Pharmacogenomics
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With that background, let's turn to the pharmacogenomics, and then we will assess how we will deal with that and/or the population studies one.

Emily?

DR. WINN-DEEN: Well, our task force did meet. I assume that is because we had a staff person who is a great organizer and made sure that we actually had a conference call.

But in the process, we went through a discussion of sort of the first draft of potential things and came up with what you have in your table folders today about potential areas to discuss.

I'm not going to go through them all one by one. I guess in summary what I'd like to say is it seems like there is a lot of meat here, and it is also an area where there is a lot going on that we may either want to just continue to be informed of, or at some point, take some more affirmative action to either support things specifically, or provide some feedback to some of the programs.

What we tried to do in terms of setting out potential topics was to group them into four areas. Setting the stage was basically designed to get everybody on the committee up to sort of the same level of basic understanding.

Translational efforts was basically, again, sort of state of the art. Where are we? What are the issues that we're facing? The ELSI issues again, you know, are there specific ELSI issues that are unique for pharmacogenomics? What might those be?

And then finally when we started listing all the government agencies that we thought HHS had purview over and were involved in this, the list started to get pretty long. We felt from the point of view of the task force at least, that there definitely was some meat here, which because of the involvement of so many HHS agencies, might make this a good area for our committee to spend some time on, and try at least to assure that there is coordination of effort and knowledge of what is going on in the different arenas.

So with that introduction, I'm happy to take any comments and questions. I put Dr. Gutman on notice that we might ask him about some of what is going on at the FDA level, because there are some guidance documents under development and under comment.

I know that there are things going on within NIH. I'm not sure if they are specifically at NHGRI as much as in the Institute of Medicine, or NAS.

DR. GUTTMACHER: The Institute of General Medical Sciences.

DR. WINN-DEEN: General Medicine. But there are definitely things going on within the agencies that I think would be of interest to this committee. The question is just should we let those sort of trickle along or do we want to take some proactive stance on that?

Comments? Ed?

DR. McCABE: Yes. I think there is one topic, and maybe it is buried in some of these others.

But as a department chair who was threatened with a pharmacogenomics legal suit a couple of years ago because of a child who had a hearing problem and had received an aminoglycoside antibiotic, I think there is also a medicolegal issue related to these drugs.

When I speak about this, I really argue that the lawyers are going to push this probably more quickly than the clinical side of things.

I don't know if that is something, maybe we don't want to bring that up. But I would think that we have to look at what the medicolegal implications are of ignoring this area.

DR. WINN-DEEN: Right. So that seems to me that that fits under the ELSI issues. But maybe what we didn't cull out was specific, you know, physician or drug company liability if a test was known, available, and not used, and then there was an ADR, what is going on in that front which I think maybe the guys from Pfizer might have something to talk about.

There has certainly been a lot of press recently on several drugs where there may be some genetic component that predisposes people to bad reactions.

Agnes?

MS. MASNY: I think also to dovetail with our discussion this morning about the coverage in reimbursement where we were looking at sort of the overriding principles that might help look at specific genetic tests, and I think the area of pharmacogenomics will probably be the area that is going to advance most rapidly.

So that I think it would be helpful to have some feedback to the committee regarding that, because I think this will be the area where we could then help move the topics of coverage and reimbursement along specifically with the issues of looking at what do we need then to have in place for the government agencies for private insurers to even know when a pharmacogenomic test will be ready to be used.

DR. WINN-DEEN: Steve, could you comment just for scheduling purposes on when some of this sort of guidance revisions are coming along, and when would be appropriate to maybe hear about those?

DR. GUTMAN: Sure, sure. There actually is a fair amount of activity, both in the Diagnostic Center and in the Drug Center at the FDA. We have published a document on general diagnostic uses related, actually not specific to pharmacogenomics or pharmacogenetics, but to the platforms that support testing in this arena, which would be multiplex products.

We published that about 18 months ago. We have gotten some useful comments, including the thought that a single document is trying to do too much, and that the issues were ? - and we appreciate it. As a result, we are moving forward with a more narrow genetics-oriented document from pharmacogenetics, which we are hoping to publish by the end of the year. Although I hesitate to be certain we'll meet that timeline.

We have within our office a working group. Joe Hackett continues to take the lead. That is very aggressively interacting particularly with industry, but with other academic and government groups to try and educate our core review staff so that we'll be prepared for the diagnostic nuances of this new technology.

In the Center for Drugs, Dr. Lesko is taking the lead. They have published a document encouraging the submission of voluntary data sets. I actually am just absolutely flabbergasted, because I didn't think anybody would submit voluntary data sets. But in fact, that program does appear at least to be generating some light as well as heat.

There are companies that are willing to come forward and share information. There is a working group that is being established to deal with the companies that are brave enough to do that, and to create the appropriate firewalls and controls so that the companies won't be harmed. There are efforts to create an interdisciplinary working group and to create SOPs.

That guidance document establishing the core of that program is also being revised with a target time of being the end of the year. Again, I don't promise it will actually make that deadline, but I expect both will be early next year.

We have recently initiated an effort which is not centrally focused on pharmacogenomics or genetics, although certainly it plays heavily off of them, which is the issue you raised before about theranostics. There has been a long effort between Drugs, Diagnostics, Biologics, and Devices to better coordinate diagnostic and therapeutic products when linked.

It has been a colorful, problematic, and imperfect past on which to build with some interesting successes, and also some interesting failures. There was a workshop actually that was held earlier this year over the summer with PhRMA, with CDER, and with CDRH, Devices and Drugs, all collaboratively involved. There may be many people in the room who were actually present at that meeting.

There was general discussion about the science that underpins how to connect a new diagnostic, or for that matter, an old diagnostic with a new drug or an old drug. And based on a very rich and interesting discussion, there is a joint working group that involves all three human product centers, Biologics, Drugs, and Devices.

For us, it is an aggressive guidance document timeline. It is hoped that we will complete the internal draft of the document by the end of this year, and have it vetted in time for the third pharmacogenomics workshop, which Drugs will be sponsoring in April of next year.

Although I suspect that workshop will have a wide variety of topics on its agenda, certainly front and center, and from my perspective, the most important, will be vetting of the joint diagnostic therapeutic guidance document.

And then most recently, the Agency has promoted as part of its perhaps in the wake of Dr. McClellan's influence, its interest in making sure that it is a partner rather than an impediment in translational research. They have introduced a program called the Critical Path Program which is to actually in a more proactive way seek out ways to bring products to market more quickly, and pharmacogenomics has been targeted as a pilot, or as an opportunity within the product lines that we regulate to be exploited in a positive manner.

DR. WINN-DEEN: Ed?

DR. McCABE: Yes, I think about this. There is some overlap between the two topics we're discussing, large population studies and pharmacogenomics. Because to get at the genetic basis for rare side effects will take large populations.

I don't know, it sounds like these are somewhat competing, and I don't know if there is a staging. I don't have an answer to this. But perhaps there could be some discussion of staging if it is better for one to go before the other.

DR. WINN-DEEN: Well, it certainly sounds like there is a lot of things going on actively that might be ready to make some report on at the whatever it is, end of February or early March meeting. At least from the regulatory side of things.

Alan, do you know in your large population studies, was there a pharmaceutical component to that? Or was it more trying to understand the genetic components of common complex disease?

DR. GUTTMACHER: Well, the folks are clearly understanding genetic and environmental factors and common disorders. Very much the thought is if one is going to do a large study, it would be foolish not to take advantage of that in this day and age, to look at pharmacogenomics issues as well. Absolutely.

DR. WINN-DEEN: Steve, I don't know, you're probably not the right FDA person to ask this, but I'll ask you anyway. Do you know for the two big drugs that have been taken off the market recently, if there is any feeling that they have some possibility for rescue based on any kind of test segmentation?

DR. GUTMAN: Yes, I actually don't know.

DR. WINN-DEEN: I think this is an area of fairly substantial concern about trying to understand what health risks we are putting people to, and whether there are simple tests that could identify who those folks at highest risk are.

MR. MARGUS: Emily, one thing that came up I guess last March maybe when we were still discussing whether to make this a priority, or there was a discussion about pharmacogenomics, and we did have some visitors, right?

With regards to CMS, besides the concern that tests would be covered, the other issue is that if hundreds of millions of dollars are being spent reimbursing people for drugs of which 40 percent of the people who have taken the drugs aren't actually responding, there is a real economic value to pharmacogenomics that CMS and certainly the private carriers should be very interested in. As a different aspect of how CMS might be interested or how we might encourage CMS besides just covering the test.

DR. WINN-DEEN: Any other comments?

(No response.)

DR. WINN-DEEN: I know we're short on time, so I'm going to yield the floor.

DR. TUCKSON: Thank you for leading that, Emily.

Let's just remind ourselves that if you go back to your little grid chart here, as Sarah took us through it, first, the genetic discrimination issue, we've got a lot of work that we're going to be doing between now and the next meeting, and probably we'll have something on the agenda around genetic discrimination. That is going to occupy some considerable attention. So that is an active ball in play.

The genetic education and training is probably not a ball in play, but certainly the next ball in play that is serious is the coverage and reimbursement. That is going to take a lot of our time at the next meeting, and we're going to have to nail down some considerable work there. So those two are big.

The other thing that is big, and let me just make sure I've got it in my list. I'm keeping track. Let's see. Those are the big ones. We're not going to wind up doing much on the intellectual property one until after the other committee meets.

So we really do have the opportunity I guess to really start to think about do we want to grab onto for the next meeting, both or one of the large population studies of the pharmacogenomics, and mature those. Then we have these other potential topics as well.

Thank you, Sarah. Why don't you take us through those, Sarah?

MS. CARR: Well, the first one is reflective of an interest expressed by the committee in June, and it sort of came up I think in the context of the discussion of education and training resolution. It was some rather significant interest expressed in what is going on in health information technology.

So we just wanted to make sure to just put it on the table here for the committee to decide whether you would like to be briefed in a fuller way about what is going on.

DR. TUCKSON: Let me, on that one, just say that given the discussion we had at this meeting regarding the family history, I think that to leverage that discussion, we may want to have a brief update on this. Clearly the implications for the electronic medical record and all the technology stuff that is going forward.

I will tell you from some other hats that I wear, that whole area is moving so rapidly. The idea of creating standards for the electronic medical record is moving from yappa, yappa, yappa, to implementation at rapid rates. So given that we spent as much time as we did today at this meeting on the family history stuff, we may want to well start to connect those in and leverage our time.

DR. WINN-DEEN: I just wanted to say that also has a lot of relevance to the pharmacogenomics. Again, this is information that you would be tested for once, and then that information would be good for the rest of your lifetime.

DR. TUCKSON: So we may want to well try to squeeze in at least a presentation on this.

MS. CARR: And then there is a third aspect to it, too, which Ed McCabe might want to speak to. That is that the way in which electronic health records might help enhance privacy.

Ed, I think you mentioned that you had had a conversation with Mark Rothstein about the growing realization that rather than diminishing privacy, it might actually enhance it. So that might be a way, an aspect of it.

But the second issue is the presentation from the HRSA Committee on Newborn Screening about the recommendations they are making to the Secretary. Chris Hook, for one, was very interested in having such a presentation.

DR. TUCKSON: And given that we are, again, officially liaison to that, and given that that has come up pretty directly today, I think this committee really does need to hear at least a brief update on that.

DR. FEETHAM: And the word I had in talking to Dr. Puryear that that would be timely, and that report would be ready.

MS. CARR: Thank you for checking on that. Then the last two are presentations that we could request of CDC on rare disease testing. There was a conference, a public/private-sponsored conference, that came up with a lot of recommendations about how to enhance access and quality genetic testing for rare diseases. That group is interested in presenting their recommendations to this committee and getting some sense of your perspectives about them.

And then CDC could provide a very quick presentation on some of the work that they are doing to enhance quality assurance and quality control through the laboratory services program.

Is Joe Boone here? In case he wants to say anything further about those two topics. They were suggested by Joe.

DR. WINN-DEEN: So I have been involved in those things. I think they would be quite germane, to at least just get an update on what they are doing to try and fill what is a really big void right now for genetic testing.