Q&A and Discussion of Ethical, Legal, and Social Implications of Pharmacogenomics

DR. WINN-DEEN: I'd like to move right to Q&A because we're really running short on time here. So are there any pressing questions for any of the folks on the panel?

Julio?

DR. LICINIO: I had one question. It was a very interesting presentation. This panel has a long history of our discussing issues related to genetic testing but which are not unique to this panel. There is a whole literature and line of thinking around that which has a lot to do with privacy and right to know and all of that. So let's say in a consent document, unless it's very clearly specified that the person wants to be contacted in the future, you don't contact. When in doubt, you don't over-expose the person to the information, because you're talking about genetic susceptibility, which may or may not happen, to a disease that they may or may not have, and some people don't want to know. For most diseases in this case, there is no cure, and I think they would (inaudible).

In the case of pharmacogenetics, I see this very differently because you're talking about the drugs that the person may be exposed to. So let's say in terms of the ethics of the testing, if you do it for research purposes, that person was not considered in the consent, should be recontacted, and you know for a fact that a person has a variant of a gene that can cause adverse reactions to a drug or can result in no effect to treatment that could be for cancer, for example, where if they don't respond they can die, or they should have chosen another treatment, is it ethical not to give the person the information when there is no clarity about that, or even when the person says "I don't want to know about my genes in general," but if you know something that another person is going to contract, you know that they have a mutation that something bad is going to happen, how ethical or unethical is it?

In other words, do you use the same standard of ethics as for genetic testing, or should the standards here be different?

DR. DEVERKA: I think it's important to always allow folks the option not to be recontacted, and I know that's common practice with some genetic testing for disease susceptibility. I think you're right, that pharmacogenetics is different. I'm trying to imagine a scenario. I guess it would be that you would have information that would affect their outcome where there would be no other treatment, for example, for a serious condition like cancer. I think that you have to respect their decision.

In fact, in most cases people don't even really have a means of recontacting folks. Either the samples are permanently anonymized and there's not a mechanism to do that -- so I think from an ethical standpoint, I would say that I would follow their wishes in the informed consent.

DR. WINN-DEEN: Tim?

MR. LESHAN: Thank you for your presentation. I thought it was very good. I just had a point of clarification, and one point I didn't say earlier is that Rochelle couldn't cover everything, but we are doing some ELSI research at the Genome Institute to look at some of these issues as well.

But you talked about the higher cost of implementing some of the privacy standards, and I'm not aware of any data that shows that. I wonder if you could talk about that a little bit more.

DR. DEVERKA: Well, folks have certainly talked about the cost of implementing HIPAA, right? I mean, people have complained about that a lot. That graphic that I gave was really just sort of a hypothetical, what are all the potential sources of increased cost, as well as what are all the cost offsets that would decrease overall health care costs. So I'm not aware of any specific studies that talk about the cost of protecting genetic information. It's just sort of logical to me to think that if we're somehow treating that information differently, that it will have a cost associated with it.

DR. WINN-DEEN: Kevin?

DR. FITZGERALD: I know you were trying to go back and forth and balance yourself here between is it a paradigmatic shift, isn't it, what's the impact going to be or not. So how do you see the way forward for a development of this technology and an emphasis on the importance of this technology while at the same time avoiding the genetic reductionism, essentialism, determinism and all those other things that cash out from this sort of naturally in people's minds when they hear about all the power of this technology?

DR. DEVERKA: Well, in addition to what I already said, we have sort of a framework already for evaluating new technologies. It's got a lot of deficiencies, but I don't think we're well served by putting this in a special, separate bucket.

I just lost my train of thought. Sorry. Can you say your question again? About how we're going to advance it when people think it's --

DR. FITZGERALD: Right. It seems to be, and not just from empirical evidence but also when one looks at its various frameworks, if you push this and hype this or just even talk about the potential for this, that it's going to be interpreted, absorbed or seen by many people as furthering a genetic essentialism, reductionism, determinism sort of thing.

DR. DEVERKA: Well, I think one major step is the vocabulary. I think that people have talked about not using the word "genetics" when we talk about these medicine response profiles. I think if we said to a patient I would like to do a test that would help me guide what drug is best for you, I think that that has a completely different connotation than we want to do a test to see if you're at risk for getting a really bad disease in the future, and I think people understand that difference.

So I think one big thing that we could do is pay attention to the vocabulary, and that's sort of my remarks in the clinical setting. I think in the research setting, our ethical obligations are to disclose all of the potential risks, which unfortunately, I think in today's environment, do contain some of the potential risks for discrimination or stigmatization, and that we need to disclose that and allow them to make an informed decision about that.

DR. WINN-DEEN: I had a couple of FDA-oriented questions. So I'll splat them out here on the floor and let whichever of you guys from FDA wants to respond.

I think we heard a comment this morning from the folks that are involved in developing laboratory-developed tests that they would like to see some recognition from FDA that those tests have some status in terms of if the biomarker is validated, that a test developed in a home-brew kind of situation could still be used in pharmacogenetics, why or why not. Currently it seems, from the comments that we heard this morning on TPMT and in the white paper on companion diagnostics, that there's really no formal recognition or utilization of that mechanism by FDA as a way to provide pharmacogenetic services.

DR. HACKETT: If you're talking about the biomarker as described in the guidance document, and you're talking analytical only, and there's no clinical validation, so you get an answer but that won't tell you what the possibility is of being responsive to the drug or developing a toxic reaction, that's a problem there. If you go ahead and develop the test, then you can go ahead and probably get it marketed. That's the simple answer.

DR. WINN-DEEN: Okay. So let's take TPMT as an example, where we have, I think, clear evidence that there is something there, but FDA did fall short. While they said tests are available, they didn't really acknowledge that the only way those tests are available today is through laboratory-developed tests. Is there a requirement that we move to an IVD assay before we can have something that's formally recognized in FDA labeling as a pharmacogenetic test?

DR. HACKETT: Other than a biomarker, yes. If you want something beyond that, then you have to go through the regular approval process.

DR. WINN-DEEN: Are you talking about the ability to make a clinical utility claim?

DR. HACKETT: It's still like a research product. It's not an FDA-approved product.

DR. WINN-DEEN: You're saying that a test result produced by a CLIA-certified laboratory is a research product?

DR. HACKETT: No, the test itself is research. It's not an FDA-approved test. CLIA, again, is also only analytical result. It's not clinical validity. Does that help?

DR. WINN-DEEN: it raises concerns.

DR. HACKETT: The test is not FDA approved, and the only way you can get that approval is to go through the process.

DR. WINN-DEEN: No, that I clearly understand. But I'm talking about in the practice of medicine, does that mean that we can't recommend that in a practice guideline or in a drug label, a test for this entity be performed? I mean, it seems like for gleevac, we recommend BCR analysis be performed, and to my knowledge there's no IVD BCR assay out there.

DR. HACKETT: Do you want to try that one for labeling?

DR. FRUEH: I think there are two separate issues here. One is a combination product or a co-developed product where a test is required in order for the drug to be used. Those tests need to be FDA approved. Beyond that, in many, many drug labels, probably 100 or more, we point to pharmacogenomic information, and that's particularly in the area of short metabolism. I think TPMT, irinotecan, are two extreme examples where we actually went and we visited the label because of the toxicities that are associated with it.

If you're looking at 2D6 polymorphisms, for example, in drugs for depression and so forth, where it's well known that the drug is heavily influenced but it's not toxicity that is immediate, the recommendation is just not there yet. This has also been addressed earlier. A lot of this information has come forward over the past few years and the drug actually is a lot older. So we don't yet see it in the label. But the development in recommending that the test is being done is definitely going to be part of the label, and there is no problem in putting that in the label, even in the absence of an FDA-approved test.

DR. WINN-DEEN: Other questions for this group of speakers?

(No response.)

DR. WINN-DEEN: Thank you very much for your presentations.

We're going to take a 15-minute break -- sorry, 10 minutes -- and resume promptly at 3:15.

(Recess.)