Continued Discussion of Oversight and Pharmacogenetics

Now we have about an hour and a half of discussion before we are visited by Ms. Kristin Fitzgerald from the House to talk to us about the House's plans for genetic anti-discrimination. How we're going to use this time is to return to our discussion from this morning and early afternoon regarding oversight of genetic technologies, the role of pharmacogenetics. We've had briefings from the federal regulatory agencies on their roles, activities and plans in regard to oversight, marketing and laboratories. You'll all recall, especially those who were involved in the Secretary's Advisory Committee on Genetic Testing, that our predecessor committee spent a lot of time and a major focus of the work was on oversight and a number of the recommendations about how oversight might be enhanced.

I think it's important, and I'll organize what I heard today into three areas. We heard about oversight through CLIA and FDA, we heard about FDA and pharmacogenomics, and we heard about oversight of advertising and promotion. One of the things we need to do now is discuss that further, and also discuss our future agenda and how we're going to focus our efforts.

Fundamentally, do we need to pursue oversight as a major agenda item of this committee, or do we feel that the FDA and CLIA are proceeding down a course that was set by SACGT and we want to monitor that? Are there other areas that we want to focus on now?

So I'll open it up to discussion by the committee.

Chris?

DR. HOOK: Chris Hook. Thank you, Dr. McCabe.

I go back to the end of our discussion this morning when we were talking with folks from the FDA about using pharmacogenomic information to understand the potential implications, negative consequences of certain drugs in various subgroups of the population, and the call or the need, the express need for more information to be generated. I think that should be a priority issue for us to consider.

As you said, perhaps the FDA cannot mandate those sorts of studies in terms of approving a drug, but if there are ways in which we can, through looking at the drug development process of Phase II and Phase III studies, through government funding as a means of requiring that type of investigation, we should at least talk about it, what would be the expenses that would add to the research overall, how can we provide them the information that they need. So I'd like to see that on the table.

DR. McCABE: Debra?

DR. LEONARD: Well, even beyond -- what you're talking about is prospective drugs. The Japanese government has mandated a pharmacogenetic analysis of all drugs that are out on the market being used in the Japanese population because the reactions there are different than the Western reactions. So prospective is one thing, but what can we learn about the drugs that we have and some of the toxic reactions that physicians are well aware of that they might see? Is there a way to test for those? Also, for drugs that are even out on the market.

DR. McCABE: I think it was maybe you, Chris, but maybe somebody else mentioned that this

should be funded by the NCI for cancer drugs, and I noticed that our NIH representative was taking notes since the National Institutes was mentioned. Alan Guttmacher is sitting in for Francis Collins from the NIH. Would you like to comment on that?

DR. GUTTMACHER: Sure. I think we certainly believe that this kind of testing is important to do. The question, of course, is that the NIH tends to fund fairly little actual drug testing in any aspect, including pharmacogenetics. It tends to be more drug companies and others. We tend to focus more on that basic science research that doesn't get funded by private industry, for obvious reasons. That's not to say we're not involved in any drug studies in any early drug development, and it's also not to say the NIH particularly -- supported largely by the National Institute for General Medical Sciences is a large pharmacogenomics group that's funded a number of institutes, et cetera.

So the NIH is clearly involved in these things and is interested very much in pharmacogenomics applications and pharmacogenetics, but I think that it would be false to think that NIH alone is going to be able to take care of this issue.

DR. McCABE: Chris, then Emily.

DR. HOOK: But isn't it true that through most Phase I/II programs, they have to receive NCI approval in order to proceed with human subjects trials in that regard? And couldn't the NCI mandate, if nothing else, the pharmaceutical companies pay for this? In other words, make it a requirement in order to do the Phase I/II testing?

DR. GUTTMACHER: I don't think the NCI -- I must say I'm not from the NCI, so I can't answer for them, but I believe that they don't have as much involvement as you're crediting them with.

DR. McCABE: Emily?

DR. WINN-DEEN: I think one of the issues -- so there's two issues in pharmacogenetics. I think we should probably address both of them. One is the issue of what to do to get the data from marketed drugs. Who is responsible for basically paying for the studies, designing them, paying for them, running them, the whole thing, so that the general public would have the information. Some of these drugs are generics. I mean, there isn't even one drug company to go to. So there's that issue. That's personally where I think somehow NIH could help with funding.

For drugs that are still in the pipeline, in Phase II/Phase III, working for a pharmaceutical company and also talking with a number of my colleagues who work for other pharmaceutical companies, there is still a big cloud over that whole process, and until FDA finishes its safe harbor guidance on what, if anything, it is or is not going to do with information that might be gathered and whether or not that information would be required to be submitted, I think that is still influencing the way trials are designed. That is, some trials are still purposefully designed not to include a pharmacogenetic component or to include it only in a blinded retrospective analysis should an efficacy or a safety issue arise because of fear for how the FDA would use that data and inhibit their ability to launch a drug.

So I think there are two different issues that really need to be resolved in two different arenas. But I do think from a public health point of view, if we're going to get to the point of really utilizing genetics and pharmaceuticals together, we're going to have to solve both those issues.

DR. McCABE: Steve, do you want to comment on the FDA? Steve Gutman from the FDA.

DR. GUTMAN: Yes. I'm not in the greatest position to comment on at least the drug side, but I do know that they take this very seriously, and I do know that they're working on documentation to strengthen that, and I think that's on a fairly tight time line. So I think there's a reasonable ability to have a short-term expectation that they'll produce guidance that I think will be industry friendly and address exactly the issues that you've raised.

DR. WINN-DEEN: So my comment back is to just sort of encourage that to reach its logical conclusion, because there is a couple of year time lag, two or three years. People today who are designing a Phase II trial for a drug that will probably reach market in about four or five years are not going to do things until the FDA guidance is clearly there. So there's this time lag phenomenon. So we need to keep moving along on the FDA front so that we can see the benefit sooner rather than later on the drug front.

DR. GUTMAN: I do believe CDER appreciates that.

DR. McCABE: So is there a way now to focus this discussion? Is there a way that you wish this committee to weigh in on this topic? Is there something that you want other than an update in a year from the FDA? How do we stay involved, become involved again in the future on the topic of pharmacogenetics?

Yes, Debra?

DR. LEONARD: Well, we can have updates from the FDA. I don't know that we're going to move their process along for the new drugs any faster than they're going to move anyway, and they're hearing us say we want them to move as quickly as possible. But is there a way to explore funding mechanisms for, if you will, retrospective drugs on the market and that pharmacogenetic analysis through NIH, through an RFA? I mean, I don't know which part of NIH this would come under or be funded through, but is there a way to explore mechanisms to get funding for these types of research?

DR. McCABE: What we have done before, "we" being the Secretary's Advisory Committee on Genetic Testing, when we had questions about this was -- and I'll tell you, it's a huge burden on the agencies, but that is to ask them to explore what they are funding at the current time in these arenas. It is a huge amount of work on their part, but that's something that we could ask.

My impression is, having lived in academics and seen the flow of money, that once you get out of -- I know pediatrics, so once you leave the Children's Oncology Group, there's very little drug testing that's done in kids that's funded by the NIH. So I think we would find that there's a relatively small amount of money that's flowing. If we then say that we need to explore postmarket surveillance in terms of pharmacogenetics, that's going to have huge ramifications throughout the industry.

So I think this is a very large ticket item that we're talking about. What I would suggest is if other countries are exploring this in their own populations, like the Japanese government, one thing we could do is try and find out what other groups are doing around the world and see how they're supporting it and how they're going about it and whether any of the things that they're learning could have any effect on us. We've got some guests from the European community here. I don't know if they're prepared to comment on this.

Reed, do you want to --

DR. TUCKSON: I think that one of the challenges that we face here, and I think you're sort of getting at it, is that we obviously in this country have a -- whatever the trillion dollar deficit is. I think we all understand going forward what that's going to mean for the budgets of any of these HHS agencies.

So I think what we might want to try to find a mechanism to do is to -- if we're talking about retrospectively using new tools, what would be a grid, and who could help us to develop a grid that would say sort of where are the priorities here? What are we trying to achieve and what are the priorities as you look back? I mean, if at the end of the day -- and part of this is my own naivete trying to get up to speed here. If we're saying that there are drugs that are in use today whose use could be made safer, give us better quality outcomes, and more cost effectively, if we had the ability to apply to them new knowledge around pharmacogenetics, then how would one make those choices of where you would look? I think that's what I'd be looking to for more guidance as to how to think that through.

On a prospective, going-forward basis, I think the thing that I'm most interested in from this morning's discussion is to assure that the data that is available going forward around pharmacogenetics and drugs is made available in efficient ways for the multiple constituencies that need to have it to make the most intelligent decisions regarding quality, cost and safety.

DR. McCABE: Before I call on Brad, I'll tell you what I teach when I teach about pharmacogenetics and pharmacogenomics. My Ph.D. happens to be in pharmacology back in my deep past, and so I get to teach this to the medical students. The people we need to have sitting at the table would be the American Bar Association. I really argue that it is the lawyers who are going to drive the development of this technology, because they're going to demand it for their clients, and that's why we will start to have testing.

Having had my nursery be threatened with a suit two to three years ago for Connexion 26 -- it turned out that the child who failed their hearing test did not have that mutation, the glycoside-induced hearing loss -- it made me begin to think about this.

So I think we will see a building of testing resources, and it will become a demand of the public, and it will be influenced by their legal counsel. Having said that, that takes us back to the question of how do we build the evidence base for this and how do we begin to try to protect the public and the professionals rather than just being reactive?

Brad?

MR. MARGUS: I talk to a lot of pharmaceutical (inaudible) pretty much daily about pharmacogenomics, and in fairness, so far, as of today, it's been pretty disappointing. The problem is there isn't a lot of great evidence yet that's driving this forward. I mean, the examples -- those of us who go to the conferences for these things see the same old examples of cytochrome P450 and HER2 and a couple of others, and then you run out of them. It's really been promised but it hasn't delivered. I think that will change because I really believe in the next few years there will be a lot more associations and markers, and that may drive a lot more.

I think if we could encourage the Secretary to encourage the FDA to continue working with industry in keeping up to date on what's happening so that they're ready for this onslaught, that would really be good. I think the safe harbor thing is obvious.

The other thing that we mentioned today is that we should also encourage that trials incorporate diversity. That's certainly important.

On the issue of how do you get people to do pharmacogenomics and find markers that could be valuable for either old drugs, drugs that are off patent in particular, or marketed drugs, for one thing if it's marketed drugs, the other fear is that no pharmaceutical company wants to cut their market size, so they're afraid of that. Obviously during development, they're worried about the safe harbor thing we discussed. And then on the drugs that are off patent, who in the world is going to pay for it?

I sit on a council right now at the NIH, and I can tell you -- it's the Neurological Institute -- they spend some decent money on clinical trials, but it's not going to go over really well if you tell them that you want to take out $100 or $200 million of R01 grants to do a few clinical trials. So what I was wondering, and maybe Alan could think of this, is there any other mechanism that would turn pharmaceutical companies on to revisiting pharmacogenomics in some of the old drugs?

For example, I have no idea what the mechanism is, but something along the lines of the Orphan Drug Act, how it provides some patent protection to encourage companies to work on it. Is there any way you could motivate pharmaceutical companies to revisit old drugs or off-patent drugs in exchange for doing pharmacogenomics that would end up actually helping the world?

DR. McCABE: Alan, do you want to respond to that before we move on?

DR. GUTTMACHER: Sure. It's a difficult question. I thank Brad for bringing up the reality that if one was to do retrospective testing, the multi-hundreds of millions of dollars that would be involved in that clearly just doesn't exist, even though the NIH has relatively deep pockets. It just doesn't exist. I think the question is how you would encourage those who are making profits from the drugs to use that kind of testing.

My -- I hope it's not cynical, maybe just reality-based kind of thinking about this is that that kind of testing, as much as it would be helpful today, probably will not become a reality until the cost of doing it becomes much less. The good news is I don't think we're decades away from that, but we're also years away from that. But I suspect that that kind of testing really needs to await the cost of genetic testing just becoming so much less that it becomes easier to do the research.

MR. MARGUS: Actually, the biggest problem I don't think is going to be the genotyping. The genetic testing is going to be. And for these old drugs, no one collected or banked any DNA, so even if you can get genotyping down to zero, you've got to still run new trials to go get the DNA.

DR. GUTTMACHER: That's right. It's going to be hugely expensive.

DR. McCABE: Emily, do you want to follow up on that point?

DR. WINN-DEEN: Yes. I just wanted to say one mechanism that we might consider is the cooperative group mechanism that's used in oncology today not for this particular application but for looking at best practices and combination therapies. Those cooperative group studies I believe receive a basic level of funding through NIH to create the cooperative group, and then the drugs that are involved in patient treatment are generally donated by the drug manufacturers. So it's truly a multi-funding source thing where everybody puts in a little bit and the patient community benefits.

Now, this is aimed at a different kind of best practices where no single pharmaceutical company really has the ability to combine its drug with a competitor's drug, so you need sort of a neutral venue where that can happen. But that's the kind of thing where maybe -- let's just take an example. Maybe all the manufacturers of statin drugs could contribute their statins and we could look for markers that predict response to statins, those kinds of things, and some of that is actually going on in the PROWESS trial, so I don't want to make it sound like that's not happening. But those are the kind of things that might be mechanisms for funding, where it's not on any one organization's shoulders.

DR. McCABE: Is this a follow-up, Reed?

DR. TUCKSON: Yes.

DR. McCABE: Okay.

DR. TUCKSON: In addition to the comments of my colleagues, I want to continue to be less ambitious than they. I'm still worried, quite frankly. I'd like to hear more, in an organized way, from the Secretary's subordinates, leaders in issues. They're too brilliant and wonderful to be subordinate, the people that run these agencies. I'd like to hear sort of the collective understanding from them about the potential value and when can we recognize the value of this new knowledge and this new science, and where are we with it.

Because, quite frankly, I keep having in my mind's eye the new report from the Census Bureau that just said there's another 2.6 million uninsured people, that the pharmaceutical costs are still continuing to go up and up and up. There are so many issues before us, and I want to be sure that somebody in the government, and I think it should be the Secretary, should be looking at the cost effectiveness of these things, knowing how these tools can be applied in a responsible way to make sure that the American people get access to pharmaceuticals that they aren't getting access to now. There's a lot going on here, and I want to make sure that this is being precise.

So I would sure love to hear in a much more precise way from the presenters that we have available to us, the experts, as to where and when are these tools going to be available and how can they best be used, and I think we can then start to give better recommendations about how to go forward. But I'm not sure we know enough yet, and maybe others are just a lot sharper around these things than I am. But please keep in mind that there are a whole bunch of people who don't get access to fundamental digoxin, much less being able to start to do some of these other kinds of tools. So let's just make sure we know what we're doing as we recommend it. I'm not against it. I just want to know a little bit more.

DR. McCABE: Debra, and then Hunt.

DR. LEONARD: I have the impression from talking to pharmaceutical companies -- and Brad, maybe you can comment on this, and I was hoping Steve would be here but he's gone -- in talking to some people, medical directors and stuff at pharma companies, they say that there is pharmacogenomics and genetics going on at pharma companies up the wazoo, tons of it, but they don't let it out of the company.

So I don't know that it will be an additional cost to pharma, like they're waiting for the FDA to tell them that they have to do this. I think they're doing it because they learn a lot from that process, but they aren't submitting that information because it runs into the marketing issue of

they cut down their market if they can identify who will benefit and who won't benefit from taking a drug with a particular disease.

So can anybody clarify that as to whether pharma is doing this?

MR. MARGUS: I will say that there's a lot of money being spent by pharma on pharmacogenetics right now, but the number of discoveries and associations where they've found a large enough percentage of genetic variants to have any predictive value, to have utility in a diagnostic test, a bar code that predicts drug response, either who is going to have adverse reactions or who is going to have efficacy, is really, really barren out there. There are very, very few examples of that, very few successes.

But the technology is moving along, so I think there will be, but I don't think they're sitting on things that would really help just because they're concerned about the market being shrunk.

Sure, some drug companies were thinking -- and it's changing, but were thinking why put money into this, why have these initiatives if it risks making a smaller market? But the flip side of that is that a lot of drug companies are hoping that pharmacogenomics will actually reduce attrition in drugs that wouldn't have made it to market will make it to market because of pharmacogenetics. So they're actually pretty high on it. But whether they're high on it and spending a lot of money or not, so far there isn't a lot of useful stuff coming out, I think.

DR. LEONARD: But part of the issue is that that's not transparent. I mean, it's not out there so that someone other than the pharma company itself is making that judgment about whether it's useful or not.

DR. WINN-DEEN: Debra, I think one issue is that a tremendous amount of the money being spent -- I'm going to be very careful in my wording -- in pharmacogenomics is aimed at finding new targets for drugs and then taking those drug targets forward. This is very different than having a test, a diagnostic test that would predict either response or safety. So the vast majority of that pharmacogenomic spending is on the way, way upstream part of things, and that's where it's been spent for the last four or five years, sort of during the heyday of the Genome Project.

Now we're starting to see some of the things from that effort coming forward, getting to Phase I/Phase II, and now you're starting to see companies having maybe a little more pathway knowledge. Instead of just having a drug that somehow works, they actually have some idea of how that drug might be having its effect. So potentially things are coming along, but I agree with Brad. From what I've seen in my interactions with pharma, the biomarkers to predict safety and efficacy are just not there. There's just not proof enough, and it's not that they're hiding it. It's that they just don't have them, and they're not motivated.

Let's be honest, they're not motivated to do a huge amount of searching unless there is some issue with the drug. If the drug is efficacious in 90 percent of the people they try it on and there's no apparent safety issues, there's no reason to spend a lot of money on those kind of studies.

DR. McCABE: Hunt?

DR. WILLARD: Just as a quick follow-up to that, and then to my original point, Debra, my understanding is exactly yours, but Emily makes a very important point. They're not going to release the data because it's their competitive edge at the early, upstream end in terms of how they figure out which darts are going to be the most likely darts to stick. But you hear it at meetings

all the time, that there's tons and tons of data at the front end of this and that the concept is there. So I'm not sure there's much we can do except perhaps bring a few folks from pharma and figure out at what level they can share some of that information with us.

But let me move to my other point on other people we can hear from. It in part reacts to what Reed said. One group within the government to hear from would be CMS. Their pockets may not be as deep as the NIH's, but on the other hand they have an incredibly vested interest in trying to figure out how to best improve the efficiency of health care delivery and reduce health care costs. So it is certainly in their best interest to think about funding, even at the level of pilot projects, albeit large pilots, a few large pilot projects, whether, in fact, this is going to reveal a data set that's going to be of some value. So bringing someone from CMS I think might be useful for the committee.

But also the other group that has an incredibly vested interest is the health insurance industry, not that I'm so naive as to think they're going to voluntarily spend their money to allow us all to collect those data. But nonetheless I think they certainly have a vested interest in trying to reap the benefits of genomic medicine downstream even if they're not ready to do it today.

DR. McCABE: Does CMS wish to comment on this?

DR. SULLIVAN: Yes. I'm sitting in for Dr. Tunis. I'm Dr. Bill Sullivan, the Deputy Chief Medical Officer for the Centers for Medicare and Medicaid Services.

We're very cognizant of that. I've been at these meetings. We're going to other meetings. We're sitting in on other pharmacogenomic sessions in other venues. We are working the best we can to try to keep ahead of this issue, and Dr. Tunis is very much attuned to everything that's going on here. He'll be here tomorrow in person. He might add some more to that.

But our research budget is fairly well defined already. We have a lot of devices that we're looking at that are in the billions of dollars over years -- ICDs, the long-volume reduction surgeries, the left-ventricular-assisted devices, a slew of oncolytic agents which will dwarf anything financially that you will come up with in the near future in pharmacogenomics. But this is very much on our horizon, and it's a topic at our medical technology council.

DR. LEONARD: Can I make a comment about CMS coming? Can they please come also to comment on reimbursement for genetic testing? Because the codes that are used currently for genetic testing are so low for reimbursement, they are nowhere near realistic of what it even costs to do the testing.

DR. McCABE: Do you wish to comment on that?

DR. SULLIVAN: I'm a CPA and an MBA, as well as an M.D., and I think I've heard in the prior sessions and this session that we don't have a lot out there. It frankly is something that we're looking at to see how we should reimburse and should we reimburse for the test that would determine whether someone is going to be susceptible to the drug, or how do we reimburse for the drug. I have something of a dichotomy. I was listening to Reed earlier, and it's somewhat humorous. I'm sitting in the morning approving -- well, I don't approve, Dr. Tunis does -- billions of dollars in cancer drugs, and then in the afternoon I go down to Medicaid and take 20,000, 30,000, 40,000 people off the drill rolls for fecal incontinence.

So I'm a little bit schizophrenic on this because where do you go when you have a drug that's

working for 90 percent of the people, and then you have an expensive test that will determine whether some more people will be better benefitted, and at the same time people aren't getting the basic drug? So we are looking at reimbursement. At one of our recent meetings we had a discussion about reimbursement for pharmacogenomic agents, and I think some of the people in this room have visited us in our OCSQ offices recently. So it's very much on our radar. It's not at the top of our radar. We've got a few other things with Medicare reform and Medicaid.

DR. LEONARD: Right, but I'm not talking about pharmacogenetic testing. I'm talking about the CPT4 codes that are used for simply doing any kind of molecular-based test. I mean, you can't do a PCR for $5.71 or whatever the reimbursement is. I mean, it's not realistic. They were set so long ago with no data on what to set them at that unless this is fixed, we're not going to move forward with genetic testing. We may as well stop discussing genetic testing, let alone pharmacogenetics.

DR. SULLIVAN: Well, let me say there's a long line of people in front of you saying that they don't get reimbursed enough. I will be taking this back to Dr. Tunis to see how we can pay more money for pharmacogenetic testing as soon as we get a better handle on how much it should be reimbursed.

DR. LEONARD: Genetic, not pharmacogenetic. And there are only about eight codes.

DR. SULLIVAN: Genetic testing is what you're talking about. Okay. Excuse me.

DR. LEONARD: That's okay.

DR. McCABE: Reed?

DR. TUCKSON: As I try to follow all the balls that are in the air, I think I'm encouraged by what I start to see. First is that as a result of our last conversation, our last meeting, we clearly identified the areas that we've talked about today as being important, and we've learned a lot so far in this meeting. I think what we're hearing is that we've learned enough that we have interest to know more because we think this is important and we think there are some opportunities that the Secretary can use in his bailiwick to intervene.

I think that the work that we have to do next, Emily helped a lot by saying we have to be very clear in defining exactly what it is that we are interested in, and the use of words are important. So I think we have to have some mechanism either before we leave or in a subcommittee on the telephone, but starting to really clarify with more specificity what it is that we are interested in learning.

Secondly, I think it is important to bring with more specificity of questions the people from the pharma industry in to help us to really understand the answers to some of these very specific questions, whether the question is how do you view pharmacogenetics for the purpose of designing new drugs and improving the clinical trials process; and secondly, if I understand Emily's point, how do you use pharmacogenetics as a way of better targeting the use of drugs in their safety and so forth? There are two different issues as she presented it, and I think both of them are important.

I think we ought to specifically try to understand more about the safe harbor issue and have somebody who really can explain that to us in another level of detail, because I think there's something there that's relevant here.

Third, I think we really do need to have somebody help us to understand better what would be the research infrastructure and the relationship between the public research dollar and the private sector research dollar that would start to answer these questions. If, in fact, as Debra has just taught me, there's a lot of this going on in the private sector, then what is the best way to leverage that so that, in fact, we get these answers, and what is the rational use of public resources given the private sector initiatives? I think that's a question that I think we're beginning to say we're interested in, and I think it's reasonable.

Finally, I think this idea of CMS coming forward to us is also important, because if I understand Hunt's point, what he's saying is let's get the federal government agency reporting to the Secretary which has to make cost decisions and coverage decisions. But where I want to go beyond what my good friend Dr. Sullivan has said is that I think the question we want to ask them is what do you, CMS, need from your sister agencies to be able to answer these questions? I think it's going to be important for us to know what they need. I'm not happy with this being thrown into the CMS research budget.

Basically, the government agencies are supposed to work together, and if we're advising the Secretary, I think what we ought to be doing is helping to provide at least some input for how to coordinate the rational use of scarce public resources to answer critical public questions, and I think that maybe what we ought to start doing is making the CMS person say what do you need from these other people.

As far as the other people who have to make payment decisions, such as plans and others who are also in this drama, I think that also makes sense, but getting them very specific questions about what information do they need if they're going to meet their real-world needs. So I think I'm encouraged that we're moving along a trail here.

DR. McCABE: Emily?

DR. WINN-DEEN: I actually thought that the prioritization comment that Reed made was maybe a place we could start to actually do something concrete. So we definitely would need to understand how and who would fund studies, but we also need to understand, out of all the things that are out there in the global world that could be done, what are the things that are most important to be done, and that's something that this committee I think could work on independent of where funding might come from in the future, and then have something very concrete with some specifics surrounding it regarding what are the criteria to get on the priority list.

Is it known frequency of adverse events, or is it that there's already something in a drug label that refers to a gene but we just haven't gotten a test out for it? What are the things that we could do to move things ahead in a real practical way so that we can make -- I'm very concerned that this committee just doesn't make these sort of broad, hand-wavy recommendations, but we need to make some very specific actionable recommendations. So I thought the priority list might be something we could work on, and I know our friend over here from CMS is anxious to say something back, so I'll stop here.

DR. McCABE: Yes, Dr. Sullivan, and then Cindy.

DR. SULLIVAN: What do we need? Sharing of information among all the agencies, and we're working on this, but there are legal hurdles to that, there are cultural differences. It reminds me of when I was in the military. We had the Army, Navy, and Air Force, and we're all doing the

same tasks. We're wearing different uniforms with the same mission. I see a lot of positive developments.

I wanted to talk earlier about how FDA, AHRQ, CMS, CDC were all knowing that we need to work together, thanks to the Institute of Medicine report about federal leadership in many areas, and we're trying to do that. There are a lot of bureaucratic and legal hurdles to that, but that's what we need. We need to share information so that we can apply it to the benefit of our beneficiaries.

DR. McCABE: Cindy, Brad, and Debra, and then I'm going to actually wrap this up. I'll give you my thoughts on it and then we'll move on to another topic that I think we need to discuss.

MS. BERRY: What would be helpful for me -- and I don't want to bring the rest of the committee down because I know there are so many here who are scientists and physicians and already have this knowledge. But what I'm struggling with is I don't have a good sense as a layperson what is out there already that we know has practical implications for the practice of medicine and improving health and health outcomes, versus what's the big unknown. I realize the big unknown and the work yet to be done is a larger bucket than what we currently have.

But when we were talking about CMS, it occurred to me that perhaps some of the research that's already out there that's proven, the tests that are out there, a lot of that could have practical applications in perhaps disease management, demonstration projects that HHS is already undertaking, and in other real and currently existing programs.

One of the mandates I've always felt this committee has is how can we improve access to genetics, genetic testing and these services to improve health outcomes. So in the first bucket, that's where I would want to focus the attention, to actually work on that. What we were talking about this afternoon I get the sense is more what is the promise of the future, what research has yet to be done, and what is the private sector doing? What can the government do to facilitate additional work in this area? That's what I don't have my arms around.

I don't have a good enough sense of what exactly we're looking at, and the time frame. Are we talking five years, ten years? I realize it will be an ongoing thing. We'll never reach a point where we'll say we've done all we can do, we know everything. That will never happen. But what time line are we talking about before we get to real applications in the health care system?

DR. McCABE: Brad, and then Debra.

MR. MARGUS: I get to answer that question?

(Laughter.)

DR. McCABE: Debra, do you want to answer the question? Go ahead.

DR. LEONARD: I was at the CLIAC meeting recently and Muin Khoury was talking about what the CDC is doing, and they have a very interesting project where they are identifying the 50 highest-impact genes on health care, I mean on actual outcomes. So I think the CDC is beginning to address what are the high-impact areas. I don't think it's pharmacogenetics necessarily, or pharmacogenomics. But as far as genetics in general, the CDC is making an effort to do that, and maybe they could talk about that.

DR. McCABE: Tim, do you want to comment on that?

DR. BAKER: I think Muin offered earlier to come and address a lot of these issues that we're trying to assimilate, the population knowledge and the efforts to fit this into the evidence-based approaches that are important in guiding the kind of decisions you've been talking about here. But we are looking at the project you referred to and characterizing at least the top 50, and we're finding through learning about technology that it's just as cheap to do five of them as it is to do 50. So we're looking at how many gene variants have public health significance and what does that really mean.

But we'd be happy to come and address the committee and describe some of those projects in some detail, but we're trying to take the public health approach and say when does this mean something. To borrow a phrase from our friend Elliott, what do we know and what do we not yet know?

DR. McCABE: Brad?

MR. MARGUS: So Reed, one thing I wanted to clarify was on Hunt's idea on the CMS. It wasn't about maybe the CMS should -- some money should come out of the CMS' budget to do this. The whole point was that the CMS should have interest because it actually could reduce the amount of money that CMS spends. So the idea is if you had $100 million being reimbursed for a drug that only 80 percent of the people respond to, a very expensive drug, and you had a genetic test that could eliminate or reduce not all of them but a large number of the nonresponders, you'd pick up $20 million or $15 million right there. So if it costs a couple of million dollars to do this study, it's a no-brainer that you ought to do that study to find the markers that could cut your cost.

I would say that means it hasn't been done yet, Cindy, and we'd like to have it already done and saying there's an obstacle here, let's get that test out there right away. But at the same time, if the technology is getting to the point where you can do it, I think we can have a role to also say let's make sure that people are working on getting those answers so that they can be applied.

I think it would be great if the CMS -- I don't know if it's possible, if the CMS came back at another meeting and said here are the top -- I don't know if you can do this, but here are the top 50 drugs you reimburse for by the dollars each year that you reimburse, and of those, here are the response rates, and you look down that list and you see in many cases clinicians thought it's 90 percent or whatever, but in some cases it's only 50 percent. That's where pharmacogenomics could be applied.

Not only would we all be much more excited about it, but that would also give tremendous teeth to any recommendations we make about why pharmacogenetics needs to be pushed and why the FDA needs to work with you, and maybe even the NIH has to chip in too. But that would be a concrete thing, to see where there's really value in it.

DR. McCABE: That's a great lead-in to what I wanted to talk about next, and that is what I would like to do is ask for volunteers to join a task force, not a working group, not something that's going to take on a life of its own and last for the next year or so, but a task force to get together and try and identify and prioritize these issues and really identify among the issues what CDC is doing, what we're hearing that pharma is doing, what Debra mentioned about reimbursement, because it's all academic if we're not going to have any molecular genetic diagnostics labs because they've all had to shut their doors.

But of the topics that we've just talked about, coming up with prioritization and where this committee could really have an impact. So we'll be accepting volunteers, then, at the end of the session today. If anybody wants to volunteer publicly now, feel free. I certainly think that a few of the agencies have been involved in the discussions. I hope they will volunteer, like CDC, CMS, NIH. They have certainly been a big part of these discussions this afternoon.

DR. SULLIVAN: CMS volunteers.

DR. McCABE: But then the others I won't be so Draconian in naming names. But since Reed is always speaking up so much --

(Laughter.)

DR. TUCKSON: I volunteer.

(Laughter.)

DR. LEONARD: Could you clarify how this task force will do its work, as opposed to a work group?

DR. McCABE: First of all, I think of a task force as --

MR. MARGUS: False advertising.

(Laughter.)

DR. McCABE: I think of a task force as having a much shorter time horizon. We had work groups in the predecessor committee, and they seemed to go on and on. This is really to just help us organize and plan for our agenda for the future. So it's not coming up with a work product. It's just to really help us gather from all of you in a group that's smaller than this committee so it can really help to set our agenda. So that's what the purpose is, really to set the agenda.

The other area that I want to be sure that we cover because it also, when we were talking about it, had a lot of interest, and that has to do with the oversight of advertisement and promotion.

Debra?

DR. LEONARD: You posed the very first question, and we went off on the pharmacogenetics tack -- not tangent, but relative to the question you had asked. You said does this committee want to focus on oversight or is CLIA, FDA and FTC doing okay with oversight? I think this is a really crucial question to me. If it's not important, we can just take a yes/no vote and then be done with it.

DR. McCABE: No, that's fine. But I do want to get to the DTC stuff also. I don't want that to be left on the shelf this afternoon.

So do you wish to weigh in on that question? You clearly have an opinion.

DR. LEONARD: I say this committee doesn't have to focus on oversight. But I think that CLIA, FDA and FTC -- I mean, CLIA at least, and FDA are regulating what they're regulating. I find that the fringe is the problem, and I don't know that we need more oversight of what's being done

because I think it's being done well for those that are following CLIA and being CLIA-certified laboratories for the most part. So that's just my opinion.

DR. McCABE: Well, I think that I probably shared my bias in a Freudian way, probably by skipping over the oversight issue, having seen the predecessor committee get really bogged down in that, seeing that CLIA and the FDA are moving forward. And also I shared my bias at our last meeting that I think labeling is an important part of education, and I see it also from the presentations that labeling is getting a lot of attention as well. So I agree with you. I think that in terms of those processes, they're moving forward. I agree with you also that the problem, as always, is the negatives, those who aren't CLIA-approved, those who are not a part of the process and how does one include them.

DR. LEONARD: Right. I just wanted a definitive statement from the group.

DR. McCABE: Hunt?

DR. WILLARD: I would support your definitive statement, with one exception. I think before we leave it, this committee could provide a service to the Secretary and to those agencies by coming up with a crisp statement of to what extent -- and I've alluded to this several times today -- to what extent genetic and genomic testing is different and therefore deserves special attention from them, as opposed to just do your job. What aspects of it are the same as everything else they're doing, and which aspects really deserve to be flagged?

I think we're the group that can do that, because otherwise every single agency is examining that question from the ground up. We could advise the Secretary on that point, where it deserves special treatment and where it absolutely doesn't deserve special treatment.

DR. McCABE: Debra?

DR. LEONARD: And if you look, for example, at CF screening as an example, the issues that have been raised with CF screening since it's been implemented have been in the post-analytical phase. I don't think there's anything that CLIA is going to do to regulate a laboratory that's going to improve that post-analytical phase of interpreting the result properly to the patient. So that gets us to the topic, one of the prime topics that we had targeted and that we'll be discussing tomorrow, which is education and how you educate physicians to communicate results properly.

Laboratories know an awful lot about that, and so they can help physicians, but physicians sometimes don't ask and sometimes that information isn't communicated. Even when it is, then on the next generation communication to the patient it's not communicated properly because the person in the middle, the physician, the other health care provider, doesn't understand really what the laboratory is telling them.

DR. McCABE: Steve, do you want to comment? Because one of the messages I got from the presentations was that your focus is on high-risk tests, not so much on genetic tests, except to the degree that they're high risk.

DR. GUTMAN: Yes. The internal discussion that was sparked by SACGT was one which stepped back and thought that while there are clearly unique features about genetic testing -- many genetic tests you might order only once, and many non-genetic tests you might order endlessly. But it was our general notion that the issue of ASRs and/or the issue of home brews was one which was better approached either generically or device by device on the basis of risk

per se, not its specialness as a genetic test. So at least the deliberations that are going on now, long as they may be and as big a struggle as they may be, are trying to focus on the general principles of risk that the entire device program is based on.

DR. McCABE: Reed?

DR. TUCKSON: Yes, I would agree with you, Mr. Chairman. I think that we don't want to get overwhelmingly bogged down in revisiting all that work on the oversight of CLIA and so forth. I was particularly heartened to hear how much the predecessor committee to this one, their recommendations are alive and are part of the fabric of what's going forward. So I think that's terrific.

If I understand Hunt's point, which I think I like, I'm not sure whether you were saying we should do it or ask the Secretary to do it and report back to us, but at some level defining, then, based on all that we now know, what are the special areas of concern which merit attention, and then to be able to determine from the agencies how well are we doing now in being able to attend to assuring the public that those concerns are, in fact, being well addressed.

I think that's very specific. I think it doesn't put us into an awful lot of complexity. It's just saying where are the danger zones here based on where we are today in genetic testing, and then based on what we know, with all the oversight that is going on, what are the danger zones, and what do you consider to be -- do you know if you're in danger? I mean, what are the data points that you're looking at? I mean, that's the question that we didn't get answered this morning.

What are the data points that FDA, CDC, and somebody --

PARTICIPANT: CMS.

DR. TUCKSON: CMS. Thank you. What are the data points that those three organizations -- and by the way, again, what I keep getting nervous about, even though at some level we know it's not true, but CMS has their issues, FDA has their issues. At some point, what is the Secretary's office, whoever is like the superstar monitoring all this, what does that person who has a little checklist saying we are going to be in deep doo-doo if the following things are happening, what does that list look like? I just want to know what that list is, and then find out how we're doing. That's all I think Hunt is ultimately saying. If that is what he's saying, then I think that's all we want to do is get that report.

DR. McCABE: Emily?

DR. WINN-DEEN: So I guess my reason for getting into public policy and out of just the lab is that I think we need to think about how to take the promise of the Human Genome Project and make that promise a reality. We have to affect the health of our society. We didn't do that just -- it's cool that we've got the sequence, but if we don't do something with that, then we've really spent a lot of money, our NIH money, on something that isn't benefitting society.

So what I would like to see us do is really to look carefully at what is the current landscape, and I think that the reports that we had last session and this session have gone a good deal into telling us where are we today, and then I think this committee could really help the Secretary by saying where do we want to be, where is the promise, and what are the gaps, what are the barriers. Is it that we need better reimbursement? Is it that we need more translational research? Is it that we need better, friendlier guidance from FDA? Which are all things that we've talked about. There

may be some other things.

Then we can make specific recommendations about what the Secretary could do to move us from where we are today to where we want to be in the future. I think if this committee could get focused on -- I mean, first we have to have the information to assess where we are. I think we need some external experts to help us describe where we would like to be, and we can set a time horizon on that, five years from now, ten years from now. And then let's identify some very specific steps that could be taken with the right federal support.

The Genetic Non-Discrimination Act is one thing. Physician education. I mean, we have to prepare every aspect. We can't have the consumer being afraid of the testing, we can't have them being misinformed, we have to have educated health care providers who know how to do it, we have to have good validated tests, we have to have qualified laboratories to perform them. There are many, many things that all have to be in place to make this a reality, and I think it's up to this committee to try and identify what is that vision that we're striving for, and what are the steps we need to take to get there.

DR. McCABE: Hunt, you started this off.

DR. WINN-DEEN: Sorry, Hunt.

DR. WILLARD: Well, my fear in responding to Reed is that maybe there is no one in the Secretary's office who has that deep doo-doo list that you want to get your hands on, and in part we're the group who is going to both say someone needs that list and here's our best thinking on the items that ought to be on that list or should not be on that list. My fear is if we simply say oversight is being taken care of and move on, that we will have missed what I view as an obligation to try to clarify those issues and really define which things you shouldn't be afraid of, because genetic testing isn't uncovering any -- you know, this is the brave new world -- and where might it be the brave new world and the public's ill ease is perhaps well-founded and it requires more study.

DR. McCABE: Well, that's a nice segue to think about another thing that we raised at the very beginning today, and that was about taking the minutes from the first meeting and whether we turn that into a report. If we say we'll wait until we get the minutes of this meeting, I'm afraid that will delay it, because we'll wait until the next meeting to approve the minutes for this meeting.

But what are people's thoughts about turning at least the minutes of the first meeting into a report to the Secretary? Because we began to lay out some of the issues and certainly said we needed to hear about the oversight and the progress in oversight at this meeting. Any thoughts on this?

Debra?

DR. LEONARD: I think a report would be very useful to the Secretary as long as it was no longer than two pages. You've got a tone in there -- he's never going to read something like that, I don't think. I don't know him personally. So I would think that whatever report is generated, it has to be very brief and targeted.

DR. McCABE: There will be a one-page maximum executive summary.

So do I hear any objections to turning those minutes into a report that we could bring back to the next meeting, discuss at that meeting, and then take any suggestions from the next meeting and

incorporate those but move them forward? So there would be some documentation and work product, and there will be additional prioritization that will come from the task force. But at least it will begin to have us thinking about priorities.

DR. LEONARD: I think that the executive summary is also over time. I mean, this committee is going to have a life. It's useful to be able to look back at what we've discussed and refresh and see what we've missed when we're moving ahead.

DR. McCABE: And also it's good to see the cycle, as Elliott Hillback pointed out from this morning's conversation. He's been talking about these issues since 1991 was it, Elliott? And they're continuing to be the same. So it's important for us to document so that we see the same topics coming up, and that helps us know where to focus as well.

So we will also take that as guidance from the committee, and Sarah and her staff will work on putting those minutes in the form of a report that we will bring back to the committee at the next meeting.

Hunt, did you get satisfaction on -- okay.

Now I do want to talk a little bit about advertising and promotion of genetic testing, because that was an area that people seemed quite interested in at the time we were discussing it. So where should we go from there?

Oh, by the way, we won't drop the oversight issue. We will continue to monitor it. We enjoy seeing Steve at these meetings, so we wouldn't want him to disappear and not come back to brief us. So we will continue to be updated on oversight, but I think it's my sense of the committee that that doesn't need to be a highest priority issue, that it will be more a monitoring task on our part at this point. Should we feel that it's gone astray, we will certainly discuss that, but I think quite the opposite from my view. I feel that I'm really pleased with how it's moving forward.

Hunt?

DR. WILLARD: My concern is that if we simply monitor it, we won't do what I tried to articulate, which is to actually as an action item come up with a statement of where is genetic and genomic testing different and where is it not in terms of an actual report or action item of this committee to allow the Secretary and all the various alphabet soups of agencies, to help focus our attention given our best recommendations.

DR. McCABE: Sarah was commenting what I was also thinking, and that is I think that's important to have in this first report. I'm not sure we'll come up with full agreement. We never came up with agreement on the SACGT. The discussion was some of the things that people thought were the same other people thought were different. But we can certainly come up and frame the issues and at least where we agree and where we are willing to disagree on these issues. That may be important as well.

So I think probably from the discussions that we had with SACGT, as well as we review the transcript from this meeting and your comments and the comments of others, Hunt, that we can begin to frame those issues, and then we can make that a point -- I'm sure that will be a point of discussion at the next meeting, to firm those up. Is that okay?

Back to the advertisement and promotion.

Yes, Chris?

DR. HOOK: This is an area that I have a lot of personal concern about, but as Brad very eloquently pointed out, direct-to-consumer marketing isn't necessarily a bad thing. It all depends upon how it's done and the nature of the test and so on. But that involves a number of complex requirements, such as informed consent, can informed consent be done simply by checking a box on a computer screen when all of us know, who have to obtain informed consent, it usually requires much more open-ended questions to ensure that the patient or the prospective individual truly understands what they've put their name on, and ensuring that the counseling mechanisms with the results are available and how can that be ensured.

I'm not sure that that's something that this committee can articulate, but I think that the industry would have a significant interest in making sure that there were mechanisms in place, and it might be -- I don't know if I'm imposing too much on Elliott or others from BIO to perhaps give us a model to shoot for of what would be doable and achievable by those who would want to market things directly and how they would be able to ensure that the concerns, the basic concerns are met.

DR. McCABE: I'm past president of the American College of Medical Genetics, and I know from our board meeting that the College is working on a statement. It should be published early next year, I'm not sure how early in 2004. But it might be one of the things we might do is to invite the American College of Medical Genetics to at least discuss, if they haven't published their statement yet, at least where they are and some of the background to that.

Yes, Reed?

DR. TUCKSON: Two things that I think we heard today -- and again, I just really think that the presentation of the FTC was just terrific, and I think his openness was commendable. I think what he's basically saying is send me, send our agency some areas of concern and prioritize those a bit. Send us some of the things that we as a committee and/or professional experts like the American College and others, that you feel represent important things, potential egregious sins that ought to be looked at. I think he's sort of asking for that. I'm overstating, of course. As a government agent, he's not allowed to come and ask us that, but whatever.

Anyway, I think he's really interested in this issue, and I think we ought to send him something. I think we ought to say, whether it's Francis' example on the nutriceuticals, maybe what we need is a couple of people again just in a little small group to determine what the priorities are. Should it be one that's based on nutriceuticals or one on face cream? I mean, clearly we had that good discussion, so maybe there ought to be some categorization of what makes it more important than others.

But they want to get started looking at this, and I think we ought to at least start them on that, and I think we also ought to solicit from the American College and from responsible manufacturers who have seen corporate competitors do scurrilous stuff that makes the good guys look bad. Maybe they can give us some examples.

The second thing I thought he was particularly good about is the potential of at least exploring as one of our future goals some kind of education of the public, which could be part of some of our other public education themes which we'll discuss in the coming days, something that sort of says how do you as a mature and responsible consumer wade through some of these advertisements in

this area, and just give them some keys and tools and tips that would help them do a better job of using their native intelligence.

DR. McCABE: Yes, Barbara?

MS. HARRISON: I was sitting here and came across the article in Genetics and Medicine about direct-to-consumer marketing, and it kind of seems there are two different issues. One is what Dr. Tuckson was talking about as far as junk DNA, false DNA type of testing. But the other is legitimate testing that's done that's offered to consumers over the Internet without having to have a physician or a genetic counselor involved, and they describe in here a test that's done for $165 for hemochromatosis testing with no need to go through a physician or any other kind of health professional.

I don't know under whose purview that would be, and I don't know if we can put a recommendation toward that.

DR. McCABE: The issue about whether or not direct ordering of tests, which is really different than direct-to-consumer marketing, though I would argue that if you don't know that you can order a test directly yourself, then you're probably not going to do it. So if you're going to have a business plan, you have to have some direct-to-consumer marketing as part of that. In point of fact, I think the College statement focuses more on direct access without a health professional being involved.

It turns out that's a states issue. It's not a federal issue. But that has to do with state rules about how medicine is practiced in their state, and different states have different rules about that. So that gets to be a little bit difficult for us who are advising the U.S. Secretary of Health and Human Services. But I think we could discuss that and have the College bring that and really focus on that.

Emily?

DR. WINN-DEEN: I guess what I'd like to see, and maybe this is in the ACMG statement, is some kind of guidance on -- there may be some things that actually a consumer could read about on the web, click a box, consent to, get their results, and there would really be no harm. I'm not sure what those are, but let's hypothesize that there is something. What we could do maybe is start to create a list of things that would never be on that list, things that aren't on that list today but might move there in the future, and things that might be okay to be there, in much the same way that we consider through FDA right now what things are allowed to be marketed over the counter to individuals for home testing.

You're allowed to home test for pregnancy. You're allowed to home test for glucose. You need a doctor's prescription to get the meter, but you can then do it yourself. You're allowed to home test for coagulation, again with a doctor's prescription. So how do we create some guidance document about what criteria would be used to put things in those different bins? It may be very similar to the criteria that we outlined in the low-risk, medium-risk and high-risk genetic testing, that there certainly are things that never, ever should be done without counseling involved, but we're going to face this issue in not just direct-to-consumer testing but in how much time and energy the limited number of genetic counselors can put into things as we get more and more things rolling out that are genetic-based tests and how to put our scarce resources on the right things and roll informed consent and education about testing out to a wider variety of health care providers.

So I think at some point we're going to have to start putting this list together. I'm not sure, maybe this isn't the right group to put the list together and maybe we should defer to ACMG, but I personally think we're going to have to do that.

DR. McCABE: I only mentioned ACMG because I have insight and knowledge from being at the board meeting. My guess is that it's not the only group that has discussed this. If there are other groups that have discussed this, I would ask them to notify us and we can include them as well.

DR. WINN-DEEN: But the other direct-to-consumer thing that I'll just bring up is so what if you don't market the test directly but in the drug store is available a buckle swab sample collection kit that you rub your cheek, you send it in? I mean, you could envision that some of these things could be done by a very reputable lab, not a home test for genetics, not a home CF test, but you could get the information and it could be done by accredited lab professionals, and what comes back to the consumer could be a report with a very nice explanation of what the results mean to you and how you should use that in your future health.

I think we need to explore whether that's going to be needed as part of making access available to a wider variety of people.

DR. McCABE: So one of the things we might do is try and identify groups who have been thinking about this and may have begun to consider these kinds of lists to present, and I saw some body language indicating from the audience that other groups are working on this as well. So please let us know if you're working with a group, whether it be a consumer group, a commercial group, whatever, so that we can include you in the next meeting.

Brad?

MR. MARGUS: Back in 2000 during the genomics bubble, I personally was shown at least 50 different business plans for businesses that would be typically web-based, because that was the rage, and genomics, which was the rage, and there was venture capital up the wazoo for those opportunities. They included everything from you go into a store and get a little test kit, anonymously put your cheek swab in, send it in, and it has a password. Three days later you get online and you can log in anonymously and see what the results are to whatever it is they're going to promise you, and then over the future more tests will be available as long as you have a credit card, and you don't have to take a sample again because (inaudible).

There were kiosks in malls that we would have where they'd take your sample and three days later you'll get your stuff. Sometimes, when we thought pre- and post-test counseling was important, you needed at least someone in a white coat, so it was under the Lenscrafter model in the mall, where you'd go in and there'd be a booth where you could privately talk to your counselor before and after.

Some of those were probably legit, and the idea was that the sequence of the genome was almost done and there was going to be such a landslide and waterfall of genetic information that the current infrastructure of physicians and counselors could never handle it, and it's all converging and you should take advantage of it. Maybe fortunately, the capital for all those ideas ran out, and so nothing has happened. The only thing that has happened is the content, the things you would test for that you could tell people anything useful or actionable hasn't come along as fast as people had hoped.

But I assure you, there were lots of innocuous, entertaining, good science genetic ideas that were out there. One was we can test you and your three siblings and tell you which sibling you're more like, things like that. Have you seen the market data? All you need is one-tenth of 1 percent of people to want to pay for that thing, and if you extrapolate over the U.S. population, at Christmas time it's a great gift for marketers to have in the catalog.

So the opportunities are out there, and I'm just hoping that some real content comes along so that the junk science isn't sold or given a bad name.

The one thing I wanted to say is if you do have this question, in the future there is going to be genetics delivered directly as well as through the traditional channels, so how can you insure some standards? Well, I imagine there must be a lot of models out there. So those of you who know that I have a strange background know that I used to be in the seafood business. I'm like Forrest Gump in shrimp.

But in that industry -- and unfortunately I think the USTC guy is gone. But in that industry it's a particularly slimy industry in more ways than one and people cheat a lot, and there's a lot of bad stuff out there. And yet the fine restaurants want to know where to buy good things from, and there are standards.

The USTC has Grade A, right? In other industries you have Good Housekeeping. So you could imagine, I think, the day coming where some agency or someone promotes a particular label like that, or a Seal of Approval, and if you're a website with a legitimate thing -- and who knows, maybe even Roche will have a website someday selling good stuff. But if you have a legitimate test with really good science behind it, you can get that Seal of Approval, and it's been advertised enough so that consumers trust it.

The big problem then comes with two things. One is the responsibility. What we heard today is there's kind of a gap that doesn't have to do with people being really, really sick, or if it doesn't have to do with a test that you sell or the reagents you sell, then nobody seems to be responsible for those things, so that's a big problem I have. The other problem is, of course, this thing about "good science." I can only imagine us putting 50 scientists in a room to decide whether a particular thing is good science or not. That's going to be a big challenge.

But I think if you can reach some standards on that thing, there are ways to convey to consumers what's real and what's bogus without actually killing the idea.

DR. McCABE: Other comments? I think we've gotten some guidance for the next meeting.

Debra?

DR. LEONARD: Just two points. One is I was just at a meeting called Lab Institute. It's by G2 Washington Reports, and there was a whole section on direct access testing and exactly what you're saying. In Seattle there's a company that goes around and collects your specimen and in three days you get your results and you can pick them up. In Nebraska there's direct access testing in a mall with the white coats. Actually, they make it more like a living room setting so the people are more comfortable walking in. In New York City they have one.

So these are people who are actually doing direct-to-consumer marketing of tests, but I didn't hear any genetic tests on there. But they were regulated by state regulations, like Ed was saying. So

this is coming, and I don't know what's happened to all the genetic ones, but it's being done for other kinds of testing, and we may be able to learn what they're doing. I could get Sarah the names of people.

The other thing everybody keeps talking about, informed consent, if you're doing direct-to-consumer marketing of genetic tests, informed consent is something that we say is needed for genetic tests, but my question is will informed consent become less important with the genetic non-discrimination laws if those are passed, since a large part of genetic counseling is describing the risks and benefits, and the risks as well as the interpretation of the test? I think interpretations of tests could be provided. I mean, we do this with CF screening. It's a little piece of paper with ten lines on it that ACOG created that describes what you're doing when you're getting CF screening, and many tests could be done in that same way.

One of the things we need to think about is how important will informed consent be when every test you do in medical practice is a genetic test because genetics is part of everything medical, and can we continue to require informed consent for genetic testing, which gets to what Hunt keeps pounding on, is genetic testing really different than other kinds of medical testing? Informed consent is one of the things that sets it apart, but that's historical because genetic tests were relatively rare. Single-gene diseases are still.

So I think we need to think about informed consent, as to whether that's something that we'll continue to need in the future or can realistically do in the future.

DR. McCABE: I think, again, I would refer you back to Fred Ledley's commentary that was in Nature Biotechnology, which is in your packet. I don't know if it's age or what, but the concern about direct access, there will be direct access. The movement of autonomy, the movement away from a health professional controlling our access to medicine, that's well on its way, and this is really one of the things that Fred talks about in here is direct access to testing, personal control, generate data to guide consumer choice. It's the natural course of things.

So I think it's really important that we chart that course and that we recognize where the Class 4 rapids are in that course, because it's going to happen. It's part of the whole -- it started with the printing press, and now with the Internet, and people want more control and have more access to information. So we need to recognize that, but then also identify where the problems are there. So I think it's a good idea if you can get Sarah some of the names so that we can learn from other areas that will be very important.

Other comments? Are there other areas that I may not have picked up on that people feel are critical that we take up within the next meeting? Or we may have given Sarah enough for the next two meetings here. But I know one had to do with the breadth of genetics, how broad is our charter. Debra has just said that everything is genetic, and many of us feel that there's certainly something to that.

DR. LEONARD: Will be.

DR. McCABE: Will be. Well, some of us think it already is, we just don't realize it yet. But I think the charter was pretty broad. I see the discussion which really has to do with the limits or even existence of genetic exceptionalism being discussed next time, taking that up. Even though our charter is broad, what do we choose to focus on within that charter? So I think we will discuss that at the next meeting.

Our 5:00 guest has arrived, but are there any other issues that people wish to make sure that Sarah highlights from today's discussion? We'll have more tomorrow.

(No response.)

DR. McCABE: I think the education, workforce, some of these issues were coming up, and they will be informed by tomorrow's discussion as well.

Okay. Let's move on, then, and I think we have had a very profitable day today and have learned a lot and are beginning to help focus the committee.