted, get precise, targeted mutation analysis as well. Andrea.

DR. FERREIRA-GONZALEZ: These are practices of pricing on diagnosis for cystic fibrosis. Have you looked at the pricing for carrier screening, since there is a specific panel that has been recommended?

DR. EVANS: No, that is not included for carrier screening.

The role of patents and licensing practices and the availability of this testing is pretty clear. It is offered by 64 laboratories nationwide. There is no evidence to suggest that the CFTR patents and the broad licensing have limited consumer utilization.

With regard to future harm, development and commercialization of new tests and techniques have continued a pace. As techniques for genomic analysis have progressed, they have regularly and rapidly been applied in the context of cystic fibrosis. Broad, non-exclusive licensing practices have clearly been compatible with competition as well as innovation, as evidenced by the fact that there are 64 labs offering a variety of different products.

Therefore, I think it is quite fair to say that patents and licensing practices of the CFTR gene most likely will not result in future harms to CF genetic testing.

The last case is one that is still in flux. Hence the disclaimer. Long QT syndrome is a shifting and currently changing landscape. The authors of this case study are continuing to update the report. I don't want to imply that the conclusions or interpretations in the following slides are final. We do not know the whole story when it comes to Long QT, and there seem to be surprises that regularly pop up with this situation.

Long QT is an interesting, from a clinical standpoint, and a tragic, from a clinical standpoint, condition. It is a mendelian condition. That is, it is inherited in a mendelian type of pattern. It affects about one in 3,000 newborns. For those of you who aren't geneticists, I can tell you from a genetics standpoint it is not rare. We are used to dealing with rare diseases.

There are mutations in 12 susceptibility genes that account for about 75 percent of familial Long QT syndrome. Mutations in three of those genes account for the vast majority of cases.

It is called Long QT because when one looks at the EKG of somebody with Long QT syndrome, under certain circumstances and at times, one of the intervals between those little blips is prolonged between the Q and the T waves.

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Unfortunately, the EKG is not sufficient to make the diagnosis in many circumstances. You can't just do an EKG and determine whether the sibling of this child who died suddenly and turned out to have Long QT syndrome is affected. It really matters clinically. If that sibling is affected, they may need an implantable defibrillator. They obviously need very close follow-up.

If, on the other hand, they did not inherit this condition from the parents, then they can forego screening and procedures.

So, clearly, this ability to diagnose Long QT is, with no hyperbole, a matter of life and death for the families in which it is being transmitted.

Moreover, knowing the particular mutation involved can guide therapy. There are particular genes that have a more malignant phenotype than others and necessitate the implementation of an automatic defibrillator at an earlier age, et cetera.

Testing is offered through Clinical Data Corporation. That is a subsidiary of PGx Health. The FAMILION Service was launched in 2004 for Long QT testing. Prior to the launch of the FAMILION Service, there were at least two other fee-for-service providers of genetic testing for this syndrome, screening approximately a third of the five genes' combined coding sequence.

The story behind Long QT is difficult to unravel and it is still being unraveled. The majority of these genes were discovered by a researcher at the University of Utah in the '90s. The University of Utah exclusively licensed its Long QT syndrome patents to DNA Sciences for a period of several years, from '99 to 2003.

Then in 2003, DNA Sciences and all of its assets were purchased by Genaisance Pharmaceuticals. Genaisance Pharmaceuticals launched commercial testing in 2004. In 2005, they were acquired by Clinical Data, Incorporated, a subsidiary of PGx Health. If you guys aren't lost at this point, let me know.

Clinical Data has since overseen the rapid growth in commercial testing for this disorder, and there has been rapid growth.

Testing is offered by Clinical Data Corporation for \$5,400 per patent and \$900 per confirmatory test in additional family members. The cost per amplicon is \$74. That is a bit of an outlier compared to, for example, the \$38 per amplicon test of, say, BRCA.

Did the prospect of patents encourage the search for gene-disease associations. That prospect didn't appear to stimulate a race for gene discovery, most likely because of the relative rarity of Long QTS and the presumed small market for such genetic testing.

With regard to the role of patents in test commercialization, there was perceived value in the Long QTS IP as both Genaisance and Clinical Data appear to have made testing for Long QTS a substantive part of their genetic testing business plans. Both GeneDX and Boston University, however, it should be noted, offered fee-for-service testing from 2001 to 2002, before patents were enforced, suggesting that IP certainly wasn't the only incentive to offer this service.

I think that gets back to a recurrent theme that clearly patents are by no means the only reason, or even a reason, that many labs pursue such analyses.

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So, how do patents and licensing practices affect price. The test currently costs \$5,400 per index case and \$900 to confirm that test in other family members. So you find a specific mutation in a child. Say you want to discover whether the siblings have it. It costs \$900 to look for that particular mutation.

It is more expensive than most comparable testing. As you will recall, BRCA confirmatory testing targeted for an individual mutation costs about half that and, on a per-amplicon basis, the initial test is also more.

There is incomplete coverage of the test by most payers, and the role of patents and licensing practices in test availability is hard to sort out. Enforcement actions of DNA Sciences and perhaps those of Genaissance from 2002 to 2004 may have adversely affected consumer access. There is concern that there was a period of time during which testing was not available at all due to the sole provider-enabled exclusive licensing.

This is a serious issue with a condition that can result in sudden cardiac death and for which there is an intervention that is available if you know it. Moreover, it is difficult to diagnose, if not impossible to diagnose, without DNA analysis.

Clinical Data doesn't offer prenatal genetic testing for Long QT. So this gets to the more general issue of concerns about an exclusive licensee offering one genetic test but not offering another type of related test that many individuals may want. So the issue of prenatal genetic diagnosis is a complex and a somewhat controversial issue in our country as a whole, but nevertheless there are certainly people who elect to pursue prenatal testing for a host of conditions. It is up to an individual licensee whether they want to offer it or not. If they are the sole licensee, that can obviously create problems.

That takes us into the realm of potential future harms. To date there is no evidence that a virtual Long QTS monopoly has had a stifling effect on the development of an improved test. Oftentimes noted is the exception of allelic dropout. This is a problem that is inherent to PCR-based tests. I'm not sure how unique it is to this particular situation. Andrea.

DR. FERREIRA-GONZALEZ: I was just curious to see if this company also has a program that allows individuals that cannot pay for that test to have access to the testing. Have you looked into that?

DR. EVANS: I don't know. Mara, do you know?

MS. ASPINALL: I don't know. We may have some representatives here who can talk to that. But again, it is the same problem. If you want to offer access to the test you need tax returns. You need to go through a major process to do it, and most patients are not able or willing to share that level of financial information.

DR. FERREIRA-GONZALEZ: But those who decide to do it, do they have that capability?

DR. TEUTSCH: I don't understand why that is the case. For drugs you don't need that level of documentation.

MS. ASPINALL: It is a great story. It is actually different for testing than it is for drugs. In many examples, and I know we didn't look at drugs in this instance in terms of patents, but it is an area where there is non-comparability in terms of the anti-kickback and the rule about providing

services, for which the requirements are actually higher so there is no sampling technique. It may go back to a point about 10 years ago, but the challenge is very great in terms of offering this.

DR. EVANS: I would go on record personally as saying that I don't think the answer to our cost issues and affordability of genetic testing or, for that matter, other types of things in medicine, is really going to be solved by those kinds of programs.

Clinical Health has been criticized for its difficulty in processing paraffin-embedded samples from deceased individuals. I'm not sure how relevant that is personally because that is not routinely done in many situations. It is very hard to get payment. Who is going to pay for analysis of a dead person's tissue, et cetera. So I'm not sure how valid that particular criticism is. It is not something that clinically is done very often.

DR. LEONARD: But wouldn't this be done in the setting of BRCA testing?

DR. EVANS: Very rarely. Very rarely.

DR. LEONARD: Because you always have to have the proband.

DR. EVANS: Yes. I would say it is almost never done.

So, what is the potential that this patent situation may cause some harm in the future. Clinical Health has declined to add genes to its Long QT testing panel or sublicense rights to its panel to other companies due to the rarity of mutations in the other genes. Now, they currently test for mutations in five genes, and rare mutations in seven other genes are known to predispose to this same, oftentimes clinically undifferentiable syndrome.

I would add this is not unique to Long QT and is unlikely to be able to be linked directly to the patent licensing issues. This is a common dilemma in clinical genetic testing. When is it worth adding an assay for a gene that plays a very rare role in a disorder. So, to some extent, this dynamic is a natural result of the nature of genetic heterogeneity. I think hemochromatosis is a good example of that, in which HFE is the major player but things like Ferroportin can occasionally cause a similar condition. I think this is more a nuanced issue with regard to Long QT.

DR. WILLIAMS: Jim, just a clarification. Does Clinical Health hold the patents on the rare genes?

DR. EVANS: Shubha, Bob? I think that Utah holds all the patents involved in this. What has happened, and that gets to the next point, is that there has been exclusive licensing of different loci to different licensees. There has not been, that I can make out, a really broad, coherent policy with regard to this. So I think Utah holds the patents to all these genes.

DR. WILLIAMS: The harm would then result from holding a patent, not developing the test, not making it easy for somebody to develop the test, and then having people that literally do not have access to testing because the test is not available or being developed.

DR. EVANS: That is precisely where harm could come up: when you have a patent holder that has refused to license a particular gene to somebody else who, even though it is for a rare subset of that disease, might be willing to test for it.

DR. TEUTSCH: We might invite some comments from the audience.

DR. EVANS: Paul Billings, and then to Bob. Paul?

DR. BILLINGS: I just had two quick questions. On your slide, are Clinical Health and Clinical Data the same thing?

DR. EVANS: I believe so.

DR. BILLINGS: I think it is a mistake. I don't think it is Clinical Health.

DR. EVANS: It should be Clinical Data.

DR. BILLINGS: Yes. Clinical Health doesn't exist. You may want to correct that.

DR. EVANS: Yes, we do need to correct that.

DR. BILLINGS: Secondly, the Long QT syndrome is caused by mutations in ion channels and there are, as you say, quite a number of them. There is no evidence that we have found them all, by the way. Some of these patents are owned by the University of Utah. There may be others that are either out there that are as yet uncaptured or may be also unknown.

DR. EVANS: Great. Bob.

DR. COOK-DEEGAN: I was just going to make a technical point about what we can and what we cannot say about the intellectual property situation. It is not too hard to find patents and who was originally assigned a patent because you can get that from a public database. The crucial information that we don't have in this case, and we know that we don't have the full story, is the exclusive licensing status of some of the key common mutation patents. It has been brought to our attention that there might be a potential mutual blocking situation here.

DR. EVANS: Right. Lori.

DR. PRESSMAN: This is such a great example of where diligence might be the fix that I wanted to jump in and suggest it. It has been proposed that very broad, non-exclusive licensing would be the fix because then there would be many parties who would eventually aggregate all 11. Another potential fix is more nuanced exclusivity but incentivizing their adding the additional mutations that, if they don't add, they lose rights. So, add or lose.

DR. EVANS: That is a good preview in the range of policy options that we present. You will see a progression. You will see a range from more and less nuanced fixes for these kinds of things that we envision.

DR. ROHRBAUGH: In terms of the comment Marc made, if a technology had government funding and is not being developed, that would certainly be something appropriate to consider.

DR. WILLIAMS: One other thing to note with this particular case study that is also unique to this case study is that this is the single case study that you have presented where there is a strong financial incentive from two other stakeholders. It is the ordering physician, who is usually a cardiologist, who will presumably be able to generate revenue relating to implantation of devices, and the device manufacturers, who obviously will benefit from that. Of course, there is still a

wide variety of opinions about who should get the defibrillator, ranging from everybody that carries a gene should get one just in case, to more of a selective issue.

But the amount of money associated with these devices and with the insertion of these devices is not trivial and in fact dwarfs the cost of the genetic test.

DR. EVANS: That is a very good point. That is a very interesting point. Mara.

MS. ASPINALL: Two comments, one to Marc's comment. I'm not familiar with the medical history there, but just because there is a financial incentive on people's part doesn't mean they do the wrong thing. The implication there is how that works through the system.

DR. WILLIAMS: No, I understand that. One of the things that we have frequently argued to peers about is that for the vast majority of genetic tests that we are ordering there is no personal financial incentive for ordering a test or not ordering a test. It really is for the patient. This is not the case with this particular test, and that is something that could in fact promote a broader use of testing that might be defined as inappropriate.

DR. EVANS: It is an interesting issue.

MS. ASPINALL: Fair enough. I think that, more broadly, testing is probably the one area that there is no financial incentive broadly. In drugs there is an incentive. On devices there is an incentive to go back. But that is the fundamental basis of our system. Virtually all of the other interactions have some financial incentive for the ordering physician or the institution. That was Point No. 1.

Point No. 2, first let me say thank you for your presentation and giving it in such a broad, open-minded way, looking at the various issues with all of the questions. I think the way that it was put together was very helpful.

One of the things, though, that I would suggest -- and I know we talked about it a little bit in the Committee -- as we move forward with the case studies, is with that last question, do patents have the potential for future harm, we should also have the potential that the patent has future benefits. We had talked about it at one point but it seems to have gotten lost in there.

The Long QT one is an example. Earlier we spoke about the role of the people in the field going out. In this case, we talk about the fact that, without education of physicians, many physicians are not aware of this, much less have an interest in doing it. I think that is there now. Right now we are laying out the situation. There are some that work one way and some that work another. I think we need to ask the question both ways.

DR. EVANS: I think that is a point very well taken. Alan.

DR. GUTTMACHER: I would just like to quickly add, I think the example of the financial interest in the Long QT syndrome is a very illustrative and important one. I would also point out, though, that even for other testing there may be a financial implication. That is, people tend to like and refer to physicians whom they perceive as doing something. That is the reason why people often write scripts at the end of an exam, to make the patient feel like you have done something.

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For many folks in genetics particularly perhaps, ordering a test is doing something. I think that there may be a less overt, more subtle, but still somewhat of an economic interest in doing something.

DR. EVANS: That is a good point. Even BRCA1 and -2, you find a mutation in somebody and they have bilateral mastectomies. We are talking about a major financial incentive from that perspective.

MS. ASPINALL: I think that that is a very fair point, but typically you hear from physicians that, the time to do the test, send it out, interpret the test, speak to the patient about it, forget even genetic counseling, often none of that is being paid for. So the incentive may be to do something, but the actual time it takes to go through that is actually a loss rather than a gain.

DR. GUTTMACHER: Medical genetics is based upon losing money on each client you see and somehow making it up in volume.

DR. EVANS: In "Catch-22," Milo Minderbinder says, "I lose money on every sale. It's just the volume that keeps me in business." I never understood that comment until I got involved in medicine, and it is exactly right. We lose money on every sale. It's just that because we are perceived as being needed and people demand it, we somehow survive.

MS. ASPINALL: The perception of that changes a little bit for those in medical genetics, for whom it is done, but the vast majority are done by non-geneticists.

DR. EVANS: We are going to try to march through preliminary conclusions that we have made in going through this.

Now, I would emphasize what we have tried to do here is, among the task force in these grueling conference calls, come up with some of the lessons learned and the preliminary conclusions that we can make. I do not want to imply that these are the only lessons that one could learn. We are trying to present a balanced type of set of conclusions.

I would start out by saying that it is not so much whether a genetic diagnostic test is patented or unpatented, but rather, how the patents are used and enforced that result in potential barriers to clinical access. I think that a good example of that is something like CF. CF has broad access. It is patented. It has been how that patent is used that has allowed for such broad access.

The findings from the case studies suggest that it is this use and enforcement of IP rights that ultimately affect access.

Controversies are most likely to occur when the interests of medical practitioners and patients aren't taken into consideration during license processes and when exclusive licenses are issued. I think that is pretty clear. It is in those realms of exclusive licensing that we run into problems. It is in realms like Canavan where there was a disconnect between the patients, their families, and the individuals who were setting policy with regard to the use of those patents.

I think that it is surprising but demonstrable that there is no clear relationship between patents, license exclusivity, and the price of a genetic diagnostic test. The evidence from the case studies don't reveal any exorbitant patent premium or, for that matter, they don't even reveal a patent premium for most of these genetic tests that were patented and even exclusively licensed relative to tests that were either unpatented or non-exclusively licensed. This was a surprise to me, but I

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think it is relatively uncontroversial from the analysis when you look at things like price per amplicon. It is surprising, but I think it is true.

Now, why is that. I don't know. It could be because of third-party payers. It could be because of the quest for volume in lieu of price per test. Andrea.

DR. FERREIRA-GONZALEZ: I think some of the testing that you looked at to compare the pricing were sequencing tests. There are not that many providers, so there is no significant amount of competition among laboratories to be looking at price changes.

The third one is the third-party payers. They act as kind of regulators. They decide how much they are going to pay.

DR. EVANS: To me, that is probably what answers that question.

DR. FERREIRA-GONZALEZ: But again, if you have, for example, more laboratories competing for the sequencing, maybe the prices might go down. We have seen from \$76 for some of the testing down to \$48.

DR. EVANS: But those aren't clearly related to the patent status.

DR. FERREIRA-GONZALEZ: But I think you may need to see the number of laboratories that are offering the tests.

DR. EVANS: But we see a lot of laboratories in many of these situations that do offer testing. Look at HNPCC. Look at CF.

DR. FERREIRA-GONZALEZ: CF is different.

DR. EVANS: I think you are right about the etiology of this, that it most likely relates to third-party payment, to CMS, et cetera. But for whatever reason, we don't see a big patent premium.

DR. WILLIAMS: I think one of the nuances relating to third-party payers is that you may also find differences in laboratories depending on whether or not they will accept specimens from Medicare and Medicaid. A laboratory that takes all comers will charge a higher per-test price because they know they are going to be losing money on those payers because of the current payment structure, which we will go into ad nauseam on the coverage and reimbursement side, or have already done that.

But if you, as some do, don't accept those payers or you just say, we are going to bill the referring laboratory or the institution and not bill a third-party payer, you can afford to charge less if you are getting dollar per dollar as opposed to looking at a discount where you have to build that into your price structure.

Looking at the test price has so many variables associated with it that, while I don't disagree with your conclusion, I think that we shouldn't necessarily be so sanguine, either.

DR. EVANS: To be honest with you, I think it is hard to disagree with this conclusion. The facts are the facts. There doesn't seem to be a relationship. I think the reason for that is complex.

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MS. ASPINALL: Patent holders range from for-profit, not-for-profit, universities, and individuals. So there is no "they" that are all one type. To me, it is not surprising. It is like any other piece. If you look at drugs or if you look at services, the relative prices and margins vary, period.

DR. EVANS: Thus far, there is no strong evidence of large-scale and long-term barriers to clinical access to genetic tests within the current gene patenting and licensing landscape. Case studies do document several instances in which access to genetic tests may have been impeded due to a sole provider not offering a test for a period of time, disagreement regarding test cost and royalty payments, inability to combine services for testing multiple mutations, and this problem that arises when there isn't a contract between a sole provider and a major payer.

I want you to pay attention to the nuanced nature of this statement. What we are trying to say is that there are not strong, large-scale, long-term barriers that have arisen due to the patents landscape. At this point, while there have been problems and while there are problems, I think it is also fair to say that in most cases genetic testing is available at what appear to be reasonable prices for most things. Yes.

DR. FERREIRA-GONZALEZ: I think it is a very strong statement here. It might be that we are lacking some of the information. Some of your case studies are of limited nature. So I think we have to be careful with that strong statement that there is no strong evidence. I don't think we have enough data.

At the annual meeting of the Association for Molecular Pathology, there was very nice work presented where patients at Louisiana State University were not able to get access to BRCA1 mutations even though they had very strong positive clinical information.

DR. EVANS: Right. I'm going to say two things. Where you lay the blame for that lack of access is important. I completely agree with you that the field is opaque, that the absence of evidence is not evidence of absence. I think that is a very important point that we will get to in a minute. Bear with me because I think we address some of that real soon.

DR. FERREIRA-GONZALEZ: I'm sorry to keep coming back to the BRCA1 mutation, but I think if you had more providers that could offer that test we might have access to that.

DR. EVANS: Andrea, that isn't borne out by what I think is probably one of the strongest case studies, when you compare colon cancer and BRCA.

DR. FERREIRA-GONZALEZ: In colon cancer you have more people offering the test, some of which are nonprofits.

DR. EVANS: Right. But they cost the same.

DR. FERREIRA-GONZALEZ: They cost the same, but I'm not talking about the cost. I mean the access to a group that cannot afford the testing.

DR. EVANS: Bear with me. Again, these are nuanced. I'm not trying to say there are no problems. What I'm trying to say is there is not a pervasive, huge problem and people are generally able to get tests. But I think that has to be countered by this following slide.

There is an important typo that was corrected in this. Your hard copies do not reflect this very important "no" in the first line.

At the same time, there is also no evidence that gene patents and exclusive licensing practices provide powerful incentives for the development or availability of genetic diagnostic tests.

In contrast to the situation for the development of therapeutics, the threshold for developing diagnostics is low. Clinical need and academic interests serve as the predominant drivers for the development of genetic tests. It is evident that in most cases diagnostic tests are quickly offered without the need for patents or exclusive licensing. You can look at CF, hemochromatosis, BRCA, Ehlers-Danlos syndrome. You could go on and on.

The incentive structure could change as the regulatory environment for genetic tests evolves. That is something we have to keep in mind. But patenting does not seem to be required for driving discovery of genetic associations or the proliferation of clinical laboratories which offer a given test.

I think, as we will get to in a minute, this is a very important point. One has to think about what the purpose of patents and licensing is. People can differ about what those purposes are. But if the purpose is to have tests available and to promote innovation, it is arguable that we have uncovered no evidence that suggests that exclusive licenses and patents are necessary. Yes.

MS. ASPINALL: If you would go back? I'm not sure it changes the conclusion, but you say "The threshold for developing diagnostics is low." I think it is important to, at a minimum, say "is lower than therapeutics." But it is increasingly changing. Several companies have spent in the tens of millions of dollars. One spent \$100 million. Is that a billion dollars? No. But the relative benefit is not like it once was or like it is perceived and portrayed.

DR. EVANS: Right. That is why that third sub-bullet, I think, is important. We can talk about that more as we get into the various policy options. I think the incentive structure could definitely change with regulatory requirements.

I do think that the phenomenon of clearing the market, which has occurred so many times in the history of gene patents and licensing, is empirically instructive to us. What it tells us, I think, in no uncertain terms is that tests get developed. We find an association and entities that do not have deep pockets -- clinical labs and academic environments -- quickly fill the gap and start offering testing. Then what exclusive licenses do is they clear the market.

I think when that happens over and over it is telling you something important. It is telling you that you don't really need incentivization to get these tests out there.

MS. ASPINALL: That may or may not be true. I guess I'm making a different point. Regardless, if the incentives don't change today and they don't change in the future, the first statement about the cost for developing diagnostics is rapidly changing and some would say already has changed.

DR. EVANS: That is why Sub-bullet No. 3 is there.

MS. ASPINALL: I'm saying it is not related to the incentive structure. If the incentive structure never changes, the hurdle to make a diagnostic that is clinically accepted today is changing or has already changed. I think if you look at the IVDMIAs that are on the market and what is public

information, it is tens of millions to do that. So the third point may also change that, but it is a separate issue because today the incentive is what it is.

DR. EVANS: That makes sense.

DR. ROHRBAUGH: Jim, I think that is a strong statement in that there hasn't been a look at the null set. What is the negative. What is not being developed adequately because it is not being patented and licensed in this way. By selecting examples of products that are developed, it is a selective set and not looking at the null set.

Also, there may not be a powerful incentive, but I think there are those who would agree that there is an incentive. I certainly know of companies who would say, we are not going to spend several million dollars even on certain clinical studies if there isn't some degree of exclusivity.

DR. EVANS: That is, again, why I think of these two slides as a spectrum. I think that there has been disagreement with both of these slides, which is exactly what we wanted, because they present the strongest statement of both sides. I think the reality of these situations is nuanced.

DR. WILLIAMS: The point I would make to John's reference to the null set is that were there not issues relating to that, particularly in the rare disease area or the ultra rare disease area, we wouldn't be investing in something like a SEP program through CDC to try and bring some of these tests to the market.

So, at least in the ultra rare disease community, there are definitely some places where incentives would be necessary to bring that in. Perhaps you could argue that patenting is not an adequate incentive to bring those forward just because of the volume.

DR. EVANS: Yes, Lori.

DR. PRESSMAN: I would just ask Bob and Shubha a question about Myriad. I thought there was some suggestion in some of the phone calls that there has been desirable behavior at Myriad where they correlate genotype to phenotype. Do you think that that in any way was incentivized by their position? I guess, could some exclusivity further incentivize such clinical utility?

DR. EVANS: That is an interesting question. I don't know. Bob, Shubha, do you have any insight into that?

DR. COOK-DEEGAN: I don't know how to answer the question about whether patents are related to that. It is clear that Myriad did that. It is also clear that it is not a universal finding for all of our case studies. So I don't know what to make of that. It is cool that they do it. Is it related to the fact that they are the sole provider? I think it probably is related in some ways. I think it is also related to the constituency community they are dealing with and all sorts of other variables.

DR. EVANS: I think that it is instructive to think for yourself about what do you feel the purpose of patents and licensing is. I think this is, arguably, a question that reasonable people will differ on. But the answer to that question is incredibly important in how we go forward in crafting policy. It gets to this.

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Are patents and, for that matter, exclusive licenses an inherent right? Is it that we should be able to have these patents and these exclusive licenses as a value in and of themselves, or do they exist as a tool to achieve some other, positive goal?

I think that is important because it all turns the threshold of action. If one says that they need to accomplish a goal, then that second slide that says, it doesn't seem that there is a lot of need for these things, weighs very heavily. If one feels that patents and exclusive licenses are an inherent right, then that first slide that says, there aren't huge problems, rises to a greater significance.  
Rochelle.

MS. DREYFUSS: I didn't chime in earlier when you talked about the goals of patent law. You did put in this notion that people have an inherent right or a moral right to patents. I would say that is an odd statement about American law. I don't think American law recognizes a moral right to intellectual property.

DR. EVANS: So, the Natural Rights argument that people discuss?

MS. DREYFUSS: The Natural Rights argument, to the extent it exists, mostly exists for copyrighted works or where a piece of a your personality is involved. But even that is more a statement of European or civil law intellectual property, not American law intellectual property.

In fact, I would say it is quite the opposite. Thomas Jefferson, who was in some ways the founder of the patent system, was very skeptical about the idea of needing intellectual property rights at all. He has a letter in which he talks about the fact that if I have a candle and I light yours, I have not diminished my own fire. I have only added more to the world.

So, if anything, that moral claim goes the other way in American law. Ideas are things that should be shared if there is no special utilitarian right to keep it not shared. The copyright clause which you put up on the board is purely utilitarian, to provide for the progress of science.

DR. EVANS: That is exactly what I was going to go back to. The U.S. Constitution is totally utilitarian in its context. It says "to promote the advance of arts and sciences." It says nothing about inherent rights. I think that is important.

MS. DREYFUSS: The notion that a state could create its own patent rights, that has completely been quashed by the Supreme Court.

DR. EVANS: Kevin and then Mara. Kevin.

DR. FITZGERALD: I don't want to juxtapose European law and tradition versus American because I think in the European law tradition you would get a different sense of that. But I don't think you have to set this up as an either/or. This can be a both/and. One doesn't necessarily have to have an exclusive natural rights framework. One could argue natural rights within a larger framework, which I think is what they do in the European tradition. So it would be seen as a both/and.

DR. EVANS: This comes from your own Kantian/Mill type of thing. Mara.

MS. ASPINALL: On this philosophical issue, the only thing that I would add is, my understanding of it is that is why there are time limits. Time limits are the balance in patents. Whether you call it a right or a privilege that is owned, that means that you have it for a certain

period of time and then it is broadly open. That time period was put in place and recently revised in the U.S. and internationally to be able to say reward but then step away and ensure broad access.

DR. EVANS: The second bullet, how does patenting and health care differ from patenting in purely commercial arenas. I think this is also germane to what kinds of policy recommendations we ultimately come up with. Is health care the same as a widget, to use the economic jargon. I would maintain that no, it isn't, that there are other important considerations in health care.

I think that that is demonstrable that we hold different views about health care. We have examples like the Ganske-Frist bill, which implies, I think, quite clearly that we separate healthcare issues when it comes to patents and licensing in some ways from more purely commercial arenas. I think that, again, these are important things for us to think about as we go forward with a possible policy range.

Is the patenting of diagnostics inherently different from other uses of patents. Since diagnostics elucidate something about an individual, is it relevant to ask whether discovering that information through a diagnostic test should be treated differently or should be controlled in some manner. I think those are, again, reasonable things to take into account. I think people will differ on those.

Maybe, Rochelle, this is a good time for you to speak. We had a conversation at the break about my statement at the start that patents of genes are a fact in every jurisdiction that has looked at it. Rochelle countered I think really instructively.

MS. DREYFUSS: I think the notion that genes are patentable is very heavily dependent on this idea that what you are doing is isolating something from nature and purifying it. Those are the cases that you cited. They were all cases where you isolated and purified something, so a great deal of human intervention was required and that made something different in kind from what was in nature.

Now, all of those cases are about therapeutics. They are about actually purifying something and then you have a nice little liver pill or whatever that you then swallow. It is the isolated substance which is the thing that is commercially valuable and the thing that the patent protects.

When you are talking about DNA, you are sometimes talking about the same things, perhaps. There might be some therapeutics that you do with DNA. But in actual fact, the isolation and purification of it is not the commercially valuable thing. It is the information content of it that is commercially valuable. When you are talking about diagnostics, that is what you are talking about: utilizing the information content, not utilizing the purified version of the DNA sequence or whatever.

We really haven't had any cases on the question whether that itself is patentable. The Supreme Court has recently, in two cases about things that are quite different, hinted that pure information may not be something that is patentable.

So one question here is whether or not the information content is patentable or just the actual substance. A related way of thinking about it is, even if you get a patent on the DNA, what is going to be considered infringement. Is use of the knowledge going to be considered infringement.

I think there is some real question at this point based on a couple of Supreme Court cases and based on a federal circuit case about how far the patents on this stuff actually go.

DR. EVANS: I think that is a really interesting issue. One thing that we need to keep in mind is that our power as an advisory committee to the Secretary lies in making concrete recommendations. Those issues will be decided by the courts and they are out of our control.

DR. FITZGERALD: I also think Rochelle makes a good point. I thought the Metabolife case indicated the opposite.

DR. EVANS: Could we actually wait on the Metabolife case? Because we are going to talk about associations.

DR. FITZGERALD: Oh, you are. Okay.

MS. DREYFUSS: I guess I disagree about that. You like evidence-based medicine. I agree when I'm a patient that that is the way I would like to be treated. But law doesn't always work quite that way. Law works on looking at the pros and cons of different positions. Is the potential harm greatest this way or greatest this way.

So this kind of data, these case studies that Bob worked on and the conclusions of this Committee, could weigh very heavily for a court. Bracketing this when it is really an issue that is very much at the forefront right now seems to me to be a mistake.

DR. ROHRBAUGH: Jim, I think there are also a lot of other patents that one could imagine and that exist around diagnostics, not just DNA. You mentioned biological and biochemical assays as well. There are formats and other kinds of things.

We are also in a time period of a bolus of DNA patents that will eventually expire. Perhaps the number of new DNA patents is diminishing and ultimately will come to an end, and so we will be dealing with a different set of patents with respect to diagnostics and their framework and also in light of the judicial and statutory interpretation of utility and all these other cases.

So it is a period in time looking at DNA. Patents issued, many times, long ago and were licensed in the past, and we are looking at the consequences today. What happens today will be different in the future.

DR. EVANS: Debra.

DR. LEONARD: The committee also looked at international perspectives. Bob and I were talking this morning that it is not only Ganske-Frist. Bob knows this better than I, but Belgium and France also have diagnostic exemptions. So the Ganske-Frist type of concept of accepting healthcare practice from patent infringement lawsuits includes diagnostics there where we excluded those. So there is precedent internationally for this kind of thing.

DR. EVANS: Absolutely. They include diagnostics in that kind of exemption.

Moving on with preliminary conclusions, the regulation of IP rights may not necessarily be the optimal primary point of action for resolving problems regarding quality of genetic testing. We put this in here because frequently as you read about the controversies regarding gene patents and licensing the perceived and potential detriment to quality is brought up.

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The argument is made, reasonably, that perhaps with a sole-source provider one is unable to have the kinds of quality control that are inherent when there is competition. This was touched upon by Recommendation No. 13 in the NRC report regarding verification.

What I would argue and what I think came out of our task force discussions is that intellectual property rights and their application are in some ways a peripheral matter with regard to quality. They perhaps are not the best place to focus if one is concerned about quality. Issues related to quality are perhaps better assessed through mechanisms that address quality instead of trying to do it in a roundabout way.

I think that this Committee has weighed in on it. It is a complex issue. But I'm not sure, and I think that the sense of the task force was, that quality perhaps takes our eye off the ball and isn't so much an IP issue. What people do have to say to that?

DR. WILLIAMS: Yes. The other way of stating that would be to say if we had a robust oversight of genetic testing quality and practice, I don't think this issue would arise within the context of a patent discussion. I would agree with you that I think that the quality issue is a very poor lever to try and say we shouldn't have patents. It really is reflective of another problem in the system. We have addressed it, and I think you are right on.

DR. FERREIRA-GONZALEZ: I think there are two different issues on the quality where you have external proficiency or alternative assessments for performance and quality. What I'm concerned about here is something that we discussed earlier for hemochromatosis where the design of the assay was limited because of the patent.

DR. EVANS: But that is not a quality issue. That is an exclusion of ability to test issue.

DR. FERREIRA-GONZALEZ: It plays into the ability to identify the disorder.

DR. EVANS: I think we are using "quality" in different senses here. I'm talking about quality as in does this test do what it says it does, is it robust enough to detect, et cetera. That is a different issue than, we can't test for this condition because it is under exclusive license.

DR. FERREIRA-GONZALEZ: But if you are going to use a test to detect specific disorders and you are not allowed to add another mutation that would allow you to really detect the disorder, it is an issue of quality.

DR. EVANS: I disagree. I don't think for these purposes we want to broaden quality in that way. I think that is an issue of can you test for this allele.

I think when we talk about quality maybe what we need to do is define quality in a more precise way for this.

DR. FERREIRA-GONZALEZ: I'm going to go back to this specific issue because it is not the quality of actual analytic validity. I'm okay with that. But you might be missing the issue.

DR. EVANS: Right, right. What I'm getting here too is mainly analytic validity issues. That is a great way to think about it. Thank you.

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The field of genetic testing is rapidly evolving and the existing landscape of patents and exclusive licenses might cause significant problems in the future. I think there are a few things we can probably all agree on. Imagine that.

Most diseases with a genetic component are genetically heterogeneous, which necessitates multiplex testing. This is not up for argument.

Technology is rapidly moving towards the ability to engage in robust, deep genomic analysis. Here is where the interpretation comes in. I think that patent thickets may become more of a logistical problem as multiplex testing increases.

This seems to be rather obvious to me. Maybe other people want to argue with me on it, but it seems to me that, as you test more and more genes, if some of those genes are exclusively licensed or patents are held and not licensed, you have a problem.

I think what is really looming is this issue of sequence analysis, which will materialize. I think that you can argue about whether it will be three years or 10 years, but I think most of us agree it is going to happen. It is very hard for me to envision this not being a serious challenge to the current system of patents on individual genes and exclusive licenses.

I knew Brian would raise his hand. Brian.

DR. STANTON: I'm just going to ask two questions, rather than make a statement. The question of patent thickets, the examples of the 802.1N, the new network standard that has been preliminary forever, could be considered a patent thicket. The DBD standards could be considered a patent thicket where standards of patent pools came up.

My question would be, I don't know whether there is evidence of patent thickets occurring. If there are, the community, or at least the commercial community, doesn't know how to deal with them. So I think that there is a potential issue, but I'm not sure that the solutions are not in the toolbox.

DR. EVANS: Right. I think that is very fair. This is a concern that I think may arise in the future. Now, whether the remedies currently exist to get around them or not, I don't know. I'm skeptical, but there are people who know a lot more about the patent system than I do. So I would love to hear how they are going to get around that.

Kevin is next.

DR. FITZGERALD: Just on that note, if I remember correctly, somebody brought up a similar kind of example talking about the HD TV. There were 1,100 different patents and everybody gets their little piece. I thought that was brought up as an example.

DR. EVANS: I think it was in software. Software development is an example of where there has been great potential for this. I think as we get into the policy recommendations that we have to look closely at other models that might get around that.

Who is next? Rochelle is next.

MS. DREYFUSS: I wouldn't draw too much happiness from these other examples.

[Laughter.]

MS. DREYFUSS: Think about the DVD, for example, or the HDTV. You have a patent on a tiny piece. You have no product unless you agree with everybody else. Nothing comes out unless everybody agrees. But if you have a patent on a gene, you can still market your test. There is absolutely no need to agree with everybody else because you can still go out there and market.

Now, there might be good reasons to want to agree, but you are not driven to it in the way that you are all in all of these other examples. That has been the problem in agriculture, where there are some places where you are seeing some of these pools. But the pools are much harder to create because of the fact that people can make money even if they are outside the pool. You don't need everybody else to market a genetic test.

DR. EVANS: Incentivizing a pool is very difficult in this context.

MS. DREYFUSS: It is completely different.

DR. FITZGERALD: On that note, I agree that is an issue that we have to look at. However, as you talk about moving ahead to the \$1,000 genome, and we are also keeping personalized medicine out there as the horizon toward which we are moving, when we get a greater sense of what is out there in the "healthy" population, my guess is the relative simplicity with which we look at some of these supposed deterministic genetic conditions is going to become a lot less deterministic.

So even if somebody does have a patent even on the CAG repeats in Huntington's, we may discover in the population that there are people sitting out there with 42 or 45.

DR. EVANS: We already know about the vast majority of them.

DR. FITZGERALD: Right. But things will become less deterministic rather than more. In that case, then you are incentivized, in a sense, to engage with other people to get the information in order to pull together in an integrated fashion, which is what personalized medicine is supposed to be anyway.

DR. EVANS: It is hard for me to see how that is going to solve what Rochelle brings up.

DR. WILLIAMS: To Kevin's point, even though the association studies are showing genes of relatively low level of effect, the reality is the market for those is enormous compared to any of the case studies that we are looking at.

DR. EVANS: Perhaps. I don't know. I would still say perhaps. We have no idea clinically if assessing somebody at a 1.3 relative risk for diabetes is ever going to be valuable.

DR. WILLIAMS: I would argue that we do have examples not in the DNA realm but certainly in the protein realm, looking at things like CRP and HPA and some of those sorts of things.

DR. EVANS: I think those exactly prove my point. They are of minimal clinical utility, for the most part.

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DR. WILLIAMS: Although the new APP3 guidelines suggest that they are going to be very important in terms of what LDL target you treat for. There is relatively good evidence around that.

Again, the issue here is not necessarily the science but the convincing and the uptake. We know that the adoption curve for physicians in terms of new testing is relatively slow. So it may take 10 to 20 years, basically.

But the bottom line is, once it does take off, it takes off very strongly. So I wouldn't necessarily again be sanguine that because we haven't seen high adoption of some of these biomarkers at the present time that that doesn't mean within five years that we are going to see that.

DR. EVANS: Absolutely. I think we could. But again, I don't think that takes us out of the realm where we should be sanguine about the prospect of patent thickets and holdouts. I think that this is a looming problem. That is my impression. Alan.

DR. GUTTMACHER: I think it is a very good slide because it helps prevent us from being generals fighting the last war. The case examples we went over this morning I think are very useful and very informative, but of course by definition they examine the past. This field really is changing very quickly.

A point that Marc made before, that Claire Driscroll from NHRI has made to me eloquently, is of course that many of the patents which we have talked about are going to expire very soon. Then when we look forward, we really do need to think about the time of being able to sequence the whole genome.

At that point, there will still be some of these which will become an issue, but the larger problem in terms of patenting then is going to be simply the technology of the genome analysis and how that is patented and licensed. I think we have an opportunity now to look forward to that. If we are going to make recommendations or other kinds of things, we should make sure that those are recommendations which look forward and emphasize how we deal with that kind of perceivable but not yet here world, as opposed to simply how do we fix the past.

DR. EVANS: That is a good point. Who is next? Lori.

DR. PRESSMAN: Around the technique and the physical sciences, there is a lot of competition, which I won't get into.

On that slide, I wonder if instead of "patent" you should put "information thickets." One concern is to be mindful of creating incentives for people to disclose phenotypic to genotypic correlations. Those won't be patented.

DR. EVANS: Or will they? Association patents. Maybe we should weigh in on that.

DR. PRESSMAN: Maybe they will be patented, or there will be secret databases. That seems like something really not good because those don't expire.

DR. EVANS: Right, right. Brian.

DR. STANTON: I was just going to advise the Committee that in March of next year when the new cabinet comes in, the new patent bill will be coming up again. One of the things they will be

considering, as somebody mentioned, is the Lab Corp. case, which deals with the simple correlation and what the standard is. That will be on the table, or is supposed to be. The leadership has been saying in the Senate that they want to bring it up in the next Congress.

I just wanted this Committee to be aware of that. The next meeting is, I think, in February. There might be some chance to bring your opinion to the Senate.

DR. EVANS: Thank you. Marc, then Debra.

DR. WILLIAMS: This relates to the point that Alan made about looking to the future. I think the other thing that we have clearly been promulgating is that in order to make any of this work, at least for common disease variants, it is going to require robust clinical decision support in terms of combining information. That of course in some sense now is being treated as a device in and of itself. That is another area that, whether or not combining that information is going to actually be a device and patentable, will also dramatically impact how we are going to be able to use this information.

DR. EVANS: Preliminary conclusions. I think this one is a fairly straightforward one. The field is opaque. It is difficult to assess the current landscape of gene patents for diagnostic purposes, associated licenses, and whether the IP rights are directly affecting clinical and patient access to diagnostic genetic tests. I think that is pretty clear.

The lack of transparency also has implications as well for the future. When it comes to multiplex testing, how does a potential provider know if their test even infringes on another's rights. We even jumped beyond that when we said that we might have infringement problems. How are you going to know, as you develop this test, if you have infringement problems. In other words, the transaction costs of this begin to rise quickly because of this opacity.

I want to explain something because I think that unless we frame this correctly there could be considerable misunderstanding about what we are trying to do with this range of potential policy options.

We are not saying as a task force or, if we approve such a range, as a Committee that this is what we are telling the Secretary. This is a very complex landscape. We are trying to frame the issues with a range. Some of them are virtually "mom and apple pie" kinds of things. Others will have vociferous objections from some people. But I think it is reasonable and instructive to bracket this field and put out a range of options.

I will say it again. Some of these will be mutually exclusive. Some of these will be ones that depart considerably from what I think and what you think, but I think it is reasonable to have them out there and get public comment. Then, next time we can have a really friendly conversation about what should go into the final recommendation.

We have divided this range of options into eight categories. They are categorized by the nature of the action, how the change would be effected, and the entity to whom the recommendation is directed.

The categories of potential policy options include advocacy efforts by key stakeholders to ensure access, enhancing transparency in patents and licensing, filling data gaps, federal efforts to promote broad licensing and patient access, licensing policies governing federally funded research to facilitate access, study federal implementation of IP laws or recommendations related

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to that, improving and clarifying PTO policy, and finally, seeking or recommending statutory changes be sought.

Again, why present this range? To present a number of options to the public to help frame the issues. The public perspectives will then help guide formulation of final recommendations to the Secretary. Yes.

DR. FITZGERALD: Just a procedure question. My sense is from this what you are saying is you are looking at this issue as at the same time complex and yet opaque. You want to get this feedback without necessarily indicating that the next meeting is going to be the meeting where this report is finalized. It could be, but it may not be.

DR. EVANS: It is not so much that. It is that we feel like just putting out an unstructured call for comments would be far less productive than putting out a framework of possible options that people can then comment on.

The other side of the spectrum would be to just have come up as a task force with the recommendations. That would not be fair to the Committee and it wouldn't be fair to the public. I think this is a nice amalgam of that.

But we do very much hope to move along quickly on this. There is 60 days for public comment. Then we will have some more of those really fun conference calls and we will come up with something. Then, in a full meeting we will nail down our recommendations.

MS. ASPINALL: Just to clarify the process, we are going to have public comment live today with people? No?

DR. EVANS: We will.

DR. TEUTSCH: But not on this.

DR. EVANS: Some people may comment on this. The main public comment will be in that 60-day period.

MS. ASPINALL: That is what I wanted to understand. It will be written comments like we have had on the last couple.

DR. TEUTSCH: Yes. It is the formal process.

DR. EVANS: Then we will do all that laborious culling.

MS. ASPINALL: Then we may have live comment at the next meeting as well.

DR. EVANS: We always have live comment.

MS. ASPINALL: Right. But then we will be looking towards finalizing this or putting it in writing at the next meeting.

DR. TEUTSCH: Correct. But we really want the public comments in writing before then so that we have as much as we are going to have so that we can reach some recommendations.

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MS. ASPINALL: That is what I wanted to clarify.

DR. EVANS: The public has 60 days.

MS. ASPINALL: After this meeting, the documentation we have talked about today will be available for public comment.

DR. TEUTSCH: Yes. Once we approve it today.

DR. EVANS: Once we approve the draft.

DR. TEUTSCH: It will go out for that purpose.

DR. EVANS: Let me keep moving here because we will need all the time we can get.

I will just make a plea for balance at the start. I don't think this is a particularly controversial statement, but the patent system in this country works pretty well. We should be mindful of unintended consequences that could result from suggested changes. It is the baby and the bath water argument. We don't want to muck up the whole system by trying to fix things.

On the other hand, if there are problems or likely future problems, I don't see it as unreasonable to recommend judicious policy changes. The key is balance. We need a proportional response to identify problems and potential problems. That would be my plea.

The questions for the following draft options are the following. I want you to keep these in mind as we go through them. Are there policy options that should be added, removed, or modified prior to releasing the draft. We have heard some suggestions. We could get that input. I'm sure the task force came up with the perfect document, so I can't imagine there would be changes.

Is the range of policy options presented supported by preliminary findings. Are there any other issues that need to be addressed in the report before it is released for public comment. Overall, and with the understanding that further editing may be needed, is the draft report ready to be released for public comment in early 2009 for that 60-day period.

With those kinds of instructions in mind, let's tackle the first ones. Some of these, as I mentioned, are kind of "mom and apple pie" types of things.

"With regard to advocacy efforts by key stakeholders to ensure access:

"A) In order to optimize patient access to and the quality of genetic tests, stakeholders -- that is, for example, industry, academic institutions, researchers, patients -- should work together to develop a code of conduct to encourage broad access to technologies through licensing agreements for the diagnostic use of gene patents."

Comments?

DR. LEONARD: But, given the discussion of quality, I think the quality issue --

DR. EVANS: Right. As I read it I thought, wait a minute, why do we want "quality" here. Why don't we leave that out. "Patient access to genetic tests." Mara.

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MS. ASPINALL: I have some issues with a number of these, but I'm wondering whether it makes sense to edit these or really leave them as they are and then have the comments on them.

DR. EVANS: That is a good point.

MS. ASPINALL: I think this presumes a lot of things. Otherwise, we will never get through it.

DR. EVANS: Right. I don't want to do too much wordsmithing here because the whole purpose of the subsequent phase of this is to get people's input. I do think that [we should discuss] if there are really substantive reasons not to have things or ones to add. I think your point is good. Unless there are huge issues, I think we should proceed.

MS. ASPINALL: The only issue that I will say is, that implies that as a result of the patent system we don't have broad access, which some of the case studies said we do and some of the case studies said we don't.

DR. EVANS: It says "in order to optimize." I don't think this necessarily implies it is bad. I think that we want the most access possible.

DR. WILLIAMS: The other point I would make relating to the quality thing and the reason to maybe recharacterize it or restate but not take it out, is the point that Andrea brought up before that some of us include within the general term of "quality" the idea that if you are not operating certain parts of the test, that affects what might be considered to be the utility of that test. So you might want to characterize that as utility as opposed to quality, leaving out the "analytic validity" piece of it.

DR. EVANS: So, how would you phrase that?

DR. WILLIAMS: "In order to optimize patient access to and the utility of."

MS. ASPINALL: Can I ask, does that include the issue that sometimes we are having very many companies or labs doing one test who actually may have lesser quality because there are variable, different standards and not a clarified ability to show one reference standard?

DR. WILLIAMS: You are talking about analytic testing?

MS. ASPINALL: Yes.

DR. WILLIAMS: That is not what I'm talking about.

MS. ASPINALL: No. I'm saying it should include that as well if you want to include that.

DR. WILLIAMS: No, that is a different issue.

DR. EVANS: That was the point. We wanted to separate analytical validity from clinical utility and clinical value.

DR. FERREIRA-GONZALEZ: We were talking about adding different mutations, Mara, here that will have different clinical utility. Clinical utility will cover that portion of being able to only detect 95 percent of the mutations versus 50 percent or not being able to add that mutation to the panel.

DR. EVANS: Kevin.

DR. FITZGERALD: It might be helpful for our own reflection if you add into (A) that HHS should bring together these stakeholders to develop a code. Then we find out from the public whether they think HHS is the place actually to do that or there is some other group to do that.

DR. EVANS: We could say "should work together (perhaps facilitated by HHS)."

DR. FITZGERALD: Just put that in there so we get that feedback and we can see whether that is the place that that is supposed to happen or not.

DR. EVANS: "B) When different stakeholders -- for example, academic researchers, industry, and patient organizations -- work together to advance the identification of gene mutations and the development of diagnostic tests, the owner of any resulting invention should consult with those stakeholders regarding whether to seek patent protection and how any resulting patents should be licensed."

Does that seem controversial to anyone?

MS. AU: What is the action step on this one? Who is enforcing this?

DR. EVANS: Believe me, we get to ones that have big teeth. Have no fear. This is a recommendation. This is a statement that we should all get along.

DR. WILLIAMS: Actually, this is a statement. It is not really a recommendation. The recommendation could be that DHHS provide a role or a forum by which the stakeholders could actually get together and discuss these issues.

DR. EVANS: That is interesting. Maybe we could consider that as another option to put out there on the table.

DR. BILLINGS: What I don't understand about this one is, I thought the patents were held in some level of secrecy until they were filed. How are we going to have these discussions within the context of how patent information is handled?

DR. EVANS: I think what this is saying is that when different stakeholders work together to identify a gene and develop a test, the owner of the resulting invention should consult. I think that it doesn't preclude not consulting. It is a recommendation or a suggestion that this is the most beneficial way of proceeding.

DR. BILLINGS: But when? After the filing, before the filing? When, exactly?

DR. EVANS: I don't know. We didn't approach it that way.

DR. TEUTSCH: It is probably not about whether but it is about how it gets implemented.

DR. BILLINGS: This actually has something to do with marketing of tests.

DR. COOK-DEEGAN: Paul, this is Bob. I think what this is trying to get at -- I'm not absolutely sure -- is let's use the Huntington's disease and cystic fibrosis model. The constituencies were at

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the table when the decisions were made about how and when to file patent applications. The fact that something can be secret does not mean that it has to be secret. In this case they were not.

That is in contrast with the Canavan case, which I presume is what this is mainly aimed at. Don't screw up your relationships with the constituencies that contributed to your invention.

DR. EVANS: Maybe Paul's objections could be overcome by saying instead of "the owner of any resulting invention," "those stakeholders should consult with one another regarding whether to seek patent protection. I think that would get around some of the ambiguity that, Paul, you highlight there.

MS. ASPINALL: Either way, there may be patents in process that people may not choose to share. I think you could phrase it either way, but as a live entity under today's system there very well may be things that people do or don't want to share. Maybe some would say, I don't want to sit here because I don't want to learn things that will impinge upon this.

I think in and of itself this is meant to be draft and then to have more substantive comments on it later. I think Paul's point is a good one as to how logistically this will work. There are those who may want to do it but they are unable to.

DR. EVANS: Right. So, what if, instead of "the owner," we said "those stakeholders should consult with one another." This is more of a general admonition in the field.

DR. LEONARD: Actually, this could be a recommendation to patient organizations, when they are beginning to interact to advance identification of gene mutations and the development of diagnostic tests, that they proactively make their input a condition of their involvement.

DR. EVANS: That is a little different. This is an admonition to, really, all those stakeholders. I think you are right. It is instructed by our experience with the Canavan experience, where this didn't happen. Now, I don't know whether us just saying, you should play well together, is going to do anything.

I don't want to dwell too much on this because these are "mom and apple pie." We want people to get along. I think it is useful for our Committee to mention this, but I think when we have things that have no enforcement we shouldn't spend that much time. We do have to break for lunch. Mike.

DR. AMOS: I just want to say, to the extent that this is sent to the Secretary of Health and Human Services, what is an actionable statement that we can make to get to the point where the Secretary can set up a commission or set up a forum to promote this. "Where possible, HHS should promote," blah, blah, blah.

DR. EVANS: That is a really good point. Maybe at the lunch break we can do that.

MS. ASPINALL: In thinking about it, something like that may be necessary at least post granting of patents because I think there is an aspect of this, which I don't think was the intention, which is restraining free trade. If you haven't filed your patents you can't say, I'm going to file this one first, so-and-so is going to file this one second.

DR. EVANS: Yes. Collusion is not something we want to encourage.

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MS. ASPINALL: So if part of the idea is, you have these patents, so how do we make the world better for health care. It may be after granting as opposed to before granting. That gets to Paul's issue as well.

DR. EVANS: At the lunch break we can talk about that. We are going to have to finish up with this one and then go to lunch. Joseph.

DR. TELFAIR: My question is more of a point of both clarification and information. It is a feasibility question. I agree with the statement made about what is actionable, but I have to back up and ask the question how realistic is this? Maybe it can be answered here. Do we have adequate information about how often this actually occurs in the development process such that we could spend reasonable time getting this done?

It seems to me that if we are going to make this a recommendation, it should be a strong enough recommendation on accessible data and information that we can actually say, do something about it. If it's just not done often enough, [it may not] even be something that is reasonable to consider.

DR. EVANS: Again, I think that the case studies clearly demonstrate there are times that when this didn't happen there were problems. I don't think it is unreasonable to admonish --

DR. TELFAIR: I'm sorry. That is not what I'm saying. I'm just saying I recognize from the case study that it happens sometimes that it's not. I'm just worried about when the "not" occurs.

DR. AMOS: My guess is that it is not going to happen that many more times for individual genes. It might, but when you start multiplexing these tests and trying to put them together on one platform, the issues are going to become very, very complex. That is something I think we may want to consider looking in the future.

DR. TELFAIR: Then, can I just recommend that that actually become the focus more and that is considered when we talk about more actionable steps and what to do? It seems to me that that would actually help focus a little bit more whatever recommendations that we make in terms of something very concrete to do.

DR. EVANS: I think we can focus this some. We will do that during the break and then come back with some wording. One more comment.

DR. WILLIAMS: Again, thinking about actionability, speaking as someone who is really naive in terms of how these agencies work together, would there be a role for the Secretary to convene something that would involve the Patent Office, Commerce, and different people at the governmental level who have a stakeholder's interest in this as well, to say here are the issues that have been teed up by our advisory committee. We think it impacts you. Can we get together and discuss your perspective on this. I don't know if that would be reasonable or not.

DR. EVANS: Again, what we need to do is now take a break. Anybody who is interested, come on over here and we will talk a little about adjusting this.

We start back at 1 o'clock with public comments. Then, 1:30 to 3:15 we will try to soldier through. Just be warned we will take the break away if we aren't done.