Overview of Final Draft Report on Pharmacogenomics and Goals of Session
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DR. FITZGERALD: Thank you very much, Reed. Following up on what Sarah was telling us, I have to make an announcement that I have a significant personal interest in getting this done today. So I have a little bit of a conflict here. If this doesn't get finished today, my personal well-being will probably be at stake. During the break, if any of you want to see the psychological scars that I have received sitting here between Suzanne and Reed, I would be happy to make those manifest.

In any case, what I would like to do right now is give you a little bit of a history and an overview of the report, where we have been, what has gone on to bring us to this day. As you can see on our first slide, indeed as we reiterate what Reed has said, we are all about the finalization of this report.

The "we" of course is significantly dependent upon the taskforce. Now, it is not exactly a village. It is more like an extended family. As an extended family, we were very open and frank with one another, and that is how we got to where we are. As you can see, it is a great group. We had Jim Evans, Andrea, Julio, and Steve from the Committee itself, and of course, everything was begun by Emily. I too would like to thank her. She got the ball rolling. All I did was let it run me over and hang on.

I would also like to thank very much the input that we had from our HHS representatives, Gurvaneet, Muin, Steve, Liz, Alan, Greg, and Rochelle. Without their input, this report would be nowhere. We really did rely a great deal on their expertise and insight.

At the end of today, I will do a few more acknowledgements of the people who were instrumental in getting us where we are today.

How did we get here. Well, we began with some informational sessions which gave us the direction and the goal for the report. The first thing we had to do subsequent to that was a compilation of all the activities that were already ongoing. This is not something that we initiated out of thin air. As the report from the Secretary indicates, this has been building for some time and is now really taking on a great deal of momentum.

To get a good sense of that momentum, we also did a review of the literature to see the different perspectives that are out there, particularly to try and pick up the concerns that different experts from different perspectives have about how to move ahead with the idea of pharmacogenomics.

This led to the development and the revisions of a draft report. In that draft report, we came up with a certain number of recommendations. We then sent that draft report out to be reviewed by some experts that had been identified as people who could give us a more comprehensive sense of where our report was situated at that time in the thinking about pharmacogenomics.

In response, we then did a few more revisions and then sent it out for public comment. What I would like to do now is give you a better sense of that public comment process.

The public comment period was from March 23rd to June 1st. Again, as you can see, ample time for people to get a hold of the report, take a look at it, and give us their responses. To facilitate that process, there was a directed targeting of some people.

As you can see, after the March 23rd announcement, it was put on the website but it was also put on the SACGHS listserv, which totals 936 different addresses. In addition to that, there was a "Dear Colleague" mailing to an additional 283 addresses. And then finally, some specific requests to organization membership, and that was about 31 different organizations. So we really did attempt to get a broad and deep response from people because of the significance we feel of this report.

In this slide, we tried to break down for you a sense of the terrain of the responses. Now, one thing I would like to point out here, it does say at the bottom the total is 57. That is not 57 individuals. That is 57 different compilation responses that we received. If you look at the public responses, many came from multiple individuals or from entire institutions or organizations, as you can see, so obviously representing the thought of multiple people within one response.

As you break down those public comments, you can see in our little pie chart, four were from government, 10 came from companies, 18 from organizations, and the largest group from groups of individuals or individuals themselves.

On the right just gives you some of the idea of the specifics of those subgroups. So from the government, you have NIH, OCR, Veterans Administration, companies such as Abbott, Amgen, Eli Lilly, Genzyme, GSK, and Pfizer. The organizations, a whole list of acronyms there. This is Washington, D.C. You don't exist if you don't have an acronym. So we met all of those. And then at the end, the individuals that were covered came from academia, healthcare providers, researchers, et cetera.

What was in the comments. It really ran the gamut. It covered a broad spectrum of concerns and suggestions, and some were fairly focused, looking at the text itself and offering corrections to inaccurate statements, inaccurate data, or data we needed to update; update of various activities that were ongoing about which we were not aware; and also, general ideas on how we might improve the report overall.

Then there were also comments on the recommendations, that area that most people take a look at when they look at one of these reports. So as far as modifications to existing recommendations, thoughts about which recommendations we should prioritize over others, and finally, whole areas that we had not considered. So, new recommendations that we thought about adding to the report.

That was the sense of the overview of these public comments. Now to give you some more specifics just so you get a feel for some of the content itself.

One of the comments that we heard more than once was that the report was somewhat overly optimistic about the long-term potential of pharmacogenomics. That certainly was not our desire. It doesn't do any good to put something out that isn't an honest, realistic appraisal of where things are and where things might go. So we took that very seriously and wanted to in fact make sure that the report as it goes out is the best that we can do to give people a sense of the terrain and the possibilities.

It was suggested that we need greater discussion of the international efforts that are ongoing. Obviously, we are advising the Secretary of the Department of Health and Human Services in the United States. However, when one looks to see what decisions one might make certainly on a policy level, one always wants to know what is going on elsewhere just to get a little compare and

contrast. So that was beefed up and we looked more in detail at some of the collaborations that were going on internationally and also in a public-private venue.

This raises the question of whether our conceptualization, our definition of pharmacogenomics, is adequate. I think it is a moving target. I certainly do not want to claim that what we are going to put out in our report is going to remain true for all time, but we certainly hope that it provides a platform for the Secretary to move ahead.

Also mentioned several times was the desire for SACGHS to address oversight of genetic tests. As you know, we are responding to that desire in an entirely different report.

There were some more focused suggestions. A call for the federal government to encourage collection of DNA samples in clinical trials to facilitate pharmacogenomics research. This is addressed in the report.

Need criteria to define what pharmacogenomics information should be included in a drug label. Obviously, another important aspect.

More emphasis on the need for more clinical effectiveness evidence to secure payer reimbursement. Call for value-based approach to reimbursement of pharmacogenomics products.

Interestingly, a disagreement within the comments we received about whether pharmacogenomics will necessitate genetic counseling. So again, something we attempt to wrestle with in the report, not necessarily saying that it is going to come out one way or another because we can't predict exactly how things will go in the future. But certainly, an issue that needs to be continually revisited.

We received, as you saw from the timeline before, the full set of comments in June of 2007. Each of the taskforce members was assigned eight comments to review so that we would get two people on each comment and then hopefully get a little bit of variety of opinion from our own taskforce members. Then the staff, i.e. Suzanne, reviewed all 57 public comments. After the therapy, she seems to be doing okay.

[Laughter.]

DR. FITZGERALD: In our review of all the public comments, we tried to answer a series of direct questions. First of all, looking at the comments that one had to address, which should be in the next draft of the report. In other words, should something actually be changed in response to a particular comment.

Of the comments that should be addressed, which would require the entire taskforce to discuss or which could just be addressed directly by staff. Primarily, the updates were something that could be directly addressed by the staff because that was just putting in the new information. So that was one of the examples for how we would take something and not necessarily bring it to the entire taskforce.

Of those that warranted discussion by the entire taskforce, how then did the taskforce see we should go ahead with those comments.

How did we do this logistically. We had conference calls. Long conference calls. Two long conference calls. Both T-W-O and T-O-O. One was October 16th and one was September 10th,

and if any of you have done these three-hour conference calls, you know after a while you are practically worried about having to have the phone surgically removed from your ear.

But in any case, a lot was done. We reviewed the discussion guide compiled by the staff. The comments were organized by the sections, as you will see, as the report is structured. And then action was taken upon the recommendations of the taskforce, primarily focused by the members who responded to a particular comment and also by then the comments of the taskforce members as a whole.

So we discussed the items. We flagged the ones that we had to discuss as a whole, and then we just made decisions about whether and how to incorporate those comments into the report.

I will mention this, too, at the end, and Reed has already mentioned it. There are, as with many of these things, people behind the scenes without whom nothing like this would get done. Again, the Lewin Group's staff has been fantastic. They have just been absolutely cooperative. They have been professional and also have responded well to intense psychological pressure. A very handy thing to note for the future.

So in collaboration with them, the report was revised and the recommendations were revised, and then we went forward with that. The revised report is in the briefing books under Tab 3.

So as we have heard already several times and we wanted to reiterate once again, the goal of today's session is to finalize the recommendations. We need to get even the wordsmithing done so we know what is going to move forward from here. This is what the Committee needs to vote on.

Now, if anyone, again, has specific editorial suggestions to the report itself, we would be very happy to hear those and receive those. Those we don't necessarily need to address today. Those can be incorporated in a continual editing process that will go on after this meeting. So I would recommend, if you have anything specific in the report itself, the body of the report, that you somehow indicate what that change would be and please give that to Suzanne so that we can compile those and look to see how they can be incorporated into the report.

Our focus today is on the recommendations. We need to get the wording down for all of them so that we can go forward with those.

Why do we need to do that today. Because after this we pull together everything so that in December the Committee members can see the final report, what exactly is going to go to the Secretary. Then that report will be copy-edited and made camera ready and then printed. Finally, in February, we target that time to send the report to the Secretary so the Secretary's Office, as we all know, has a month to look over the report and all and respond and then release it to the public, hopefully within a month. That is where we hope to be able to go in the immediate future.

So my understanding is everybody is to get a break before we get into the report, or no? You want to keep going? Should we get started? All right.

See, this is the way it is. Every time I suggested a break, Reed would say, "No. Go, go."

[Laughter.]

DR. FITZGERALD: All right. Forward we go. The organization of the report. As you noticed, as we mentioned before, the report is in Tab 3 of your books. I believe, due to a specific recommendation from Andrea in one of our early meetings, the report -- we all agreed -- was organized into three overarching themes. These were areas where we thought important aspects of pharmacogenomics could be broken out into subgroups and addressed in a way that would allow us to keep contained within that subgroup our comments and yet, at the same time, make them into an integrated whole, which the whole report is supposed to be.

So the three overarching themes were research and development, the gatekeepers that are responsible for moving pharmacogenomics ahead, and then of course implementation of pharmacogenomics to improve outcomes in clinical and public health practice.

It would be impossible for me to overstate that third piece and the focus there, to improve outcomes in clinical and public health practice. This is something again and again to which we return. This is the goal. This is where we hope and we think the good of pharmacogenomics can go.

There are 15 recommendations. But of course, remember your college exams and the professor says, "There will be one question on the exam"? They don't tell you it will have eight subparts. Well, we have 15 recommendations and only 37 subparts. That is not so bad.

This is the first significant section of the report, research and development. This broke down into even further areas of focus. Obviously, basic research; what are the issues that are raised in that area. Then, of course, moving from basic research to clinical research and translational research overall. Raising, of course, the questions how then does one build an infrastructure that will enable and facilitate this research. Finally, the ethical, social, and legal issues that come up in research and development.

One thing you will notice as we go through the report is that the ELSI issues are raised in each of the three sections. Of course, we could have had an ELSI section, but we thought that it was better this way because we wanted to address those issues as they came along as we looked at these other subsections.

Looking at the second section, we talk about the gatekeepers, those who we identified, and others helped us identify, as the individuals critical to moving pharmacogenomics into the public sphere, getting it to those improved clinical and public health outcomes.

The four groups that were identified: industry, FDA, CMS and other third party payers, and of course, clinical practice guideline developers, professional societies in particular.

Now, if you will notice one thing here, before I said we had eight recommendations to that first section. Here we only have one. That doesn't mean that this subsection somehow is of less importance. But as I mentioned, these are the gatekeepers. This is the bottleneck, in a sense. Since you are only talking about the bottleneck, you only need one recommendation for the bottleneck: how to make it work better.

Finally then, we get to the third section. Again, this is the section that really focuses on where we hope pharmacogenomics can ultimately go. The implementation to improve outcomes in clinical and public health practice. This will involve several aspects that we need to address: education and guidance; information technology in pharmacogenomics; economic implications of pharmacogenomics; ethical, legal, and social issues in clinical implementation of

pharmacogenomics; and coordination of Health and Human Services pharmacogenomics activities.

One of the difficulties in any of these reports is being able to draw clear lines of distinction. It is virtually impossible. However, I think what one can do is try to identify foci from which one then looks out at the broader picture. So granted, education and guidance, information technology, economic implications, and coordination of activities within HHS are going to be relevant to all kinds of different issues we address: large population studies and oversight of genetic testing.

What we tried to do here is to situate some of those broader issues within the context or the focus of pharmacogenomics. We intentionally took this into consideration: parts of this report will in fact, hopefully, overlap well or coordinate well with earlier reports, like large population studies, and certainly subsequent reports, like the oversight of genetic testing. So we have tried to, in that way, formulate this report so that it is part of a continuum of the work of SACGHS.

You will see in this section we have Recommendations 10 through 15, with 16 subparts.

I hope that gives you a sense of how the report was structured and how we think, in any case, the report can best address the issue of pharmacogenomics.

What are we going to do today. We are going to stop now and listen to Reed.

DR. TUCKSON: Given now that I think we are getting ready to get into the discussion of the report itself, what we will do is we will take the break now for a second. That way we won't interrupt the discussion. Then we just plow right through it.

So here is the challenge. This is what I will call out for the new folks. We don't fool around with these breaks. I mean, I don't. So we start exactly when we say we are going to start. We do what we say we are going to do. Gurvaneet, you know that.

By the way, Robinsue Frohboese, we have read into the record all manner of incredible things about you, and I want to just say to you that we are very proud of the honor that you received, the highest award that your division gives out. You are terrific, and you are great on this Committee, and we think you are wonderful. So anyway, a round of applause for Robinsue.

[Applause.]

DR. TUCKSON: Now she will beat me up at the break. So we are going to start at 20 of. That gives you the 15 minutes. So we start at 20 of with the discussion. If you are late, oh my god, the woe that will befall you.