Discussion of Final Draft Recommendations (continued)
Facilitators: Reed V. Tuckson, M.D. and Kevin T. FitzGerald, S.J., Ph.D., Ph.D.

DR. TUCKSON: Welcome back. Apparently we have some considerations on 4B.

DR. FITZGERALD: We took care of it.

DR. TUCKSON: On 4B? We don't now? We took care of it?

DR. FITZGERALD: We took care of it.

DR. TUCKSON: You took care of it offline?

DR. FITZGERALD: Yes.

DR. TUCKSON: Wow. Some kind of controversy that turned out to be.

DR. FITZGERALD: I threatened them. It worked out real well.

DR. TUCKSON: Can you all believe this? This is perfect. Everyone came back exactly on time. They knew we were going to start.

It has come to my attention, from mean people like Marc, that apparently I once again, instead of calling him "Gurvaneet," I called him "Gurvanot," and everyone has been snickering about it the whole time.

For the new people that don't know, I mangle everyone's name regularly. That is my responsibility. But of all the people that I mangle every time, it is Gurvaneet Randhawa.

[Applause.]

DR. TUCKSON: Which really takes all the fun out of it when you screw it up.

[Laughter.]

DR. TUCKSON: So I will find someone else's name to butcher horribly before my tenure here is over. Unfortunately, Gurvaneet is off the table now. We have this new Paul the Wiser, Paul the Something, and Paul the Lesser, which is incredible.

Take it away, sir.

DR. FITZGERALD: Thank you, "Red."

[Laughter.]

DR. TUCKSON: We are on 5B. So, gearing up again after lunch. Get those synapses firing. You will find 5B on page 43 of your report, Tab 3. It reads, "HHS should initiate and facilitate collaborations between public," for example that long list of acronyms, "and private entities (for example, private health insurance plans, pharmacy benefit managers, healthcare facilities with electronic medical records, clinical research databases, or genetic repositories) to advance the

generation and sharing of knowledge on the analytic validity, clinical validity, clinical utility, and cost effectiveness of pharmacogenomics."

Yes, Michael.

DR. AMOS: Can you just add NIST there to the list?

DR. FITZGERALD: Sure. Oh, it is already up there. Sorry.

Oh, I love this. This is good. Oh no, wait. Go ahead.

DR. EVANS: A real simple thing. Again, it gets back to what I was saying on the prior one. I noticed it in the first sentence of 5A, too. It is very research-focused but [we need] the term "value." There is cost effectiveness in there, but if you insert "value" into the first sentence of 5A and also in 5B, it gets at quality and cost.

DR. FITZGERALD: Is that not under clinical utility?

DR. EVANS: Not really.

DR. FITZGERALD: So we need just "value"?

DR. EVANS: I would add it because cost effectiveness is way too narrow. I think we are looking for a bigger picture here.

DR. FITZGERALD: Let me get this right. So it is "analytic validity, clinical utility, cost effectiveness, and value"? Just the word "value"?

DR. EVANS: Right.

DR. FITZGERALD: Everybody comfortable with that?

DR. EVANS: The same phrase is present in 5A, so you may want to change that to be consistent.

DR. FITZGERALD: Great. Excellent. We have made just a couple of changes. "HHS should initiate and facilitate collaborations between public," including NIST, "and private entities," including that whole list, "to advance the generation and sharing of knowledge on the analytic validity, clinical validity, clinical utility, cost effectiveness, and value of pharmacogenomics."

Good? We are good to go. Fantastic. Next is 5C. Same page in your report.

"HHS should encourage and facilitate studies on the clinical validity and clinical utility of pharmacogenomics," and we will see about value, "and the dissemination of study findings, including negative findings where appropriate, through publications, meetings, and an information clearinghouse."

Yes, Marc.

DR. WILLIAMS: Do we need "where appropriate"?

DR. FITZGERALD: The question here was since, obviously, you are going to get lots of negative findings, some which may or may not be relevant, would "relevant" be better? I suppose it doesn't do any more specificity than "appropriate." Just say "including negative findings."

DR. WILLIAMS: Right. There is a reasonable amount of literature that says that this is a major issue.

DR. FITZGERALD: No, it is.

DR. WILLIAMS: So I think just saying "and negative findings" is sufficient.

DR. FITZGERALD: It is not too draconian for anyone? Fine. Get rid of it. Good.

All right. Anything else on this?

[No response.]

DR. FITZGERALD: Great. So everybody is good. "HHS should encourage and facilitate studies on the clinical validity and clinical utility of pharmacogenomics and the dissemination of study findings, including negative findings, through publications, meetings, and an information clearinghouse."

We are good on that? Everybody looks happy. Excellent. Next. Fantastic. Thank you.

"NIH should provide mechanisms that promote interactions among basic, translational, clinical, and outcomes researchers for the identification of endpoints and data elements to be measured. The goal of these interactions would be to maximize the value and utility of basic and translational research data for downstream assessments of the clinical validity and clinical utility of pharmacogenomics tests."

You will notice this ends here. What is in your report has another sentence. We are recommending deleting that sentence and just stopping here. Yes.

DR. WILLIAMS: Should it read "NIH" or should it read "HHS," since there are other HHS agencies involved in that kind of work?

DR. FITZGERALD: "HHS." Good. Thank you. Anyone else? This is good. We should have lunch more often.

[Laughter.]

DR. FITZGERALD: Going once, twice, three times. Fantastic. Sold. Next.

No. 6A is on page 47 of your report. Again, this is slightly different on the slide than it is in your text.

"HHS should encourage private sector entities, including academic institutions," and here is where the difference is, "voluntarily to share," we are doing a little wordsmithing ahead of time, "voluntarily to share proprietary data to advance the development and codevelopment of pharmacogenomics products. Manufacturers should be encouraged to make their data publicly available to allow others to conduct research and publish such studies."

We decided not to split the infinitive and not make English professors across the nation unhappy with us.

DR. FOX: I think "voluntarily" may be in the wrong place there. It sounds like you are voluntarily encouraging. You might want to put it after.

DR. FITZGERALD: "To share voluntarily"? No, because that splits the infinitive.

DR. FOX: "Share proprietary data voluntarily."

DR. FITZGERALD: "To share proprietary data voluntarily." Okay.

Anything else with this, now that we have finally decided where we are going to volunteer? Trust me, we had long discussions about this.

So the final is, "HHS should encourage private sector entities, including academic institutions, to share proprietary data voluntarily to advance the development and codevelopment of pharmacogenomics products. Manufacturers should be encouraged to make their data publicly available to allow others to conduct research and publish such studies."

Fantastic. All right. Moving right along. This will make "Red" very happy. No. 6B. Gurvaneet, by the way, is giving me $10 every time I say that. I just want you to know.

[Laughter.]

DR. FITZGERALD: No. 6B. "HHS should work with the private sector to identify obstacles to data sharing and to develop solutions to overcome these obstacles. For example, legal and data confidentiality assurances, intellectual property protections)."

Ruminations, suggestions? Yes.

DR. EVANS: We have been working on this extensively over the last year or two in terms of Medicare data, claims data in particular. One thing I would suggest you put in the parentheses is "funding."

DR. FITZGERALD: Funding.

DR. EVANS: You have focused in on legal issues and what not, but who will pay to collect data and share it.

DR. FITZGERALD: Oh, funding of the data collection.

DR. EVANS: Yes.

DR. FITZGERALD: So, "funding of data collection" rather than just funding? Right? Specifically data collection.

Anyone else? Marc.

DR. WILLIAMS: Just a purview question. Barry, maybe you can comment on this. The intellectual property protections, would that be within the purview of HHS or does it have to work with another agency within the federal government to deal with that? I don't know.

DR. STRAUBE: No, that can be within HHS. There are other agencies that might need to be pulled in, but definitely it could be HHS.

DR. FITZGERALD: Paul the Middle.

MR. MILLER: I'm not sure, but are confidentiality and privacy the same thing?

DR. FITZGERALD: No, no. I don't know about legally, but ethically, no.

MR. MILLER: So, do you want to also add something in here about privacy assurances in addition to confidentiality assurances, or is that something different?

DR. FITZGERALD: I think that is different, but I'm willing to be corrected.

MR. MILLER: Is it different?

DR. FERREIRA-GONZALEZ: At least my understanding of it.

MS. ASPINALL: This is for the company as opposed to privacy for the individual.

DR. TUCKSON: Are there any HIT issues here, and does that need to be put into the parentheses section?

DR. WILLIAMS: The good news is this is not an exclusive or a restrictive list. Other things could be added as HHS feels necessary.

DR. FITZGERALD: We do try to deal with the HIT issues later, but we could certainly put that in here, too.

MS. ASPINALL: I think it is a good idea, given the Secretary's focus on HIT, around personalized medicine. I think it is great to add it as an example.

DR. FITZGERALD: We could do "funding of databases and health information technology." Thank you, Suzanne.

So we have, "HHS should work with the private sector to identify obstacles to data sharing and to develop solutions to overcome these obstacles. This list includes but is not exclusive, legal and data confidentiality assurances, intellectual property protections, funding of databases and health information technology."

Everybody is happy? Great. Thanks very much. Next is 6C. This is found on page 48 of your report. Now we are into the data sharing and database interoperability.

"Research, regulatory, medical record and claims databases need to be interoperable to facilitate research on pharmacogenomics technologies and to build the necessary evidence base. Interoperability of these databases will facilitate the study of the molecular pathogenesis of disease, the identification of targets for drug development, validation of pharmacogenomics

technologies, assessment of health outcomes associated with the use of pharmacogenomics technologies, and determination of the cost effectiveness and economic impact of using these technologies.

"HHS and other relevant departments (for example, DVA and DOD) should work with the private sector to improve data sharing and interoperability among database. Specifically, HHS should work with existing organizations to create uniform genomic data standards, explore ways to harmonize data analysis methodologies, and develop an infrastructure to enable data exchange."

Yes, Ellen.

DR. FOX: A couple of points on this. First, I think the first sentence is overstated. I think interoperability is nice to facilitate those things, but I don't think you need interoperable records in order to conduct research. So I think that "need to" is a little bit overstated.

DR. FITZGERALD: I think the "need" is to facilitate.

DR. FOX: They need to be interoperable to facilitate.

DR. FITZGERALD: Right. To facilitate research.

DR. FOX: No, I'm saying it is not really a need. It is helpful.

DR. FITZGERALD: You could facilitate it other ways.

DR. FOX: Yes, yes. The second point, I think there is technically a difference between data sharing and interoperability. In the second paragraph it talks about data sharing and interoperability. So perhaps that should also be in the first sentence.

DR. FITZGERALD: Oh, I see.

DR. FOX: I'm suggesting maybe combining the first two sentences and saying "Data sharing and interoperability of various databases, e.g." and then put the list in the first sentence, "will facilitate."

DR. FITZGERALD: Let's just make sure we got what you are recommending.

DR. FOX: That is what I'm recommending. Then, a second point. This isn't on the recommendation but in the text. I think the text lists a number of barriers to interoperability which are basically logistical or practical barriers. I think it is important to note that there may also be some philosophical barriers to interoperability.

In other words, you might read this to suggest that ideally every database should be interoperable with every other database. I don't think that is accurate. I think that there may be, for example, differences in the way the data was collected, the purposes for which it was collected, the mission of the organizations, where just combining databases would not be appropriate.

DR. FITZGERALD: This is a perfect time to once again remind everybody to do this. Anybody who has any recommendations for the text itself, please get those recommendations, very specific [as to] where you want it in the text and what you want in the text to Suzanne. That can be done today or you can Email her shortly after this meeting. But whatever recommendations you have

along those lines, please get them to Suzanne and we will incorporate those into the text. So, thank you on that note.

Yes, Gurvaneet.

DR. RANDHAWA: There were two issues for me. One, the first paragraph starts out very broadly in looking at claims databases, medical record databases, and then the second paragraph ends very narrowly in just genomic database standards. Is there a reason to exclude the others from that?

DR. FITZGERALD: If I remember correctly, the idea was that yes, while we did want the more generic to be in the recommendation, there was discussion where people wanted to make sure that specifically that narrow area of creating uniform genomic data standards and exploring ways to harmonize was mentioned.

So this is one of those where we thought just the generic recommendation wouldn't be sufficient but that needed to be mentioned. That is the reason, if I remember correctly about how that came about.

MS. GOODWIN: You say the second paragraph is specifically focused on genomics. Oh, just on genomic data standards.

DR. RANDHAWA: Right. Which is not how you start out.

DR. FITZGERALD: Right. We started with the generic and the broad, but the people in the taskforce thought it was important to make sure that that was specifically mentioned. That is all I can tell you.

DR. RANDHAWA: Then the second issue was, some people are distinguishing data sharing from information sharing. Data sharing implies access to the data that is present in a database, which may or may not be feasible [because of] intellectual property issues or privacy issues but also business model issues.

Some folks have suggested that it may be feasible to share information that is present in the databases without actually sharing the data per se in the databases. I don't know if you want to make that distinction here.

DR. FITZGERALD: That is a good question. Again, my recollection of our discussion of this particular one was on the data and not the information because, obviously, if there is information sharing, there has already been a process of filtering and interpretation that has been ongoing. That doesn't necessarily give the person access to the data. The raw data, if we want to put it that way, not that there is such a thing. But the data itself rather than how the data has already been processed.

Again, we can discuss that. But that I think, if I remember correctly, was the point.

Yes, Paul.

MR. MILLER: Just a drafting issue. I'm agnostic on the point, but it strikes me that this recommendation is drafted very differently from the others. All of the others are really much more directive and start off "HHS should," "NIH should." This has an introductory paragraph

which really isn't a recommendation for action but rather a broad statement and then the recommendation comes differently.

So my question is, assuming this is done purposefully, does that make sense just in terms of creating the recommendation or is that better served being put in the text?

Because it really stands out as different in terms of format from the rest of the recommendations. If you look at the other recommendations, they are all "HHS should," HHS this, that, and the other thing. Here we have just an open paragraph of a statement.

DR. FITZGERALD: Again, this gets back to that tension that we felt before when we were talking earlier about the need to put in a little justification into the recommendations. Granted this is for the Committee to decide.

MR. MILLER: As I said, I'm about agnostic about it being there. I just want to point out that it is very different from every other recommendation.

DR. FITZGERALD: Right. I think the idea was that this was useful here, but in any case. Marc.

DR. WILLIAMS: I would just offer the suggestion that if you flip those two paragraphs then it would fit the format that the other ones have.

MS. ASPINALL: I'm quite taken by Paul's comment as to whether we need the now-second paragraph. I think it is otherwise in the executive summary in the same way the others have the assumptions.

DR. FITZGERALD: Yes. If we want to whittle this down, we certainly can.

DR. WILLIAMS: I would just note that several of the other recommendations that we passed through, 5A in particular, do in fact include a small amount of text that put them in context. I don't see any reason not to do that.

DR. FITZGERALD: Yes, sure. Scott.

LT. COL. McLEAN: There are a few locations where the Department of Defense is named specifically, and this is one of them. In this context, it seems to imply that we are going to recommend that the Department of Defense work with the private sector. Is that a recommendation for the Department of Defense specifically?

DR. FITZGERALD: The idea, I think, in this regard was [for] Department of Defense and Department of Veteran Administration.

LT. COL. McLEAN: Usually this is a recommendation for the Secretary to take some action.

DR. FITZGERALD: For HHS, right.

LT. COL. McLEAN: The way this is worded, it suggests that it is a recommendation to the Department of Defense. I just want to clarify that.

DR. FITZGERALD: Got it. Right. No, no, no, this is a recommendation to the Secretary. Maybe you are right; we could word this better. The idea, anyway, was to collaborate with the other departments in moving to the private sector.

DR. WILLIAMS: A language suggestion there would be to remove the "and" and just put "work with other" or "convene," which we have used in other recommendations. We cannot make specific recommendations to other departments.

DR. FITZGERALD: Right. It is not recommending to DOD, correct. Or DVA, for that matter.

DR. AMOS: If you are going to make that change, actually NIST has a role in interoperability and data standards. So you can just add NIST to the list.

DR. FITZGERALD: As part of the e.g. list?

DR. AMOS: Right.

DR. FITZGERALD: Let's see what we have at the moment. Now we have reversed the paragraphs. So we have, "HHS should work with other relevant departments (for example, DVA, DOD, and NIST) and the private sector to improve data sharing and interoperability among databases. Specifically, HHS should work with existing organizations to create uniform genomic data standards, explore ways to harmonize data analysis methodologies, and develop an infrastructure to enable data exchange."

Second paragraph. "Data sharing and interoperability of research regulatory medical record and claims databases will facilitate the study of the molecular pathogenesis of disease, the identification of targets for drug development, validation of pharmacogenomics technologies, assessment of health outcomes associated with the use of pharmacogenomics technologies, and determination of the cost effectiveness and economic impact of using these technologies."

That is where we are at the moment. People are good with that? Any other questions, comments, or general malaise?

[No response.]

DR. FITZGERALD: Good. All right. Excellent. Next. On page 49 of your report, Draft Recommendation 6D, "FDA should identify, initiate, and facilitate research opportunities and public-private partnerships to encourage the development and codevelopment of pharmacogenomic products (for example, through the Critical Path Initiative.)"

Yes, Chira.

MS. CHEN: This sounds like FDA is paying for the research. So, it is?

DR. FITZGERALD: "Should identify, initiate, and facilitate research." I wouldn't say paying for all of it.

DR. GUTMAN: The deal for the Critical Path is it is very largely being generated out of leveraged activity, so collaborative activity. Funding has been modest up until now, and there has been a deliberate effort to make sure that that funding is always matched in some way.

I think the funding may become more generous. We are never going to look anything like even a small nook or corner of NIH, so I'm certain that it would continue to look for partnerships with industry or other government entities.

MS. CHEN: I just want to make sure that is being done, or else why are we putting it on here.

DR. FITZGERALD: Anyone? Yes, Michael.

DR. AMOS: The NIH has their Biomarker Consortium. Is that mentioned anywhere? It could fit here as well. That is a public-private partnership that would be along the same lines as the Critical Path.

DR. FITZGERALD: Now, there is an appendix in the report, just to let everyone know, of all the various efforts that are going on in the government. Is that Appendix A?

MS. GOODWIN: Yes. There is discussion in the text of the report about the Biomarkers Consortium, and it is also in the appendix. That is part of the reason why the "e.g." is here noting that this is just one example of one of the activities that it could be done through. But, if we want to add others or not mention any specifically.

DR. FITZGERALD: If anybody notices in the report an effort or a program is missing, please, again, let Suzanne know and we will be happy to add things to the list. We want to be as comprehensive as possible. Marc.

DR. WILLIAMS: I think the thing that looks a little bit different here is we have identified just one, whereas in many of the other recommendations we have identified more than one. It may, appropriately or not, give pride of place, if you will. If we want to have a e.g., it might be good to mention a couple.

DR. FITZGERALD: So we will do "Critical Path Initiative or Biomarkers Consortium."

We haven't made too many changes to this, so it stands almost as read initially. Everybody is good with that?

[No response.]

DR. FITZGERALD: Fantastic. It looks great. All right. On to the next. No. 7. This is on page 51 of your report. This is into, now, the realm of personal information protection.

"As data access and sharing expand, it will be important to strike the right balance between protecting the privacy and confidentiality of personal data and fostering access to these data for pharmacogenomics research. Stronger data security measures may be needed as more pharmacogenomics researchers access patient data."

"It will be important to strike the right balance." Well, okay. "HHS should strike the right balance." "Should work to strike" or "guide" or whatever. Yes, Paul.

DR. BILLINGS: I have a problem with this particular recommendation because it is important now, it is important in the future, and it was important in the past as well. So, what is exactly new about this? What are we calling for that isn't already in place?

DR. FITZGERALD: I think the reason behind it was exactly what you just said: its importance. So the thought was to leave it out, its absence might suggest that it is not as important as it is. It is not to say that this is the definitive recommendation or that this changes anything from the past or reduces anything for the future but to say it is of such importance that it needed to be in here. But I think that was part of the idea, that it is in fact such an important issue.

Marc, go ahead.

DR. WILLIAMS: To address that and to expand a bit on the recommendation, I think that the issue that has resurfaced that does make it a bit different is the idea of the information technology and whether or not previous recommendations have in fact been specific enough to capture that.

What I would reference is the work that is being done through the American Health Information Community, AHIC, which is a DHHS initiative that has a specific workgroup on privacy. I think this would be a perfect opportunity to make a very specific recommendation and say that we recommend that the Secretary raise this specific issue with the Privacy Workgroup of AHIC to develop guidance as part of that initiative.

DR. FITZGERALD: Joseph.

DR. TELFAIR: I don't have anything to add to the last comment, but I thought the recommendation should start off with a much stronger statement. So the last sentence, I would actually recommend it be the starting sentence, and I would change the word "may" to "will." Whatever comes after that the Committee can decide, but I would just move that around.

DR. FITZGERALD: Done. Then I have Mara and then Barry and then Robinsue.

MS. ASPINALL: The same comment.

DR. FITZGERALD: Oh, okay. That's good.

DR. EVANS: Just in addition, Marc, to the Privacy Workgroup, there is the Personalized Medicine Workgroup.

DR. WILLIAMS: It is a different workgroup under the AHIC. But what the Personalized Health Workgroup has agreed to do is to work with the Privacy Workgroup on these issues. So it would really be captured within that discussion.

DR. EVANS: That works fine. I think what some of us within HHS are trying to do is to cut down on the number of workgroups that are there.

[Laughter.]

DR. EVANS: Thank you.

DR. FITZGERALD: Robinsue and then Paul.

DR. FROHBOESE: In response to this discussion, I just wanted to point out Draft Recommendation No. 12A, which specifically does reference AHIC. That may be the place to get some greater specificity, although it is fairly specific. Underscore the privacy and security in that recommendation.

DR. WILLIAMS: I would just note that that one has a little bit of a different orientation in the sense that it is really looking at decision support, which is a different aspect of that. We have several recommendations here around Nos. 6 and 7 that are relating to the database, so I don't know that we necessarily need to combine them, although if everybody feels strongly about that I think that would be fine, too.

DR. FITZGERALD: Paul.

MR. MILLER: As a matter of drafting, I would strike "strike" because I am not quite sure what that means. Rather than "should strike the right balance," whatever that means, "HHS should balance the privacy and confidentiality of data with the" blah, blah, blah.

DR. FITZGERALD: Thank you. Let's read what we have now. "Stronger data security measures will be needed as more pharmacogenomics researchers access patient data. As data access and sharing expand, HHS should balance the privacy and confidentiality of personal data with access to these data for pharmacogenomics research. AHIC's Confidentiality, Privacy, and Security Workgroup should be tasked with addressing this issue."

Yes, Joseph.

DR. TELFAIR: Starting with "HHS should balance," I'm not quite sure, but it seems to me that you should have --

DR. FITZGERALD: We could say "HHS should strike a balance."

DR. TELFAIR: No, I'm agreeing with that part. I'm just saying before that there should be the way you get there. I'm not great at wordsmithing, but if the first statement is there, that is a pretty strong statement. Then something about recommending how they really should do it. It seems to me that that is what is missing before the "HHS." You have that as the third sentence, showing it should be done, but somehow or another it should come earlier as a way to get to this or a way to accomplish this, or something to that effect. "Such that" and then a statement. There seems to be [something] missing there.

DR. FITZGERALD: So you wouldn't see what we said at the end there that the AHIC Workgroup should be tasked with addressing this issue with creating that balance, with delineating the balance, with something like that?

DR. TELFAIR: Yes, I agree with the part that the balance between the two should occur. But there seems to be a bridge amiss. There is a set of bridging words between the last part of that and then moving to the tasking part. That is all I'm saying.

I apologize. I am not good at wordsmithing, so I would have to think it through. This is the sort of block that methodology people get. It's just me. But there should be some kind of bridging statement, and I'm open to people who are better at words than I am. That is just a suggestion.

DR. FITZGERALD: Yes, Julio.

DR. LICINO: I think it is not only a matter of balance because the way it states there, it is like either you have privacy and confidentiality or you do research. It is a balance between the two. In other words, if you do research you are breaking privacy and confidentiality. But I think that it

should be more than that. It should be like "to ensure that research can be conducted protecting privacy and confidentiality."

I know that sometimes there is a conflict between the two, but I think the goal should be to ensure that the research is done with full protection of privacy and confidentiality.

DR. FITZGERALD: I think we have run into this issue before because of even just how you phrase that. If you say the research should be done with protection of privacy and confidentiality, people read that as the research should be done and along the way try and protect confidentiality and privacy. Others will say privacy and confidentiality should be protected and then research can be done. You see the subtle distinction there.

So the question I think we are trying to figure out is how do you say that in a neutral way to say that both the research is done and privacy and confidentiality are protected. That has been a struggle we have had all the way along. If anybody has a better way of saying it, it would be great.

Ellen, please.

DR. FOX: Perhaps related to that is, it seems to me that there is an inadequate distinction between security and privacy and confidentiality here. It seems almost to equate the two. Is this really supposed to be about data security? Then we could maybe just get rid of "privacy and confidentiality" and talk about balancing data security against access, which is a balance. You want to maintain privacy and confidentiality, but data security, if you are going to provide access, there is going to be a give-and-take there.

DR. FITZGERALD: Right. I understand that. I think the idea was to try and say why do you need data security, in part for privacy and confidentiality reasons. But, yes.

DR. FOX: But you always need data security, even if you are not keeping something confidential.

DR. FITZGERALD: Right. So here, again, up at the top it says "protection of personal information." So the emphasis is more on privacy and confidentiality than data security.

DR. FOX: The first sentence starts with data security.

DR. FITZGERALD: I'm not saying we didn't.

DR. FOX: Oh, okay. I assumed it was the opposite.

DR. FITZGERALD: Julio, go ahead.

DR. LICINO: The issue about research is, there may be a security breach, of course, and then that destroys privacy, but in the context of conducting research you may have information that makes the person identifiable. I think that is the big issue.

DR. FITZGERALD: Yes, exactly.

DR. LICINO: You can break into a database and that is a big issue, but we are not discussing that here.

DR. FITZGERALD: Right. It is bigger than just that. Absolutely. Is that not coming [through]? We are still working.

Should we look and see what we have? No. Go ahead, Jim.

DR. TELFAIR: I actually like Paul's [suggestion to] balance those two. I think that does remain not open to the interpretation that we are doing one and the other is an afterthought, and I think in truth it is a balance. There are issues that need to be balanced. Absolute privacy would preclude research, and absolute openness would preclude privacy. Thus, it is a balance. So I like the way Paul put it.

DR. FITZGERALD: So we have now two balances, "on how to balance the need to balance"?

[Laughter.]

DR. FITZGERALD: Let's try this and see what people think. "Stronger data security measures will be needed as more pharmacogenomics researchers access patient data. AHIC's Confidentiality, Privacy, and Security Workgroup should develop guidance on how to balance the protection of privacy and confidentiality of personal data with access to these data for pharmacogenomics research."

Robinsue, yes.

DR. FROHBOESE: I'm sorry to go back to this, but I want to again just pause and think whether AHIC's Privacy and Confidentiality Workgroup is the best vehicle to look at this. I raise it for a couple of reasons. One, there are plans that AHIC will be phased out next fall and there will be a successor organization that will be stepping in for AHIC. So I just don't know the continuation of that workgroup.

Marc knows this better than I, so I would like you to address it, but it certainly has its hands full right now with looking at within the context of electronic health records, looking at all of the privacy and security aspects. Is this the right group to give this very important issue the kind of expedited attention that it needs.

DR. TUCKSON: How about if we do it this way, then, just so we can move this along. I think you are right. AHIC's future is questionable; there is no question about it. We don't know what is going to happen with it. Maybe you could say, "Through mechanisms such as AHIC," and that way you signal where you are headed. You are trying to decrease the redundancy that Barry is worried about, but you don't lock in.

Let's try to bring this one to closure.

DR. FITZGERALD: Steve and then Martin.

DR. TEUTSCH: I think part of the problem is this focuses on how to balance them rather than assessing what the right balance should be. The question really is we have to recognize tradeoffs and we need to figure out where it needs to be, and this focuses mostly on mechanisms.

DR. FITZGERALD: Martin?

MR. DANNENFELSER: I just think that the way this is worded it might sound like it is a 50/50 thing, and I think that is not the right balance, if you will. I think we should maybe take the word "balance" out and do something on how to protect the privacy and confidentiality of personal data. That doesn't mean that you are going to have 100 percent success in doing that, but that is what you are striving to do.

DR. FITZGERALD: Well, we are having a pushback on "balance."

DR. WILLIAMS: Balance doesn't mean 50/50.

DR. FITZGERALD: Martin?

MR. DANNENFELSER: I still think it sounds like we are not giving appropriate consideration to the privacy.

DR. FITZGERALD: Of course, when we say "appropriate," what is appropriate.

DR. WILLIAMS: There are two issues here. This is not the only group that is assessing this issue of personal privacy. We are discussing it in the context of the databases for pharmacogenomics research, so it is really in an informatics context. So this is not taking place in the vacuum of no other discussion about how we weigh privacy and confidentiality versus the ability to do research.

I think what we are really talking about here is that there is an informatics component that is inextricably linked to doing pharmacogenomics research, and what we are trying to address, as I see it, in this is that at the present time the sense of the group is that we don't necessarily have those specific issues addressed for these types of pharmacogenomic databases that are being proposed.

It was news to me to hear that AHIC may be going away, but that is the way of things. But to address the issue, yes, they do have a lot on their plate, but it is within the Secretary's purview, that being an advisory committee, to tell them what to do and when to do it.

DR. FITZGERALD: So, what would you recommend? Are you happy with this?

DR. WILLIAMS: I am happy with it as it is currently constructed.

DR. FITZGERALD: Let me just go through it one more time. "Stronger data security measures will be needed as more pharmacogenomics researchers access patient data. HHS, through mechanisms such as AHIC's Confidentiality, Privacy, and Security Workgroup, should develop guidance on how to balance the protection of privacy and confidentiality of personal data with access to these data for pharmacogenomics research."

I'm looking, I'm looking, I'm looking. All right?

[No response.]

DR. FITZGERALD: We are good. Thank you very much. Thanks for all the good input.

Now we are on to No. 8A, which is on page 56 of your report. This is population stratification in drug response and some of the questions there.

"Because genomic factors may be more meaningful predictors of drug response than race and ethnicity categories, FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may better explain differences in drug response."

It is a very specific recommendation to address a relatively specific problem. Everybody is comfortable with this and the wording? Joseph? Wait. Joseph and Alan. Sorry, Alan.

DR. GUTTMACHER: Better than what?

DR. FITZGERALD: I'm sorry?

DR. GUTTMACHER: Better than what? In the last sentence.

DR. FITZGERALD: "That may better explain." Better than what we have now.

PARTICIPANTS: Better than race and ethnicity.

DR. FITZGERALD: Oh, yes. Better explain differences than using race and ethnicity as explanatory factors.

DR. GUTTMACHER: If others feel that that is clear in context, then I will withdraw my question. I'm not sure it does.

DR. FITZGERALD: Joseph?

DR. TELFAIR: I guess mine is not quite the same, but it is on a similar pathway of thinking. Race and ethnicity are not biological categories, so it is not appropriate to categorize them in that way. They are more sociological categories. So if you are going to use biological categories, I think you really do need to have a little bit more explanation at the end as to what you are going to do.

DR. FITZGERALD: So again, you are not going to help me with the wordsmithing because you don't do that.

[Laughter.]

DR. TELFAIR: Because I'm not a biologist. That is not my area of thought. To explain differences, you can talk about other differences but differences that --

DR. FITZGERALD: How about if we do this. "Encourage the collection of genetic and other biological factors such as biogeographical ancestry that may better explain differences in drug response"?

DR. TUCKSON: I think one of the key words here, and it may be overly simplistic but to answer the first question, "that may better explain individual differences in drug response." It is drug response of the individual that you are concerned about, not the differences in the social class of the patient.

DR. TELFAIR: I guess I would agree with that language because that is actually what I'm searching for. Even though these categories are there, they are actually sociological group

definitions. If the outcomes are more individualistic, then you need to say they are more individualistic.

DR. FITZGERALD: Although there will probably be inclusion of data from such categories as biogeographical ancestry, which is not race or ethnicity but just ancestry.

DR. TELFAIR: Right, yes. I would agree with that.

DR. FITZGERALD: Now I have Mara and Paul and Andrea. No, not Andrea? Just Mara and Paul.

MS. ASPINALL: I think, Kevin, I was going to agree with you to put it into a sociological category such as race and ethnicity, and I don't know what you do with gender, whether you put it in there. But I thought that would be useful, to categorize it in bunches and use race and ethnicity as an example.

DR. FITZGERALD: Maybe "more meaningful predictors than social"?

MS. ASPINALL: I would also do it in the first sentence.

DR. EVANS: "Than less exact proxies," something like that. The whole point of this is that these aren't very good proxies.

DR. BILLINGS: But they are not also exclusive proxies for the individual. The population genetic factors, as well as socioeconomic or others, at the individual level and at the group level may be co-explanatory. So I think you are looking, rather, for things that are better. You are looking for things that are more comprehensive descriptors, aren't you?

MS. ASPINALL: Isn't it both?

DR. BILLINGS: I'm saying both.

DR. FITZGERALD: So again, recommendations for words? Take a look at what is up there.

DR. BILLINGS: I wouldn't say "more meaningful predictors." I think they are predictors, for instance.

DR. FITZGERALD: Wait a minute. I need concrete suggestions here. Mara.

MS. ASPINALL: Let me first understand. Is Warfarin an example of this, where race and ethnicity and age only explain 25 percent of the variables but when you put in genomic factors you then explain 75 percent of the variables? Is that the idea?

DR. WILLIAMS: My interpretation, as I read this, was that we know that some drugs are coming to market using race and ethnicity as defining [factors.] BiDil is really the example of this. What we are trying to say is that genomically that doesn't make sense because within a self-identified group of African Americans there is a dramatic difference in response based on the genomic factors, which in fact give you a deeper level.

So I think it addresses a current issue, which is that these things are being used as proxies for development of drugs for subgroups and it recognizes that that is a reality, but we are saying we need to move beyond that.

DR. FITZGERALD: Paul.

DR. BILLINGS: I actually disagree. I agree with what Marc just said, though. I think that in the end socioeconomic class and the biological factors will have something to do with who takes the drug and how they respond.

DR. FITZGERALD: Right. I think the question is, is the sociological, economic data that is relevant captured by categories such as race and ethnicity. That is one of the questions.

Now, Gurvaneet.

DR. RANDHAWA: I think some of the confusion here is we don't qualify what predictor. If you are saying a biological predictor, I don't think there is any argument. If you are talking about a predictor to a treatment, then there are non-biological factors that [affect] this completely. So I think if you say "biological" to the predictor, that is better.

DR. FITZGERALD: I think one of the concerns here is that categories such as race and ethnicity, which everyone acknowledges are socioeconomic categories, are not even perhaps the best socioeconomic categories to use, right?

Go ahead. Mara and Jim.

MS. ASPINALL: I don't see them as socioeconomic categories.

DR. FITZGERALD: What kind of categories are they?

MS. ASPINALL: I wouldn't put "economic" in. I think it is sociological. While I think that is important, it has nothing to do with economics. They are sociological categories.

So I guess I would make two suggestions. At the beginning of the first sentence, although maybe it changed now -- sorry. It changed again.

DR. FITZGERALD: I know. It is evolving.

MS. ASPINALL: I had some words there. Anyhow, I don't think it should be "socioeconomic." It should be "sociological."

DR. FITZGERALD: Right. "Sociological." That's fine.

MS. ASPINALL: Secondly, in terms of Marc's comment, I understand BiDil, but to me Warfarin, which is also very current, is exactly this issue. It has been dosed based on race, ethnicity, age, and weight, and now it can be dosed on those and genomic factors.

DR. EVANS: There are major differences in response to Warfarin by race, and it turns out that VCOR and SIP explain most of that.

I think, if we go back to the original 8A that is in our book, that artfully dodges the contentious issue of defining race. Is it biological, is it all social construction. We don't need to get into that, and I think we would be foolish to tackle it.

I think 8A says genomic factors may be more meaningful predictors of drug response than proxies like race and ethnic categories. Therefore, we should encourage collection and analysis of genetic and other biological factors. That doesn't say that race is some biological issue that may better explain differences.

I think that really is -- I didn't design it, so I can say this -- an artfully worded recommendation.

DR. FITZGERALD: Are you saying we had all this discussion for nothing?

DR. EVANS: Yes.

DR. FITZGERALD: No, no.

[Laughter.]

DR. FITZGERALD: Look up on the screen and see, people, if what is up there captures things more adequately than what we had or what we had is closer.

We have right now, "FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may be more meaningful predictors of individual differences in drug response than sociological categories."

DR. EVANS: No.

DR. FITZGERALD: No. That doesn't do it. Cross that out.

DR. EVANS: What this does is it lends --

DR. FITZGERALD: Wait a minute. I have Michael, Martin, and Jim. Michael.

DR. AMOS: So, isn't the problem really when you try to use race and ethnicity as a biological marker? That is the problem, right?

DR. EVANS: Well, when you try --

DR. FITZGERALD: Wait. I have to keep other people in here.

DR. AMOS: You run into problems when you try to use race and ethnicity as a biological marker.

DR. FITZGERALD: So, what are you recommending for the recommendation?

DR. AMOS: Joseph.

DR. FITZGERALD: I see.

[Laughter.]

DR. FITZGERALD: Martin, go ahead.

MR. DANNENFELSER: I thought that, for the one that we just had up there a minute ago, if we just put "e.g." in parentheses at the end for the sociological factors and then just put race, ethnicity, gender as examples.

DR. FITZGERALD: Martin, you got it. Help us out here again. What are we doing?

MR. DANNENFELSER: The formulation we just had before we flipped back there. Where it ended was "sociological factors" or something. Then at the end of that, after "factors," put in parentheses, "e.g. race, ethnicity, gender."

DR. EVANS: But again, now you are jumping right into the controversy. Can I talk or not?

DR. FITZGERALD: I just want to make sure I get the suggestion right, that's all, before we comment it.

DR. EVANS: Gender is not a sociologic definition. I don't think we should --

PARTICIPANT: Yes, it is.

DR. EVANS: Well, sex is not.

DR. FITZGERALD: Wait a minute.

DR. AMOS: I can give you the words.

DR. FITZGERALD: Hold on. Let's see what people think about this. So we are still not comfortable. Michael, what were you thinking?

DR. AMOS: I was thinking that "differences in drug responses than when attempting to use sociological factors as biological markers."

DR. FITZGERALD: "In drug responses than when using sociological factors as biological markers." "FDA should develop guidance that encourages the collection and analysis of," "that may be better predictors of individual differences in drug response than when using sociological factors as biological markers."

We have a new recommendation up there. Now I will take comments and questions. Joe, you are first.

DR. TELFAIR: Instead of "as biological markers," just use the word "as proxies." Take out "biological markers" and use "as proxies."

DR. FITZGERALD: Next comment, anybody? Yes.

DR. EVANS: I will make one more stab at this. This last sentence as it stands defines, for example, gender as a sociological construct. It is both a biological and sociological construct, as many would argue race contains both. Therefore, I don't think that is accurate. You can say something like "in drug responses when using broader categories" or "broad proxies such as race, ethnicity, gender." How about just "when using broad proxies"?

DR. FITZGERALD: "When using broad proxies."

DR. EVANS: Then we can avoid this fruitless debate which inflames everyone as to how do you define these things.

DR. AMOS: Yes. "When you attempt to identify biological differences." Jim? "When you attempt to identify biological differences."

DR. EVANS: I think "broad proxies." Then you don't need to get into it.

DR. FITZGERALD: Wait a minute now. That you like? All right. Everybody take a look at what we have. Door No. 3. No, it is still changing.

Here we go. "FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may be better predictors of individual differences in drug response than broad proxies, e.g. race, ethnicity, and gender."

I have Martin and Gurvaneet.

MR. DANNENFELSER: Is the word "categories" better than proxies? I don't know; "proxies" to me sounds a little inappropriate there. They are not necessarily proxies. I think they are just different ways of categorizing.

DR. FITZGERALD: We have a "categories" suggestion. Gurvaneet seems to be on that, too.

DR. RANDHAWA: I agree with that. I think, if I was a pharmacoepidemiologist looking at this recommendation, I would not agree with this because if I'm looking at sociological databases and I'm saying such and such of Race A has a better response, it may be because of access or whatever else.

But it may have a much bigger predictor than any genomic factor. So then you are saying better predictor. It is not quite true here. It may be a better predictor for a biological response but not a better predictor of a drug response because the drug response has many other factors and biology is just one part of it, sometimes a very small part of it.

So unless you make it clear that it is a biological predictor and not a predictor per se, I don't think the statement is true.

DR. FITZGERALD: I guess one of the problems with race and ethnicity is they are usually self-assigned.

DR. RANDHAWA: It doesn't matter because you are looking at it from an effectiveness point of view. Someone who is not going to respond to a drug, whether it is because you can't buy a drug, you can't afford to have a complete prescription of the drug, or because your genomics are not good enough, it doesn't really matter. But if you are looking at it from a purely biological phenomenon, then that is a different issue.

DR. FITZGERALD: What was your suggestion about the recommendation? How do you want to change that?

DR. RANDHAWA: It is fine when you put "biological" in there.

DR. FITZGERALD: Good. Joe?

DR. TELFAIR: I would actually concur with that because that is really what my original thought was trying to get around.

DR. FITZGERALD: Steve.

DR. TEUTSCH: Rather than "proxies," which is pretty vague, I would probably talk about sociodemographics.

PARTICIPANTS: No.

DR. FITZGERALD: "Categories"? I thought that was going to go to "categories." "Categories."

All right. We are going to try this.

DR. WILLIAMS: I would just point out that it does say "maybe."

DR. FITZGERALD: We are not going to try this.

DR. WILLIAMS: It doesn't say "is." It says "maybe."

DR. FITZGERALD: Martin is back on.

MR. DANNENFELSER: It is just a real fine-tune here. Maybe at the end, rather than "e.g." we could just say "broad categories like."

DR. FITZGERALD: "Such as"?

MR. DANNENFELSER: Or just "broad categories like."

DR. FITZGERALD: Oh, I see.

MR. DANNENFELSER: Because a lot of other things could be in categories besides race and gender. There are all kinds of categories. I just want to make it sound like "categories" refers to those types of things.

DR. FITZGERALD: We are going to try another time here. Let's try this. "FDA should develop guidance that encourages the collection and analysis of genetic and other biological factors that may be better biological predictors of individual differences in drug response than broad categories such as race, ethnicity, and gender."

Are we happy with that?

[No response.]

DR. FITZGERALD: That's wonderful, because now I'm going to go to the next one, 8B. I'm going to turn this over to Reed because I'm going to go get a drink.

[Laughter.]

DR. TUCKSON: Population stratification in drug response, recommendation 8B. "When drugs are shown to be effective in certain racial and ethnic subpopulations (e.g. BiDil), FDA should encourage manufacturers to conduct additional post-market studies to identify biological, social, behavioral, and environmental markers that may underlie the differential drug response."

The floor is open.

DR. AMOS: Reed? Following on to the last discussion, I think you should say "genetic."

MS. ASPINALL: In the end. Instead of the whole list, just "identify genetic markers."

DR. AMOS: No, other things, too. Just "conduct additional post-market studies to identify genetic, biological, social." Just add that to the list because what we are saying in the one before is that this might be a better predictor.

DR. TUCKSON: Do you see a difference between "genetic" and "biological"?

PARTICIPANTS: Yes.

DR. TUCKSON: So you have genetic, biological, social, behavioral, and environmental.

DR. WILLIAMS: I would object to that difference. I think "biological" is broader, but genetic is biological and to have both of them implies that genetic is some other, non-biological thing floating out there.

DR. TUCKSON: Mara.

MS. ASPINALL: I'm not going to get into the last debate. Maybe somebody could help me. There aren't many --

DR. TUCKSON: I'm sorry, Mara. Let me just get this one nailed. Wait a minute. So, are we adding "genetic" or not?

PARTICIPANTS: No.

DR. TUCKSON: So we are not adding "genetic."

DR. WILLIAMS: Two points. I completely agree with what Alan said, but in the previous one we did specifically articulate "genetic and other biological." So from a language consistency perspective between the two recommendations, that would be one point.

DR. TUCKSON: So "genetic and other biological."

DR. WILLIAMS: The second point is that this is a pharmacogenomic report, and so it probably should be explicitly stated.

DR. TUCKSON: So, "genetic and other biological." Thank you. Mara?

MS. ASPINALL: I was exactly where Marc was, "genetic and other biological." But maybe somebody can explain where social, behavioral, and environmental come in in this one where

they hadn't previously come in at all. I guess, to make it consistent, I like "genetic and other biological that may underlie the differential drug response," and not to add the other three.

DR. TUCKSON: This is a fundamental difference of opinion here as to whether or not you say that we would get beyond the biological to include behavioral and environmental.

DR. TEUTSCH: I think this talks about effectiveness, not simply the biological response. It gets back to what Gurvaneet said. When you have effectiveness, that takes into lots of consideration these other things are very germane to that, rather than simply a biological phenomenon.

DR. TUCKSON: Mara, I appreciate your having raised it. Now we are beginning to see that the key word to focus in on is "effectiveness" and many different determinants of effectiveness other than the biological issues and that they want to open it up to include all of those, which is post-marketing stuff, which is terrific.

With that we have it. We will move on. No? Sure.

DR. WILLIAMS: I would suggest we add the word "more" before "effective" in the first line because otherwise there is no differential drug response, which we refer to at the end.

DR. TUCKSON: So, "when drugs are shown to be more effective in certain racial." Good. Sounds like a friendly amendment. Any last ones? Yes.

PARTICIPANT: I agree with what you just said about the difference in response and effectiveness. Should we change the very last word to "differential effectiveness"?

DR. TUCKSON: So the response is too narrow. "Differential drug" --

PARTICIPANT: "Effect," because of what Steve was talking about. That encompasses it.

MS. ASPINALL: That deals with my discomfort as well because it broadens it at both ends.

DR. TUCKSON: So, "drug effects," or "effect," either one you want.

Good. Anyone else? Say again?

DR. AMOS: Does "response" include safety and effectiveness? Because we are talking about safety here as well. It is the same?

DR. TUCKSON: It is being said effects are both positive and negative. Good question. Thank you.

All right. With that, we will move to the next one. Take it back, sir, freshly hydrated.

DR. FITZGERALD: Let's make sure everybody agrees with this one. No. 8B, "When drugs are shown to be more effective in certain racial and ethnic subpopulations (e.g. BiDil), FDA should encourage manufacturers to conduct additional post-market studies to identify genetic and other biological, social, behavioral, and environmental markers that may underlie the differential drug effects."

DR. TUCKSON: There is one thing I just realized. Although we did it for discussion, do we need the "e.g. BiDil"? What that does is to single them out.

DR. EVANS: It also has never really been compared head-to-head.

DR. TUCKSON: Yes. Let's leave the example out.

DR. EVANS: Jettison it.

DR. FITZGERALD: So we are going to take out "BiDil" now.

Everybody good? We are all set. Fantastic. Next.

DR. TUCKSON: Process check. We are at Gatekeepers section.

DR. FITZGERALD: We are moving. So when is the break?

DR. TUCKSON: There is none.

DR. FITZGERALD: No break? There are no breaks.

DR. TUCKSON: There is no break until we do a better calculation of whether we are going to make it.

DR. FITZGERALD: Here we go. Gatekeepers. Now, just to give you, again, a brief overview, these are the entities that can enable, halt, or redirect the course of pharmacogenomic technologies, effects integration, and patient access. These are the four groups that were identified. I'm not going to go through all the roles of each because you are all familiar with those. Let's go right to Recommendation No. 9, Slide 58.

DR. FERREIRA-GONZALEZ: Can I make a comment on that?

DR. FITZGERALD: Sure. A comment on what?

DR. FERREIRA-GONZALEZ: The Gatekeepers section. We have the role of the industry, the role of FDA, the role of CMS, and we have the role of the laboratories performing the testing, which are regulated through CLIA. Even though it might be a role of CMS, the way it is listed here CMS has a role of coverage and reimbursement. That needs to be moved earlier in the section or actually highlighted because I think it is a very important gatekeeper.

DR. FITZGERALD: Which slide are you on, No. 56?

DR. FERREIRA-GONZALEZ: Either. On No. 53 you have gatekeepers. You have industry, FDA, CMS, and other third-party payers. CMS should have, maybe, two bullets because it has different roles through the CLIA.

DR. FITZGERALD: So you want to change the text of the report. Why don't you write up that suggestion and give that to Suzanne to change the text. It is not going to change Recommendation No. 9 yet, though, right?

DR. FERREIRA-GONZALEZ: No.

DR. FITZGERALD: So we are going to Recommendation No. 9.

DR. TUCKSON: I will give you the language. It is Slide 56, the role of CMS and other third-party payers. "Reimbursement may not be perceived to be adequate"?

DR. FITZGERALD: Again, if you give that to Suzanne, we will take care of that. We are going right to the recommendation, as you would order us.

All right. This is Recommendation No. 9. It is found on page 74 of the report. This is on reimbursement.

"In clinical situations where a pharmacogenomics test has been shown to enhance safety and/or effectiveness of clinical management (i.e., has demonstrated clinical utility compared to alternative management strategies) and provides value comparable to or an improvement over other covered services, public and private health plans should provide coverage and reimbursement for the test and the most clinically appropriate drug as indicated by pharmacogenomic test results."

Marc, then Paul, then Joseph.

DR. WILLIAMS: This has major scope issues. We are recommending to the Secretary. The Secretary only has purview in terms of reimbursement over CMS-related payers. So that would be Medicare and to some degree Medicaid. So any reference to private health plans in this, we can all feel that way but it is not within the scope of what we can recommend to the Secretary.

The second point I would make that I think has been missed in this recommendation that is really critically important is the idea that what we really should be recommending to the Secretary is that clarification be forthcoming from CMS as to whether or not pharmacogenomic testing is going to be considered to be a preventive service and thereby not covered by CMS. The legislation basically excludes that without modification or, as at least there have been some rumors, it will be considered in the context of the disease, in which case it would be covered.

That is the critical issue that I think this recommendation needs to address, that the Secretary clarify with CMS how these tests will be treated by CMS, if that is a fair statement to Barry.

DR. FITZGERALD: Just a point of clarification. Suzanne, go ahead.

MS. GOODWIN: Well, I suppose two points of clarification. The first one, that recommendation is in the Coverage and Reimbursement Report, and I think we do in the text of the report reference that particular recommendation.

I know at one point during the development of these recommendations we did have a specific one saying exactly what you said and reiterating what the Coverage Report says, and after discussion amongst the taskforce it was decided that it would not be included in this set of recommendations. Personally, I am not recalling the discussion why it was in there.

DR. WILLIAMS: I'm sorry. This is specifically to ask for the clarification about how these pharmacogenomic tests will be considered by CMS. Is that what we are talking about?

MS. GOODWIN: Yes.

DR. WILLIAMS: If it is in the Coverage and Reimbursement Report, I think we should --

MS. GOODWIN: Oh, I'm sorry. Not specifically to do with pharmacogenomics. The recommendation that was in this report asked for clarification how the screening exclusion policy of CMS applies to PGx tests.

DR. WILLIAMS: Well, again, my personal opinion is I think it absolutely has to be in here.

DR. FITZGERALD: I have Paul, and then Joe, and then Barry and Marc.

DR. BILLINGS: In this particular one, I would prefer to take out the clause "comparable to or improvement over other covered services." This would allow for this to have to do with comparison to other covered services or de novo improvements. In other words, as long as they deliver value, what do we care if it is covered before or not.

Secondly, I would like to see the word "adequate reimbursement," or some other modifier of "reimbursement," be put in there, since we all know that coverage and reimbursement can be inadequate.

Then, finally, that --

DR. FITZGERALD: On that second one, where would you put "adequate"?

DR. BILLINGS: "Adequate" before "reimbursement."

DR. FITZGERALD: Before "reimbursement." Thank you.

DR. BILLINGS: Then, finally, to what Marc just said, it is true that we can only recommend policies that could be implemented CMS, but we could hope or we could wish that, as some payers do follow CMS protocols.

DR. FITZGERALD: That I think was our intent in drafting it.

DR. BILLINGS: You might even say that.

DR. FITZGERALD: I have to check my list here. Mara. Oh, Joseph was next. I'm sorry. Joseph. Sorry, Mara.

DR. TELFAIR: It is okay. I actually was agreeing with Paul the Lesser on the second comment that he made. That was going to be part of mine. So I would just agree with that.

DR. FITZGERALD: Thank you. Mara and then Barry.

MS. ASPINALL: I also agree with what Paul had said, but I'm struggling with the beginning piece about "in clinical situations." By definition, if it is already in a clinical situation, there either will have been reimbursement or coverage or not. So I don't think we need that phrase at the beginning.

DR. FITZGERALD: Just start with "where."

MS. ASPINALL: Right. That was number one. Number two is, does it need to meet a standard above, "when it says to enhance safety or effectiveness of clinical management" or to show effectiveness of clinical management? I didn't know what the intention was there; that it is above a standard of what existed now?

DR. FITZGERALD: Right. In order to change reimbursement policy.

MS. ASPINALL: Let me come back to that.

DR. FITZGERALD: Barry.

DR. STRAUBE: I have to agree where Marc was headed. As written here, it is again possibly a meaningless recommendation because we are governed by statute in terms of how we cover things. Safety and effectiveness is the way coverage decisions used to be made under HCFA back before 1995. Anything FDA-approved as safe and effective was covered.

That is not the case anymore. "Reasonable and necessary" we are struggling with trying to once again define. We are getting comparative effectiveness, let alone possibly cost effectiveness, that is slowly starting to work its way in.

Making a coverage decision is the way I am reading this. It is almost instructing us. We don't use value. That is not anywhere in terms of coverage decision policy.

We are already starting to do this. That is why I'm here today struggling with this issue of if the law says screening is never covered, if the law says prevention is but it has to be enacted by Congress, could we somehow construe this to be a diagnostic test linked back usually to symptoms or physical findings but possibly to family history and to other entities.

So there is a whole way of approaching this that could be extra-statutory or could be requiring a statutory approach. When you read the preamble and everything else that leads up to this recommendation, people are struggling with how do we change the Medicare program in particular to even allow us to make a coverage decision. It has nothing to do with value.

DR. FITZGERALD: Do you have a recommendation for how we can reword this?

DR. STRAUBE: Well, again along the lines of what Marc was saying.

DR. FITZGERALD: Take a look at what we have. Where we are at the moment is, "When a pharmacogenomics test has been shown to enhance safety and/or effectiveness of clinical management (i.e., has demonstrated clinical utility compared to alternative management strategies) and provides value, CMS and other federal health insurance programs should provide coverage and adequate reimbursement for the test and the most clinically appropriate drug as indicated by pharmacogenomics test results."

Is that closer; is that further? I'm going to do Marc and then Mara.

DR. WILLIAMS: I think this gets at the point that Barry was making. You are basically telling Medicare how to make its coverage decisions and you are using language that is not consistent with the CMS language on how they make those coverage decisions.

I would default back to a recommendation that would state that the Secretary

explore with CMS the issue of whether pharmacogenomic tests will be excluded from coverage based on screening or prevention language or whether there are non-statutory solutions that would allow consideration of coverage using the usual mechanisms under which CMS operates.

I think that is what we can actually tell the Secretary that can actually be accomplished by a DHHS group.

DR. FITZGERALD: Reed and then Mara.

DR. TUCKSON: I don't want to struggle with the word "adequate." Once you start putting those kind of words in this kind of thing, you open up enormous contractual issues and debates and fighting and so forth. I just think you reimburse it. The adequacy is perceived by whoever it is perceived by.

DR. FITZGERALD: Where was the adequacy part? That was in front of "reimbursement," right? You want "adequate" struck.

DR. TUCKSON: Right.

DR. FITZGERALD: I have Mara and then Jim.

MS. ASPINALL: I'm closer to where Marc was. Before I wordsmith, but I understand the need, I want to take it up a level. Was the idea here the fact that if there are tests for which pharmacoeconomics relevant, useful -- I'm not using the perfect words here -- we want them covered? That is what I'm struggling with.

There is not a comparable piece. The headline is reimbursement for pharmacogenomic products. The recommendation only talks about reimbursement for pharmacogenetic tests. So my first question is, is there an assumption that if it is a pharmacogenomic-related drug it will be reimbursed? That is probably not a terrible assumption, but I'm assuming that that is there.

So I wanted to get it up a level to not get to quite so much detail but rather say the group is in favor of tests that are pharmacogenomic, that are related to tests that are related to drugs that have gone through this process that we have outlined in the other recommendation. HHS should find a way to cover these because, by definition, if we have done all this, we have shown the basic research, we have shown the translational research, and then the test isn't covered, there will be no incentive to create these tests beyond that basic research.

DR. FITZGERALD: Reed has a question. Go ahead.

DR. TUCKSON: Let's take it outside of this for a minute and let's talk about all the manufacturers of nuclear imaging machines. At the end of the day, does CMS have to cover every new nuclear imaging machine out there?

In this case, does this open the door to no matter what it is? Let's say you have a great test for a drug that CMS may say is beyond the realm of the formulary today. Does this open the door to everything being open on the table now?

MS. ASPINALL: I look at it as it may be different options for the same thing in the same way that many different drugs are approved for the same condition. The way this is going with pharmacogenomics, my suspicion is actually there won't be multiple tests initially. A test for X

condition is covered and there may end up being three tests for X condition, but the patient only needs to go through it once. So the market may go to the lowest-price one.

Indeed there may be five manufacturers of nuclear imaging machines. A hospital only needs one, they choose the one they want, and that test or that machine is covered to get the answer to decide who best or how best to use that particular drug.

I guess I'm saying there might be multiple tests but each patient only needs one.

DR. WILLIAMS: I think I can clarify this.

DR. FITZGERALD: I hate to tell people; we are only a little over halfway through.

DR. WILLIAMS: The specific language that we are dealing with, without naming it as such, is really addressing the issue of the formulary. At the present time, pharmacy benefit managers and health managers use formularies to try and control cost. If you have compelling data that shows that a certain individual would benefit from a certain drug, then are formularies really appropriate.

Again, getting back to what CMS can do, under Medicare Part D and to some degree Medicare Part C, if there was compelling evidence that there were pharmacogenomic differences let's say within the SSRI category, CMS could say to its contractors we are not going to allow you to apply a formulary to this class of medications. You need to consider medical necessity based on the pharmacogenomic information that will lead to best dosing.

So the issue is that we are kind of talking around the issue. "Clinically appropriate drug" is really referring to the idea that there is a best drug that could be identified for an individual and getting away from using formularies.

DR. TUCKSON: I'm going to be real quick because the moderator is moving us forward. I just want to make sure that this does not get read as just because you can come up with a terrific pharmacogenomic test and match it to a drug therefore CMS is obligated to cover that test and that drug when they may not have been willing to cover that drug in the first place.

DR. FITZGERALD: I have Jim and Barry and Chira. We are going to be here forever. Go ahead. Let's focus on getting a recommendation.

DR. EVANS: I understand. I think Barry's points are really well taken. It would be silly of this Committee to make recommendations that can't be enacted or are not under the purview of CMS.

I just have a question. Is there any utility in this Committee to suggesting a categorization for pharmacogenomic tests, for example as diagnostic tests, that would short-circuit some of this and make them covered or coverable more easily when they meet criteria in improving efficacy and effectiveness? That is my question, basically for you, Barry, I guess.

DR. FITZGERALD: Barry, go ahead.

DR. STRAUBE: I'm not sure I understand the question.

DR. EVANS: Could there be any utility in us making a recommendation about how to categorize pharmacogenomic tests that would then allow more action or leeway on the part of HHS?

DR. STRAUBE: I was going to suggest a slightly different thing, and I'm not paying attention to this language at all. It would be to recommend to the Secretary that he ask CMS to produce a guidance document on current status of genetic testing as it relates to pharmacogenomics, including surveying the private sector to see what coverage was extant in that setting and to make some recommendations to him as to what options were available. Something of that nature.

DR. EVANS: Maybe say with the intent of being able to cover improved tests or improved use of drugs.

DR. FITZGERALD: Here we go. Let's take a look. "CMS should clarify how the Medicare screening exclusion policy applies to pharmacogenomic tests" -- no. That is not it. Try it again. Barry, do it again.

DR. STRAUBE: This Committee recommends to the Secretary that he request --

DR. FITZGERALD: Hold on, hold on. "This Committee recommends to the Secretary." Go ahead.

DR. STRAUBE: That he request that CMS produce a guidance document.

DR. FITZGERALD: "CMS should produce a guidance document.

DR. STRAUBE: Detailing current coverage issues pertaining to pharmacogenomics in the Medicare program, including surveying the private sector for what is currently covered extant there.

DR. FITZGERALD: Hold on. "Pertaining."

DR. STRAUBE: Forget the "extant."

[Laughter.]

DR. FITZGERALD: Keep watching what is going on in that lower paragraph, and we will keep working on this as Suzanne tries to get it down.

"CMS should develop a guidance document detailing current Medicare coverage issues pertaining to pharmacogenomics tests." No?

MS. ASPINALL: No, "pharmacogenomics."

DR. FITZGERALD: "Pharmacogenomics."

MS. ASPINALL: "Pharmacogenomic coverage" as opposed to just tests, because we have issues as to whether drugs are going to be approved as well.

DR. FITZGERALD: So, "detailing current Medicare coverage of pharmacogenomic drugs and diagnostics"?

MS. ASPINALL: No.

DR. FITZGERALD: No. Just "pharmacogenomics." "Detailing current Medicare coverage of pharmacogenomics," period. Everybody is good with that? Okay. Next.

DR. STRAUBE: "In doing so, CMS should survey the commercial sector policies and should identify future coverage issues." We can word that better.

DR. FITZGERALD: Now that, I'm presuming, is all you are suggesting in this. So the whole top part can get tossed.

MS. GOODWIN: Can I ask, what is the commercial sector policies you are talking about? Private health plans.

DR. STRAUBE: Yes.

MS. GOODWIN: What is the purpose of that survey?

DR. STRAUBE: To see what the current coverage policies are so that we can compare that to restrictions under Medicare and try to get them in alignment, if possible. We are going to find that they are different. Whether they are grossly different or not remains to be seen.

DR. WILLIAMS: That is actually be done in the area of cytogenetics and molecular diagnostics as we speak. So that is very consistent with the direction that CMS has been taking.

MS. ASPINALL: There was some interesting private sector work looking at the total cost of treatment with the addition of pharmacogenomic tests reducing the full cost of treatment.

DR. FITZGERALD: So [this is] what we have here currently. Everybody take a look so we can move on with this. "CMS should develop a guidance document." No, actually before that, "The Secretary of HHS" -- how did that begin? "CMS should develop a guidance document detailing current Medicare coverage of pharmacogenomics. In doing so, CMS should survey private health plan policies and should identify future coverage issues to identify inconsistencies in coverage." We have "identify" twice here.

MS. ASPINALL: Can I ask Barry for a friendly amendment? Do we need "inconsistencies" or just "to understand current coverage"?

DR. STRAUBE: We need to understand current coverage and also, again based on this Committee's report, how do we get to some of the other issues that have been raised and/or if we can't, why not.

DR. FITZGERALD: Right now everything has to be in terms of words that are going into that recommendation. I just want to be sure here. "Plans and policies to identify inconsistencies in" -- we are having problems capturing all this.

DR. STRAUBE: "Inconsistency." I'm not sure where that word is coming from.

DR. FITZGERALD: Don't get rid of "inconsistencies."

DR. STRAUBE: Do get rid of it.

MS. ASPINALL: "To identify differences in coverage between Medicare" --

DR. STRAUBE: I think, again the differences are not the primary issue. The real key issue is what can we cover or not right now. If we can't cover anything in terms of tests, we can cover the medications.

DR. FITZGERALD: Let's just focus on you putting words up on the screen so we can all agree to the words. "In doing so, CMS should survey private health plan policies to identify differences in" -- is this okay so far? "To identify differences in Medicare and private health plan coverage and future coverage issues."

DR. STRAUBE: "Identify differences in Medicare and private health plan coverage."

DR. FITZGERALD: "To identify differences between Medicare and private health plan coverage and future coverage issues?

DR. STRAUBE: Sure. I'm okay.

DR. FITZGERALD: You are comfortable with that.

DR. STRAUBE: Although I would put "Medicare coverage and reimbursement." In fact, "coverage, reimbursement, and oversight."

DR. FITZGERALD: Wait, no, we can't do oversight. Don't go there.

DR. STRAUBE: That's fine.

DR. FITZGERALD: This is what we have right now. "CMS should develop a guidance document detailing current Medicare coverage and reimbursement of pharmacogenomics. In doing so, CMS should survey private health plans to identify differences between Medicare and private health plan coverage." No? "And future coverage issues." "As well as future coverage issues."

They are happy so far. Paul the Not Often Heard From, yes.

DR. WISE: The original recommendation in the book and on the first slide was fairly generic. It wasn't about Medicare per se. We have just basically thrown all children out of the recommendation. That is fine if we want to be explicit about that, but there are still plenty of other issues that were originally part of the content for Recommendation No. 9 that are relevant to children and Medicaid.

So if move to what is up there now, which might be very helpful someplace else, the other programs need to be included to reflect fairly what was originally in the content of Recommendation No. 9.

DR. WILLIAMS: Is there any reason not to just have "Medicare and Medicaid coverage"?

DR. WISE: That was going to be my suggestion, if the Medicare types were happy with that.

DR. FITZGERALD: Barry.

DR. STRAUBE: Again, practically speaking though, we have less to say about Medicaid and SCHIP policies.

DR. FITZGERALD: But you have something to say.

DR. STRAUBE: We could comment on that, yes, how much we would have to say. Sure.

DR. FITZGERALD: So what I'm getting, then, is we have Medicare, Medicaid, and SCHIP. Next, Steve?

DR. TEUTSCH: I'm perfectly fine with this recommendation. I just am concerned that there were a number of things that came up in the report that related to how we tie utility and value to coverage of decision-making. I understand we were trying to push CMS for sure, but we actually got feedback from the private sector as well because they look to Medicare for guidance, or CMS for guidance and leadership on these issues. We [have to] somehow pull this together because there is also the influence that HHS has over the federal employee health benefits programs and others.

The concern was, by waiting for a report, which is great, it is going to be years until all of this really happens. We wanted to provide some guidance to the agencies that they should do this on the basis of incremental effectiveness and value. That was part of the intent to do that.

Now, we may decide we don't want to go there and this will suffice, but I just want to be sure everybody is clear that that was the reason that other recommendation was crafted the way it was.

DR. FITZGERALD: Marc. Again reminding everybody, we are only a little halfway through. Then Ellen.

DR. WILLIAMS: My response to that is basically I think that the CMS decisions have to be made on the statutory terms that they are given, which is necessity and reasonableness. So we can put that language in there, but it means nothing. We know that there are some overlaps between what we mean by utility and effectiveness and what you mean by reasonableness and necessity, but I think if we are going to reflect that here we need to reflect the language that CMS can actually act on within its purview.

DR. FITZGERALD: Ellen.

DR. FOX: I suggest you might want to survey public health plans as well as private.

DR. FITZGERALD: Public and private health plans, okay. Any other comments? Gurvaneet.

DR. RANDHAWA: Just focusing on that point, I'm not sure if we focus only on differences between the plans that that is the only thing we need to get to help inform future decisions.

DR. FITZGERALD: To identify similarities and differences.

DR. RANDHAWA: I would suggest rephrasing it, instead of making it more text, just to say "to survey current coverage policies or issues to help inform future CMS coverage," and leave it at that, whether it is similarities, differences, different criteria, whatever it may be.

DR. FITZGERALD: So you would like, "In doing so, CMS should survey current public and private health plans"? "Should survey current coverage." "Should survey private and public health plans." "CMS should survey public and private health plans to identify issues"?

DR. RANDHAWA: "To help inform their future coverage."

DR. FITZGERALD: "To help inform future coverage issues."

PARTICIPANT: Decisions or issues?

DR. RANDHAWA: "Future coverage decisions."

DR. FITZGERALD: Now we have, "CMS should develop a guidance document detailing current Medicare, Medicaid, and SCHIP coverage and reimbursement of pharmacogenomics. In doing so, CMS should survey public and private health plans to help inform future coverage decisions."

MS. GOODWIN: The second sentence needs to clarify what CMS is surveying these health plans about. That was part of the language we took out.

DR. RANDHAWA: It would be coverage decisions and how they make their own coverage. That is the intent of the survey, I'm guessing.

MS. GOODWIN: About how they make their coverage decisions?

DR. FITZGERALD: "Survey public and private health plan decision-making," or whatever. Mara.

MS. ASPINALL: I like "decision-making," and end with "coverage and reimbursement decisions," so it is comparable to the first sentence.

DR. FITZGERALD: "Should survey public and private health plans about their decision-making"; is that right? "About their PGx coverage decision-making" or just "decision-making"?

MS. ASPINALL: No, just "decision-making."

DR. FITZGERALD: "About their decision-making processes" or "policies"? "Policies," maybe? "Policies," probably.

PARTICIPANT: "Processes" if it is decision-making.

DR. FITZGERALD: "To help inform future coverage and reimbursement decisions." Now we are going to try this. No, we are not. Martin.

MR. DANNENFELSER: I don't know if the "in doing so" ties as well now to that first sentence or we should just say "CMS should also survey."

DR. FITZGERALD: Just get rid of "in doing so."

MR. DANNENFELSER: Say "should also."

DR. FITZGERALD: "CMS should develop a guidance document detailing current Medicare, Medicaid, and SCHIP coverage and reimbursement of pharmacogenomics. CMS also should survey public and private health plans about their decision-making processes to help inform CMS' future pharmacogenomics coverage and reimbursement decisions." So, just their decisions or anyone else's decisions? "Its future," okay.

"CMS also should survey public and private health plans about their decision-making processes to help inform its future pharmacogenomics coverage and reimbursement decisions."

How are we doing now? Let's see. I think most everybody has been beaten into a complete stupor.

DR. STRAUBE: Kevin, as you are surveying, as a point of interest to folks, I can, in some cases with the Medicare program, ask for public comment on guidance documents. So this might include the capability of seeking public comment, too. I don't know that we want to put that into the recommendation.

DR. FITZGERALD: No, no.

DR. STRAUBE: Just so people know.

DR. FITZGERALD: Emily.

DR. WINN-DEEN: I just have a concern that by only talking about surveying people's decision-making processes we are not going to get information on their actual coverage and reimbursement. Do we want that as well as their processes? Yes, okay.

MS. ASPINALL: Yes, I think that was the intention.

DR. FITZGERALD: So we want what now?

DR. WINN-DEEN: "Decision-making processes and coverage/reimbursement decisions."

DR. FITZGERALD: "Decision-making processes and"?

DR. STRAUBE: "And policies."

DR. FITZGERALD: "And policies," "coverage policies." That is what we were trying to get at. All right.

One of them has to go longer than all the rest, so hopefully this is it. Here we are. Recommendation No. 9, going once, going twice?

[No response.]

DR. FITZGERALD: And it is finally put to rest. There we go.

MS. AU: Kevin, before you go to No. 10, can I say something? It is not about No. 9. No. 9 is fine.

This seems to be the only place we are talking about reimbursement. Some of the other reimbursement issues we had brought up in our Reimbursement and Coverage Report. It just seems like we have to put some recommendation in there about some of the things that we mentioned in there about genetics expertise.

DR. FITZGERALD: It is referenced, certainly, in the report, that is correct. Yes, it is referenced in the earlier report on coverage.

MS. AU: I think that in our reports that have been after the Coverage and Reimbursement Report, like the Large Population Study one, we actually referenced the report in the recommendation.

DR. FITZGERALD: So you are saying we could do what we did here before and put a little footnote or something?

MS. AU: Not for Recommendation No. 9. I'm just saying as a separate recommendation. This is the only area where you talk about reimbursement. Later on you do talk about education and all that other stuff, but it doesn't talk about how you pay for some of those things to help with the understanding and education. So you are only going to talk about reimbursement in this one section.

DR. FITZGERALD: Let me get this right. You are not talking about Recommendation No. 9. You actually want Recommendation No. 9B. You are really going to hurt me.

Andrea.

DR. FERREIRA-GONZALEZ: We can say specifically that the issues that were covered in that report are still current and then the Secretary should go back and relook at that particular report.

DR. FITZGERALD: Yes. Do we want to make a recommendation to that extent?

DR. FERREIRA-GONZALEZ: That's it. We are saying that the issues dealt with in that report are still currently valid.

DR. FITZGERALD: What we are doing is this 9B right here. Come on, Sylvia. You started this.

DR. WILLIAMS: "The issues raised in the SACGHS Coverage and Reimbursement Report impact this report, and the Committee recommends that these issues be" --

DR. FITZGERALD: "Therefore, the Secretary should revisit" --

DR. WILLIAMS: "Review and apply and implement the recommendations from that report."

MS. AU: "To move forward on those recommendations." Act on those recommendations.

PARTICIPANT: Can I ask what the tenets of the other report were? We have to read all the reports if we come on the Committee.

DR. FERREIRA-GONZALEZ: Kevin, you might want to borrow from the report.

DR. FITZGERALD: No, we can't. We have to have the language.

DR. FERREIRA-GONZALEZ: "As the issues are identified in the coverage and reimbursement of genetic tests and services" -- right there.

DR. FITZGERALD: There it is. Thank you, Andrea. Here we have Recommendation No. 9B, adding to our list of recommendations. "As the issues identified in the SACGHS Coverage and

Reimbursement Report are still current, SACGHS urges HHS to act on the report's recommendations." Sylvia, is that okay?

MS. AU: Yes.

DR. FITZGERALD: It gets right to what you wanted. Excellent. Everybody is okay? Good? Wonderful.

Here we go. This is the Implementation Section. I am, again, not going to go through all these details. These are the issues we are going to try and address: education and guidance, IT, economic implications, ELSI, and coordination of HHS activities. So let's go right to 10A, which is Slide 65, and that is on found on page 90 of your report.

The recommendation is that "HHS should assist state and other federal agencies and private sector organizations in the development, cataloguing, and dissemination of case studies and practice models relating to the use of pharmacogenomics technologies."

Comments, questions, confusion?

[No response.]

DR. FITZGERALD: Complete agreement. That we like. Everybody is good with this. Good. Next.

No. 10B. This is use of pharmacogenomics technologies in clinical practice and public health practice.

"HHS should assist professional organizations in their efforts to help their memberships achieve established competencies on the appropriate use of pharmacogenomics technologies. HHS also should encourage and facilitate collaborations between the organizations and the federal government around these activities."

DR. BILLINGS: Are there established competencies on pharmacogenomics activities?

DR. FITZGERALD: Are there established. "Should assist in their efforts to help achieve established." So you are saying do we have any now.

DR. BILLINGS: That is what I'm saying.

DR. FITZGERALD: My understanding was, if there are any, they are few and far between.

DR. BILLINGS: I don't think there are any, actually.

DR. FITZGERALD: Oh, I see what you are saying.

DR. FERREIRA-GONZALEZ: For example, the ASCO and CAP, that is a competency.

DR. BILLINGS: That is about as close as you can get to one, I think.

DR. FERREIRA-GONZALEZ: Yes, so we do have one.

[Laughter.]

DR. FERREIRA-GONZALEZ: Maybe we can encourage to have more.

DR. BILLINGS: If you take out "established" you get it, I think.

DR. FITZGERALD: So, take out "established." Good. Any other comments, questions, decisions about this one? Let's accept this as it is now. Going once, twice? No. Ellen.

DR. FOX: Change "memberships" to "members."

DR. FITZGERALD: "To help their members." Those are the kinds of suggestions we like: brief.

Here we go. Everybody is happy? We are happy? Yes. We are moving along to 10C. There are a lot of 10s, people. This one is on page 91.

This is pharmacogenomic technologies in clinical practice and public health practice. "As evidence of the clinical validity and clinical utility for a pharmacogenomics technology accrues, HHS should support the conduct of systematic reviews and technology assessments to summarize the evidence base. These systematic reviews and technology assessments should be disseminated to professional organizations to facilitate the development of clinical practice guidelines."

Yes, Marc.

DR. WILLIAMS: I would just remove "professional organizations" because there are lots of groups that will develop clinical practice guidelines. They just need to be disseminated to facilitate the development of clinical practice guidelines. It may be AHRQ or others that would do that.

DR. FITZGERALD: Oh, I see. "Should be disseminated to facilitate." Good. Yes, Mara.

MS. ASPINALL: Are these reviews of the drug and this is post-market, so after the drug has been launched?

DR. FITZGERALD: "HHS should support the conduct of systematic reviews and technology assessments to summarize the evidence base." This is post-market, yes. Oh, it could be more?

DR. WILLIAMS: Well, if there is a good evidence base before somebody brings something to market, then there is no reason that that couldn't be done. I don't think it defines whether it is pre- or post-market.

DR. FITZGERALD: No, it doesn't limit it, but it is certainly post-market.

DR. WILLIAMS: What we are really talking about here is transparency of data and putting that on the public domain so that people can use it.

MS. ASPINALL: I'm trying to understand for a drug how this is different from what exists now or it is just that it is transparently available.

DR. FITZGERALD: Well, the transparency was certainly something we were attempting to achieve, that's for sure. I can't give you all the details on how that might differ from what exists now, not knowing it all, but Gurvaneet will do that.

[Laughter.]

DR. RANDHAWA: I will try. I think the intent here was focusing on the technology assessment and systematic evidence reviews, which are contingent on publicly available information, but also the fact that there aren't that many around. So even though there is a lot of information, its synthesis isn't that common, so that is what we were trying to encourage here.

MS. ASPINALL: So when you say "technology," you mean --

DR. RANDHAWA: It is broad.

MS. ASPINALL: -- microarrays, or do you mean a particular drug category? I'm just trying to figure out who is the person and what would they be doing this on.

DR. RANDHAWA: These are folks like the evidence-based practice centers, the Cochrane Collaboration, who will evaluate all different domains, whether utility, validity, anything of any drug, diagnostic device, anything that is relevant to clinical practice.

MS. ASPINALL: Those kind of organizations would be the people that you are talking about here that would have to do that, or that we are recommending to do that.

DR. RANDHAWA: Right.

MS. ASPINALL: Does that need to be clearer?

DR. TEUTSCH: No. This is already in place for other things, and this is just saying it should be applied to pharmacogenomics as well.

DR. FITZGERALD: Anyone else? Paul.

MR. MILLER: A wordsmithing thing. It may not have any meaning. But I just noticed that as we go through the 10s, 10A, -B, -C, and -D, we are using the words, "assist," "support," and "facilitate," in each of them. Do they mean the same thing? Are they asking HHS to do the same thing in each of those contexts, or do they mean different things? If so, should you use the same word? It is just sort of a general question.

DR. FITZGERALD: So, "assist," got it. "Should facilitate," "should support."

MR. MILLER: One may have fiscal or resource implications. Maybe they all do. I'm just not sure.

DR. FITZGERALD: Yes. I'm just trying to see if I'm picking up any differences. I don't think so.

DR. WILLIAMS: I don't think there is anything in the text of the document that would support the fact that we had specific intent with any of those verbs.

DR. FITZGERALD: No, I don't think so.

MR. MILLER: It may be a distinction without difference. I was just asking.

DR. FITZGERALD: Right. No, I don't think so.

MR. MILLER: Somebody just pulled out the thesaurus, I think.

DR. FITZGERALD: We didn't want to be boring.

PARTICIPANT: At Recommendation No. 10 I think it is a little late.

[Laughter.]

DR. FITZGERALD: We never said we achieve what we want, that's for sure. Brevity we have not achieved.

No. 10C is where we are now. "As evidence of clinical validity and clinical utility for pharmacogenomics technology accrues, HHS should support the conduct of systematic reviews and technology assessments to summarize the evidence base. These systematic reviews and technology assessments should be disseminated to facilitate the development of clinical practice guidelines."

People are happy with that? Looking around, I don't see any great suffering. We will say 10C is good and move on to 10D.

This is on the use of pharmacogenomic technologies again in clinical practice and public health care practice. "HHS should facilitate the development of evidence-based clinical practice guidelines and dosing guidelines by supporting consensus-building efforts among guideline developers. These consensus-building efforts should include development of standards that define the minimum levels of evidence required to support guideline decisions. These standards should take into account the clinical contexts (e.g., prevention, diagnosis, treatment) in which the pharmacogenomics test may be offered. Consensus-building efforts also should include standardization of guideline development methods."

I think most of the Committee has passed into unconsciousness, which is a good thing. This is what we have been working for.

[Laughter.]

DR. FITZGERALD: How are we? We are looking good. Gurvaneet.

DR. RANDHAWA: I think this wording is fine. I have nothing to add to this.

DR. FITZGERALD: Good. Thank you.

DR. RANDHAWA: But I did want to bring back one point that Steve had mentioned earlier, which was the original intent of Recommendation No. 9 on reimbursement. Is this a place where we can think about adding clinical utility information and how it informs coverage decisions or is that recommendation not being considered?

DR. FITZGERALD: In 9B, since we have dragged in the entire previous report, I think --

DR. RANDHAWA: I don't know that that had the clinical utility and incremental benefit in there.

DR. FITZGERALD: I would have to look. Yes, Scott.

LT. COL. McLEAN: By reference to 10C, the clinical utility is right there. It is folded in because of the adjunctive recommendation.

DR. WILLIAMS: In some sense it is a symptom in search of a disease. If there really is demonstrated utility and incremental effectiveness, only idiots are not going to adopt that, or if there is specific contract language that prevents them from doing anything genetic, which exists. I don't know that we necessarily need to point that out. If the evidence is really compelling that this works, people will try and facilitate that happening.

DR. FITZGERALD: Thank you. Sylvia.

MS. AU: Can we get rid of the last sentence by making the first sentence "HHS should facilitate the standardized development of evidence-based," blah, blah, blah?

DR. FITZGERALD: Wait a minute now. "Should facilitate the standardized development of evidence-based."

MS. AU: "Clinical practice guidelines."

DR. FITZGERALD: What you are trying to catch is the standardization of guideline development methods in the first sentence?

MS. AU: Yes.

DR. FITZGERALD: Marc.

DR. WILLIAMS: I'm not sure it is necessary because there is already a standardized process established with Guidelines.gov. I don't think we are talking about any sort of a repository.

DR. FITZGERALD: Get rid of that sentence. Brevity is good, right? How about the brevity of moving along to the next one? Everybody good on 10D?

[No response.]

DR. FITZGERALD: Let's go to 10E. This is another one of the recommendations that came directly from the public comments. "To inform the development of pharmacogenomic tests and dosing guidelines, HHS should fund clinical trials that provide evidence on whether pharmacogenomics information is clinically useful and, if so, how to use this information in addition to other relevant factors (e.g., gender and age of patient, other medications being taken)."

Joe.

DR. TELFAIR: I'm wondering if part of this has not already been covered in previous recommendations.

DR. FITZGERALD: There is a little overlap, but we are not as specific as what we have here saying HHS should fund clinical trials to provide evidence.

Yes, Gurvaneet.

DR. RANDHAWA: There are two issues here. I think one is, I'm not sure we can always get this information from trials. It may be clinical studies, some trials, some not trials.

DR. FITZGERALD: Clinical studies, okay.

DR. RANDHAWA: The other aspect is, to some extent we have discussed this in a more generic form in the other when we were trying to improve the evidence base per se. Dosing is a very specific aspect. That is only one part of pharmacogenomics. One can argue about the other part, which is targeting the drug or tailoring the drug and what drug to take. Are we focused only on the dosing?

DR. FITZGERALD: The reason dosing is in there is it was specifically mentioned as needing to be in there by the members of the taskforce, not just to leave it. They thought it needed to be emphasized. That was the reason it is there.

Yes, James.

DR. EVANS: A question. Do we really need that last clause? "If so, how to use this information, in addition to other relevant factors." What does that add to it, and is that necessary?

DR. FITZGERALD: After the "and if so," right? You want to possibly end it right after "pharmacogenomics information is clinically useful"?

DR. EVANS: Yes.

DR. FITZGERALD: So we are just saying we don't need to emphasize the fact that integrating it with other --

DR. EVANS: We are looking at whether PGx is clinically useful. I'm not sure why we need that last part.

DR. FITZGERALD: Joe.

DR. TELFAIR: I would concur because I think we have already covered this part. I would concur with him.

DR. FITZGERALD: Oh, okay. Get rid of that.

So right now, take a look at what we have. What we have is, "To inform the development of pharmacogenomics tests and dosing guidelines, HHS should fund clinical studies that provide evidence on whether pharmacogenomics information is clinically useful." Basically, we are pushing the studies.

Great. I'm looking around. Going once, going twice.

[No response.]

DR. FITZGERALD: Yes, indeed. We are on to 10F. Thank you.

No. 10F. "Professional organizations are encouraged to submit clinical practice guidelines that they develop for pharmacogenomics testing to AHRQ's National Guideline Clearinghouse to facilitate dissemination and encourage their implementation and use."

Actually, I suppose we could phrase this a little differently and say "The Secretary should encourage professional organizations to submit."

DR. WILLIAMS: Again, I would just raise the issue with are we trying to be very specific about professional society organizations. There are healthcare delivery systems that also develop guidelines. I would want it to be a little bit more generic.

DR. FITZGERALD: So, "professional organizations and"?

DR. WILLIAMS: Or just say, "The Secretary should encourage organizations to submit."

DR. FITZGERALD: Good. Am I missing somebody? Okay. Great. Up there we have now, "The Secretary should encourage organizations to submit clinical practice guidelines that they develop for pharmacogenomics testing to AHRQ's National Guideline Clearinghouse to facilitate dissemination and encourage their implementation and use."

Everybody seems happy with that. Wonderful. On to 10G. This is on page 94 of your report, still on clinical practice and public health practice.

"FDA and drug manufacturers should focus more attention on ensuring that all relevant pharmacogenomics information is included in drug labels in a timely manner. When a pharmacogenomics test is mentioned in a drug label, information should be included about the test's analytical validity, clinical validity, clinical utility, dosing, adverse events, or drug selection for clinicians to use when making treatment decisions based on pharmacogenomics test results. FDA should provide guidance on the standards of evidence that must be met for pharmacogenomics information to be included in the label."

This is our labeling recommendation. People seem to be happy with that. Good. Oh. Paul.

DR. BILLINGS: Was there a discussion about different parts of the label? That is, there is real estate on the FDA labels, and the question is I wonder whether the group thought about what part of the label we are talking about here.

DR. FITZGERALD: We did not. We thought it best to leave to FDA to decide that, not that we would make a specific recommendation to that content. Yes, Mara.

MS. ASPINALL: A related question. If a test is a laboratory-developed test and the FDA does not review it, how is that thought about in the midst of putting it on the label? Would the FDA get it from CLIA? How would laboratory-developed tests fit into this recommendation?

DR. FITZGERALD: Oh, okay.

DR. WINN-DEEN: I think it depends on what the test is. Obviously, if it goes through the codevelopment process, then you can have labels pointing at labels.

Let's use your Warfarin example. In that label it said genetic factors are a part of the other list of factors you should consider in Warfarin dosing. They didn't really go into even the specifics of exactly which snips should be tested for.

So I think it depends on what the evidence base is and what the commercial availability of a specific test is how much information you can put on the drug label. I think we wanted to just leave a laundry list of things that could go in there, but they don't all necessarily have to go in there.

DR. FITZGERALD: I have Ellen and then Steve.

DR. FOX: Shouldn't "or" be "and/or"?

DR. FITZGERALD: Where is that? Oh, you mean "adverse events."

DR. FOX: There is a long list of things that should be --

DR. FITZGERALD: "And/or drug selections," is that the "or" you are talking about? Thank you. Steve.

DR. TEUTSCH: Again, we are making recommendations for manufacturers here. It maybe should just say that FDA should work with manufacturers, and then get rid of the next phrase, to ensure that all relevant PGx information appears in labels. It would just be simpler.

DR. FITZGERALD: Oh, I see. Okay. Wait a minute. Let's make sure we get that. Steve, take a look.

DR. TEUTSCH: Yes.

DR. FITZGERALD: Paul.

MR. MILLER: I was just going to make the same point.

DR. FITZGERALD: Wow, we are getting on the same wavelength. That would be a really scary thing.

Excellent. Here is what we have. "FDA should work with manufacturers to ensure that all relevant pharmacogenomics information is included in drug labels in a timely manner. When a pharmacogenomics test is mentioned in a drug label, information should be included about the test's analytic validity, clinical validity, clinical utility, dosing, adverse events, and/or drug selection for clinicians to use when making treatment decisions based on pharmacogenomics test results. FDA should provide guidance on the standards of evidence that must be met for pharmacogenomics information to be included in the label."

Paul.

DR. BILLINGS: Can I just ask another point of clarification. Was it the subcommittee's view that the impact of the current labeling is an effective one?

DR. FITZGERALD: The impact of the current labeling?

DR. BILLINGS: I'm trying to put this in a politic way. Polite way, yes. Maybe "polite" is the right word, since I'm sitting next to Steve here.

[Laughter.]

DR. BILLINGS: But I'm just curious; is it working today?

DR. GUTMAN: Nobody believes anybody reads the labels.

[Laughter.]

DR. FITZGERALD: Yes, Steve.

DR. TEUTSCH: Just to be fair, FDA, number one, has improved the label, but beyond that, it is absolutely critical for what can actually be said about a drug. Although, I agree, docs won't sit there and read the label particularly, it is critical to what the companies can promote and educate about.

DR. FITZGERALD: Once, twice, three times?

[No response.]

DR. FITZGERALD: It is time to move on to 10H. We are picking up here.

DR. TUCKSON: It is 3 o'clock. You have the potential for a quick break. You can have a choice. You can just wander over and grab your coffee as the discussion continues to unfold, which is probably the best thing to do. You are always invited to use the facilities whenever you so desire.

[Laughter.]

DR. TUCKSON: I think we should just press on through. Just know that there is some stuff there. You just go get it quietly and don't trip over your neighbor.

DR. FITZGERALD: No. 10H. "NIH and FDA should continue expanding the Internet-based DailyMed project, which provides up-to-date, real-time prescription drug label package insert information to people with Internet access. To ensure that all sectors of the public have access to this information, FDA and NIH should develop other ways to disseminate this information."

This was a specific information dissemination recommendation because, obviously, information is power. Everybody seems good with this. Good idea, like the wording. Great. Once, twice.

[No response.]

DR. FITZGERALD: And we are out of the 10s.

Recommendation 11A. There is light at the end of the tunnel, folks, and it is not a train. This is public education and engagement. "To inform the public about the availability, benefits, risks, and limitations of pharmacogenomics technologies" -- oh, I'm sorry. This been flipped.

MS. GOODWIN: If you look at 11B, that is the new 11A.

DR. FITZGERALD: Oh, I'm sorry. Gotcha.

MS. GOODWIN: 11A and 11B are flipped.

DR. FITZGERALD: That's right. If you look in your report, this is 11A. What was handed out to you as the slides was something we did earlier in the week that we changed. Yes?

MR. MILLER: Could I just make a quick wordsmithing? It is actually Sylvia, so she gets blamed.

MS. AU: I haven't even read it yet.

MR. MILLER: No, this is on 10H.

DR. FITZGERALD: Oh, no, 10H is gone. No, go ahead.

MR. MILLER: It is a deletion. Basically, there is a redundancy. If you look at the first sentence, "NIH should continue expanding Internet-based project," blah, blah, blah, "information to people with Internet access." If it is Internet-based, it is people with Internet access. So I think you can drop that.

DR. FITZGERALD: The reason I think that is in there is the fact that in the next sentence we say people who do not have access to the Internet will also need to have this. So that was why it was there. It was a matter of emphasis.

MR. MILLER: A redundant matter of emphasis.

DR. FITZGERALD: Yes, we were trying to emphasize it over and over.

[Laughter.]

DR. TUCKSON: Do not let Sylvia lead you astray again.

MR. MILLER: I'm moving next to Paul.

[Laughter.]

DR. FITZGERALD: Now, 11A. Look at 11B, which is Slide 74 in your handout, but it is 11A in your report. This is also at page 96. We are all on the same page, or look up on the screen.

"To inform the public about the availability, benefits, risks, and limitations of pharmacogenomic technologies, HHS should ensure that credible educational resources are widely available through federal websites and other appropriate media."

Again, here the idea is to get the information out to the people and not only through Internet access but also through other means for people who do not have Internet or do not use it well.

Great. Everybody is happy with this? So am I. No, Joseph isn't.

DR. TELFAIR: I'm actually fine. There is just one tweaking of it. I'm not quite sure what the "credible" means when you talk about education material. A better way to talk about it is simple, plain language. Terms like "plain language."

DR. FITZGERALD: Oh, I see what you are saying. You are getting at more than "credible." It all has to be acceptable as far as --

DR. TELFAIR: Acceptable, right. Yes. It needs to be acceptable.

DR. FITZGERALD: What is the term for that? Sylvia, what is the term for that? Accessible?

DR. TELFAIR: Right, yes.

DR. FITZGERALD: There is a genetic counseling term that we use all the time.

PARTICIPANT: Appropriate.

DR. TELFAIR: I was trying to avoid the word "appropriate."

PARTICIPANT: It is already in there.

DR. TELFAIR: It is in there, right. That is the term that is used, is "appropriate."

DR. WILLIAMS: But HHS has standards for all of their educational materials.

DR. FITZGERALD: Thank you. So that is all part of HHS. They don't put anything on the website before it goes through those people who make it. Is that good enough? The fact that they do it already is okay?

DR. TELFAIR: Well, everybody does. If they do it already and this is going to HHS without going to the lay public, then no problem. But if it was going to the lay public, then I would have a problem.

DR. FITZGERALD: Sylvia.

MS. AU: How does the Secretary ensure that only appropriate media disseminate the information?

DR. FITZGERALD: No, no, no. Not "only." "Other appropriate media." In other words, a lot of people don't have Internet access or aren't Internet savvy, so there will be other ways to disseminate the information other than something through the website.

MS. AU: "Other media." I have to help Marc with his mantra.

DR. FITZGERALD: You want to get rid of "appropriate." Just get rid of "appropriate."

[Laughter.]

DR. FITZGERALD: "To inform the public about the availability, benefits, risks, and limitations of pharmacogenomic technologies, HHS should ensure that credible educational resources are widely available through federal websites and other media."

Thank you. Marvelous. 11B. For this one, Martin?

MR. DANNENFELSER: Should we say anything like "government websites," which could take in other states and so on? We don't have control over that, I guess, right?

DR. FITZGERALD: That is "other media." All right. Good. All right. No. 11B, page 96.

"HHS should use existing public consultation mechanisms to engage the public in a constructive dialogue regarding the potential benefits, risks, and limitations of pharmacogenomics technologies. This dialogue should include an assessment of their perceptions of and receptiveness to pharmacogenomics and their willingness to participate in clinical research studies involving these technologies."

We need to look at how we spelled "dialogue" throughout the whole report, but it is either with a U-E or not, one way or the other. There is another one up there.

Yes, Joe. Joe and then Paul.

DR. TELFAIR: I just have a question on some of the thinking. Why only clinical research studies involvement? There are other elements of engagement and dialogue that you want related to utilization and access. So I would say "research studies access and utilization related to these technologies," something to that effect.

DR. FITZGERALD: "In their willingness to participate in."

DR. TELFAIR: "In," yes, "clinical trials."

DR. FITZGERALD: "In research studies."

DR. TELFAIR: "Research studies."

DR. FITZGERALD: "And"?

DR. TELFAIR: "And providing information on facilitation of access and utilization"? No?

DR. FITZGERALD: I have Paul and then I have Reed.

DR. BILLINGS: I was going to suggest that the first sentence is a little boggy to me. You might just say "HHS should use existing public consultation mechanisms to engage in a dialogue regarding the potential benefits, risks, and limitations," because public consultation will be public. We don't need two "publics."

DR. FITZGERALD: Right. "To engage in a dialogue regarding the potential." We are still working on yours, Joe.

I have Reed and then Steve.

DR. TUCKSON: Actually, he did mine. I wanted to get rid of that "widely." So "widely" was the last one. I wanted to get rid of that one in the last one. Then this one here in terms of "constructive."

We have to be careful. We put a lot of adjectives in here that make these things impossible, so let's try to be disciplined and get rid of unnecessary adjectives. So my point was, let's be disciplined when we finish all this and make sure that we are getting rid of unnecessary adjectives.

DR. FITZGERALD: We are going to have a paucity of adjectives. Steve.

DR. TEUTSCH: I was just going to try to talk about Joe's [remark.] I would probably have just concluded the end, "their willingness to use these technologies and participate in clinical research."

DR. FITZGERALD: Does that get it?

DR. TEUTSCH: I'm fine with that.

DR. FITZGERALD: "Their willingness to use these technologies and participate in research studies." Yes, Barbara.

DR. McGRATH: I guess this gets at the bigger question of asking them what questions and what will you do with the information. So if we just ask them if they are willing to do studies or willing to use the technologies, aren't we also asking them if they are not willing to use these things?

DR. FITZGERALD: Yes, exactly.

DR. McGRATH: Somehow the tone sounds like we want confirmatory information from the public.

DR. FITZGERALD: In the first sentence I think we were trying to get at that regarding the potential benefits, risks, and limitations of these technologies. So we get from them what they see are the risks and limitations, the harms and benefits, that kind of thing. Is that okay, Barbara?

DR. McGRATH: Yes.

DR. FITZGERALD: I don't see any hands, so let's look at what we have. "HHS should use existing public consultation mechanisms to dialogue on the potential benefits, risks, and limitations of pharmacogenomics technologies. This dialogue should include an assessment of their perceptions of and receptiveness to pharmacogenomics and their willingness to use these technologies and participate in," should we do "research studies"? Just "studies" is too broad. Just studies? Okay.

Everybody good with that language? We are good to go. Fantastic. On to No. 12. This is on page 105. In fact, this may be all of page 105. We got carried away. There are a lot of adjectives in here, but this is health information technology.

"The Office of the National Coordinator for Health Information Technology, through the activities of the American Health Information Community and in consultation with DVA and DOD, should take steps to ensure the inclusion of clinically validated pharmacogenomics test results into patient records, along with decision support systems and tools to enhance appropriate test use and interpretation. Decision support systems and tools should include information about

the availability of pharmacogenomic tests, patient test results, and relevant information for making treatment and dosing decisions.

"As the infrastructure develops, HHS should account for the needs of basic clinical and translational researchers to ensure that secure, consented clinical outcomes information is available to accelerate integration of pharmacogenomic breakthroughs into clinical practice.

"HHS should support efforts to establish standards for the development of electronic clinical decision support systems and tools. Pharmacogenomic test clinical practice guidelines should be developed in a manner that allows for their integration into such systems and tools."

Comprehensive, but we thought substantively useful. Yes.

DR. WILLIAMS: I'm not sure that this really captures what the groups are actually charged to do. While DVA and DOD may in fact be developing some guidelines to implement, the AHIC and ONC are basically developing platforms that will enable these to actually work within an electronic health record environment. They are not really dealing with content at all. It is just basically making sure that the clinical decision support engines will be able to access the relevant data to generate the algorithms that would arise from clinical use.

As I read that first paragraph, it really sounds like you are calling on those groups to work to develop content, and that is not their role.

DR. FITZGERALD: Our thought, if I remember correctly, was obviously you need both structure and content. One without the other is fairly useless. So I think we are looking for both. Do you have a way of refining that word-wise?

DR. FERREIRA-GONZALEZ: For example, in here we are saying "should take steps to ensure the inclusion of clinically validated PGx." I mean, are you asking them to determine what is a clinically validated PGx?

The idea is that they have to develop the infrastructure, and the coding and so forth needs to put this information in an electronic format. So I'm not sure we are really capturing what we wanted with this language.

DR. WILLIAMS: Basically, all of Recommendation 10 relates to developing the evidence and putting the evidence out in guidelines so that people can actually use it. This recommendation, in my mind, since it is around the health information technology, has to ensure that the developments in HIT will be able to support inclusion of things like genomic information, which currently we don't have standards or ability to include in the vast majority of information systems. So that really needs to be the intent of this recommendation, in my mind.

DR. FITZGERALD: I have Reed and then Ellen.

DR. TUCKSON: It seems to me it is too much. I think it is redundant. For me, it just boils down to "The Office of the National Coordinator for Health Information Technology, through the activities of the American Health Information Community and in consultation with DVA and DOD should take steps to advance the inclusion of pharmacogenomic test results into patient records, along with decision support systems and tools to enhance appropriate tests using interpretation," period. The rest of that paragraph is just redundant to me.

DR. FITZGERALD: So, "decision" take out.

DR. TUCKSON: All that goes. Then the second paragraph. Again, I'm not sure it says anything more. Once you have said it up front, this doesn't add any more to it.

DR. FITZGERALD: You would take out that paragraph, then?

DR. TUCKSON: Take it out, too.

DR. FITZGERALD: Take it out.

DR. TUCKSON: Then this last part about "HHS should support efforts to establish standards for the development of electronic clinical decision," that is built into what they are doing. So I would, again, take that out. They are already trying to, through the AHIC process, develop electronic decision support systems.

So "PGx test clinical practice guidelines should be developed in a manner," that is a double of the recommendation earlier. I don't think you need it there. So I only come up with the first two sentences.

DR. FITZGERALD: Yes, Ellen.

DR. FOX: I'm confused as to what this is asking the VA. All of our records are electronic. If you do a genetic test, it will be included in the electronic record today. So if the issue is developing uniform genomic data standards, then that is covered under 6C, where VA is asked to create uniform genomic data standards.

So I'm not clear on what it is that VA is being asked to do. I don't know what it means "to include clinically validated pharmacogenomics test results into patient records." I don't know what that means.

DR. FITZGERALD: Before I answer that, I have Gurvaneet, Scott, Jim, Marc. Gurvaneet.

DR. RANDHAWA: I agree with Reed's point. We should at least clarify the process and the structure first, which is what AHIC is doing. But also, I think what is lacking here is the content, not only developing some content as to what exactly the decision support should look like for what tests but also learning from it. If you look at decision support systems in the past, for example the ones created for potential drug interactions, our track record of how well they are used in decision-making isn't all that great.

So apart from creating the content, the pilot study also needs to figure out what is the best way of making sure it actually gets used in practice in a useful manner, which would require some pilot studies to be done by other HHS agencies, maybe beyond just AHIC.

DR. FITZGERALD: What would you add to the recommendation?

DR. FITZGERALD: What is lacking in the recommendation right now is there is no mention of any component of HHS funding some pilot studies to actually look at the issues about how to integrate tests into clinical practice. What are the best means of improving decision-making in that context.

DR. FITZGERALD: Going back to Ellen's point, you said there is already that information in the Department of Veterans Affairs' database; is that correct?

DR. RANDHAWA: Yes. Just to go back to another point, some studies have been done in terms of when there are critical drug interactions. There is an alert that comes up on the computer screen, do you really want to do this, [and they] override it. Well, different people have different means of overriding, and we don't even know exactly what is the decision in terms of override and how it actually supports decision-making.

So yes, there are tools available. How well they are being used in practice and how well they inform current utilization we don't really know a whole lot about.

DR. FITZGERALD: Who would pilot those studies?

DR. RANDHAWA: I guess any of the knowledge-creating agencies in HHS should be able to do that.

DR. FITZGERALD: HHS could. I just want to make sure we are capturing what you are recommending up here. I have "The Office of National Coordinator for Health Information Technology, through the activities of AHIC and in consultation with DVA and DOD," which we will get back to, "should take steps pilot studies."

DR. RANDHAWA: I think that is the structure that we were talking about which Marc had mentioned. I'm talking more about the content. The pilot studies would actually be, let's take these 10 pharmacogenomic tests and use them in the CPOEs, or whatever mechanisms we have, and find out how actually it has been used in practice and if it has actually helped the physicians, the pharmacists, or whoever is using it in their decision-making.

DR. FITZGERALD: Can you say that in six words?

DR. RANDHAWA: Not right now.

[Laughter.]

DR. FITZGERALD: Let's see if we can get it up there.

Now I have Jim, I believe, right? Did I miss somebody coming along here? No.

DR. EVANS: Mine is very brief. I like what Reed did in cutting that. I think that the reason that the VA and the DOD were put in there is [as] examples of [the use of] sophisticated electronic medical records, especially with regard to decision support systems. Obviously, these things will get into the medical record, but because of the gap that exists in practitioner knowledge, the decision support systems become very important.

DR. FITZGERALD: I think the consultation part was big, Ellen, with the DVA and the DOD. Consult with [you] because you already do a lot.

Marc.

DR. WILLIAMS: Just two points. One is about having something in the electronic medical record. I haven't seen the VA system, but my guess would be that the results are represented as

images, not as coded data. An image won't work in decision support. You have to have coded data. The coded data elements are still part of the structural elements that are really necessary to be able to run decision support engines. Not all information in electronic medical records is equal.

So I'm basically arguing to say we need to keep the structural elements represented in this recommendation.

To Gurvaneet's point, I certainly don't disagree, but I wonder, as we look at the fact that this is a problem across all medicine -- and I always feel a bit embarrassed if we focus in on a pharmacogenomic test as opposed to trying to get everybody on their heart medications -- whether specifically recommending pilot studies around pharmacogenomic CPOE type of systems is the direction that we really want DHHS to go or whether there are bigger fish to fry that may in fact inform the utility.

I still struggle with the idea of where the best place is to really learn how these things work, whether it is really top-down or whether it is really something that has to be developed at each individual level.

If it really comes down to each individual level developing it, then it is really just a matter of being able to pull information from the sources to be able to run the engine that you want to run.

DR. FITZGERALD: Now, again, when we started this recommendation, we attempted to get both structure and content. That got cut down to a couple of sentences. Now we are trying to get structure and content again. Is there a way we can look at this and word it so we can get some of that in this single recommendation?

This is what we have so far. "The Office of the National Coordination for Health Information Technology, through the activities of AHIC and in consultation with DVA and DOD, should study how clinically validated pharmacogenomic test results are being incorporated into patient health records. HHS also should take steps to ensure the necessary infrastructure is in place to support the inclusion of pharmacogenomics in electronic health records and decision support systems and tools."

Is that enough? Ellen.

DR. FOX: I think the problem I'm having with it is the inclusion of the pharmacogenetics. It is unclear to me what that means. Maybe something like "support the use of decision support systems and tools relating to pharmacogenomics," or something like that. I don't think it is the data you are trying to get included.

DR. WILLIAMS: Well, it is, to some degree. I think maybe the word to use there is "to support the representation of pharmacogenomics data." Again, the data has to be in the system to do any of the other things, but it has to be in a system in the proper way. At least in the IT world, we talk about representing data or structured data elements, or whatever.

I don't know, but that is the concept that I think is really critically important in the second paragraph. We have to have the infrastructure to be able to put that data in there in a format that you can actually use it.

DR. FITZGERALD: Ellen.

DR. FOX: I'm personally not familiar with that word "representation," but I [like] the last word you used, the "infrastructure." Maybe you could use the infrastructure to support the decision support. But the word "representation," I'm just unclear on what that would mean.

DR. FITZGERALD: So, "HHS should take steps to ensure the necessary infrastructure is in place to support the representation of pharmacogenomics data in electronic health records and decision support systems and tools."

DR. WILLIAMS: So, "in electronic health records for use in."

DR. FITZGERALD: "For use in decision support systems and tools." Yes? Okay. That got Emily back on board. Scott.

LT. COL. McLEAN: Can I just ask for clarification of the meaning of the term "consultation"?

DR. FITZGERALD: Up in the first paragraph. It means that you consult with somebody. No. I think the target here is we were thinking again of getting the different groups. The Secretary is within HHS, so this is to go outside of HHS and consult with both you and the Veterans Administration on how you do it.

MS. GOODWIN: At least as you do it really well.

DR. FITZGERALD: Exactly.

MS. GOODWIN: You are ahead of the curve on this.

DR. FITZGERALD: This is HHS saying why don't we get together with the other groups that are ahead.

Gurvaneet.

DR. RANDHAWA: I will be happy to suggest some wording, but I agree with Marc's point. I want to get a sense from the Committee, first of all, is it something the Committee is going to support in terms of getting some studies about content? Now, whether it is pharmacogenomics or any other clinical decision support is a discussion we can have, and I'm sure we can learn clinical decision support from other areas and apply that to pharmacogenomics. But there isn't a whole lot going on in that area per se.

The second thing to keep in mind is, in the future when we get more funding for pharmacogenomic activities, it may be potentially viable to do this. But I want to get a sense if the Committee wants to go in that direction before I suggest any wording.

DR. FITZGERALD: Why don't we put your wording up and then the Committee will let you know whether or not they want to go in that direction. With what we have up there now, Gurvaneet, where would you -- oh, I'm sorry. Ellen, go ahead.

DR. FOX: Just one more comment. I just want to make sure that the Committee is not misled by the current state of affairs. I think VA has a very sophisticated electronic record system and very sophisticated decision support. I don't believe VA has any decision support relating to pharmacogenomics currently. This almost sounds as if we are going to consult with VA to learn how that is done or something. I just wanted to make sure the Committee was clear on that.

DR. FITZGERALD: We are just trying to get everybody talking to one another so you can learn from each other and whatever else is out there, rather than people being in silos.

MS. GOODWIN: Would you prefer that highlighted clause get moved down to the second paragraph and say, "HHS, in consultation with DVA and DOD"? Would that be a better place for it?

PARTICIPANT: Yes.

DR. FITZGERALD: Gurvaneet, how are you doing on your [wording]?

DR. RANDHAWA: I will give it a shot. I'm sure we will be modifying it as I speak. "HHS should fund pilot studies that develop clinical decision support systems of pharmacogenomic technologies." What I'm struggling with right now is "and facilitate or improve decision-making at the point of care." I would appreciate someone helping me with that language there.

DR. FITZGERALD: This is what we have so far.

DR. WILLIAMS: Let me take a shot at this.

DR. FITZGERALD: Go, Marc.

DR. WILLIAMS: "HHS should fund pilot studies that examine the impact on practice of decision support systems for pharmacogenomic technologies at the point of care to maximize evidence-based best practices."

What I think I hear Gurvaneet saying is that we know what to do and we know that there is clinical decision support. We have not been able to really figure out how to us clinical decision support to actually make the best practices go forward.

The example of the drug interaction is alert fatigue. Every time you order a drug, you get an alert and so you just tend to ignore them all. Does that capture it? I think that I can support that.

DR. FITZGERALD: I just want to recognize the fact that we started with three paragraphs, worked our way down to two sentences, and we are back to three paragraphs. So I'm going to invite Reed [to comment.]

DR. TUCKSON: I'm just a little bit concerned. We are trying to get to some consensus here, but we have spent an awful lot of the government's money today. I think we have to be real, real careful about how much stuff we are saying that they have to spend money on. It is just impossible when you add up the tab on this whole deal.

So if there is something that we can not recommend as new money but to be part of something else that is ongoing, I think we have to do that. But, keep a tab of this thing. We are out of control.

DR. FITZGERALD: We are still working on this. Don't worry. We will send you the bill, Reed.

Let's take a look as we go through. Here is what we have. "The Office of the National Coordinator for Health Information Technology, through the activities of the AHIC, should study how clinically validated pharmacogenomics test results are being incorporated into patient health

records. HHS, in consultation with DVA and DOD, should also take steps to ensure the necessary infrastructure is in place to support the representation of PGx data in electronic health records for use in decision support systems and tools. HHS should fund pilot studies that examine the impact of clinical decision support systems for pharmacogenomic technologies on clinical practice at the point of care to maximize evidence-based best practices."

Marc.

DR. WILLIAMS: In the first paragraph we somehow went from electronic health records to patient health records. Those are two very different things in terms of a lexicon. We may want to include both, but I think the focus here is electronic health records.

DR. FITZGERALD: That was probably just moving words around. All right. Take a look because it has changed somewhat substantively. Has everybody now completely lost any focus or desire at this point?

[No response.]

DR. FITZGERALD: That is where we are. Reed?

DR. TUCKSON: I guess nobody went with me on eliminating anything.

DR. FITZGERALD: No, we are sending you the bill.

DR. STRAUBE: No, I'm going with Reed because there is no money, so it again becomes a redundant recommendation. In fact, we are looking for ways to bring in the private sector. This particular Secretary is very eager to try to get things out of public-private partnerships, and in doing so, part of that requires other funding streams.

Perhaps you can work the last paragraph that HHS should explore establishing pilot studies but not bring up the funding issue.

DR. FITZGERALD: I see. "Should explore pilot studies." "Should explore" --

DR. WILLIAMS: "Development of."

DR. FITZGERALD: Or, "initiating"?

DR. WILLIAMS: "Explore development of pilot studies.

DR. FITZGERALD: "That examine the impact." All right. Gurvaneet.

DR. RANDHAWA: I agree with Reed. We don't have, especially AHRQ, a huge budget. But we are funding two pilot projects on clinical decision support. That was recently announced. So it wasn't pharmacogenomics, but at least there is some activity that is going on that AHRQ is funding.

DR. TUCKSON: That is what I'm saying. Be a little more practical about saying use the money to do this, to do this. That didn't come out right.

DR. FITZGERALD: Any other wordsmithing recommendations for this recommendation?

[No response.]

DR. FITZGERALD: We seem to be somewhat in agreement, at least in a nebulous kind of way. All right. So, once, twice, three times?

[No response.]

DR. FITZGERALD: We are on to 12B. We are getting there, folks. Slowly, but we are getting there.

Still on health information technology. "Until electronic health record systems become a universal feature of the healthcare system, HHS should identify other ways to make best clinical practices for pharmacogenomics more readily available to help providers as they are developed."

Yes, Joseph.

DR. TELFAIR: Just a few wording changes to make it a little more practical in terms of taking into account what was just recommended. If you can replace "other ways" with "systematic pathways."

DR. FITZGERALD: "Should identify systematic pathways"?

DR. TELFAIR: Right. "To make," instead of "best," "emerging."

DR. FITZGERALD: "To make emerging."

DR. TELFAIR: Right. That's all. Those are the changes.

DR. FITZGERALD: "Clinical practices."

DR. TELFAIR: Yes.

DR. FITZGERALD: Robinsue.

DR. FROHBOESE: I have a question about this recommendation. I just didn't understand it. Is this saying that HHS should make available general information about PGx or individual clinical information more readily available?

DR. FITZGERALD: I'm going to look now at our new version here. If we have new clinical practices for pharmacogenomics, "emerging clinical practices," and they can't automatically be made universal because the health record system isn't universal, right?

DR. FROHBOESE: I'm just not sure [what] the relationship [is] between an individual's electronic health record and HHS making available best clinical practices.

DR. FITZGERALD: Emily.

DR. WINN-DEEN: I think the intent was that until you have the electronic health record and then the electronic decision support tools that draw from that record, and you need both of those, there needs to be some alternative way to get information to physicians about what the current best practice is. So maybe we need to wordsmith it, but I think that is where we were headed.

DR. FROHBOESE: Then I think it would be good to make that clear.

DR. FITZGERALD: Whoa. Wait. Suddenly everybody is awake. Wow, wonderful. I have Jim, Steve, Marc.

DR. EVANS: I feel in a way that 12B is wholly redundant. We have already discussed getting things out to professional societies, how to get them out to physicians, et cetera. I don't think we need 12B.

DR. FITZGERALD: There is a move afoot, obviously, to get rid of 12B. How many people here would be deeply disturbed and wounded if we do that?

[No response.]

DR. FITZGERALD: Wow. We are getting rid of a recommendation rather than adding one. What a concept. Is everybody good with getting rid of 12B? It looks good. Once, twice, yes. Gone.

Economic implications of pharmacogenomics. Here we go. "To ensure that investments in pharmacogenomics are well spent, HHS should gather data to assess the economic value of investments in pharmacogenomics relative to other health-related investments. This assessment should encompass the cost effectiveness of pharmacogenomics technologies and take into account their short- and long-term impacts on specific sectors in society as a whole."

Yes, Sylvia. You want 12B back. No.

MS. AU: No. Given my optimistic nature, it is difficult for me to say that this sounds very Pollyanna-ish. You are asking them to do an analysis that the federal government is going to analyze the money is well spent for this health-related initiative versus all the other millions of health-related initiatives that we have? It just sounds too Pollyanna-ish to me.

DR. FITZGERALD: Does Pollyanna want to respond? Go ahead, Steve.

DR. TEUTSCH: I like Pollyanna.

[Laughter.]

DR. TEUTSCH: I mean, it is true, but this is a fundamental problem of allocation of resources and somebody needs to pull it together. This is clearly not the only thing. We talked about doing this earlier on in terms of generating information. Someone needs to pull it together and make it available in a broader context. That's all.

It really doesn't say that there needs to be an elaborate investment here beyond pulling together the information that is available.

DR. FITZGERALD: I have Reed and then Barbara.

DR. TUCKSON: I'm going to continue to come back to just being the mean grinch at the party. There are too many recommendations. There is too much money, too many things asked to do. This one is just absolutely, to me, unnecessary in the scheme of everything. If we can get rid of something, let's get rid of it. The list is too long.

DR. FITZGERALD: Barbara and then Ellen.

DR. McGRATH: I'm not sure about that one way or the other, but if we do decide to keep it, we came up with some language earlier on, on Slide 2 or 3, at about 6 o'clock this morning when we talked about it. I think we are encouraging HHS to encourage research in this area, right? So it is directed to NIH or CDC or other federal agencies. There was one early on that we used some language. Maybe it would fit better and make it more of a directive. To redistribute their funds or something like that. Do you remember that conversation?

DR. FITZGERALD: Yes.

DR. McGRATH: If that is what we are asking, we should maybe use consistent language.

DR. FITZGERALD: I think that was more focused on basic research concerns.

DR. McGRATH: Isn't that what you are asking, that there be research on the economics?

DR. FITZGERALD: No. 5A, Slide 42. If that is the one you are talking about, just to be sure.

DR. McGRATH: I just read this one as saying there needs to be more research on the economic issues, not just the scientific aspects. So it seems the same.

MS. GOODWIN: Is this the one that you are thinking of? It is talking about cost effectiveness and value of PGx.

DR. McGRATH: I guess. I thought we started off the sentence with "HHS" and something about NIH in there, "should redistribute funding." See, I didn't write them down. Maybe just never mind.

DR. FITZGERALD: So we have another move afoot here to get rid of a recommendation. Yes, Ellen.

DR. FOX: Although I generally agree with Reed that we need to be careful in the number of recommendations here, I want to advocate for keeping this one in. I think that this is an area where there is a potential to develop infinite numbers of tests at infinite cost, and this is a huge issue. This could actually take money away from other health expenditures in a big way. So I think just advocating for cost effectiveness analyses along with all the other research is important.

DR. FITZGERALD: Someone is disagreeing with Reed yet again. I don't understand it.

I have Barry and then I have Joe and then I have Scott.

DR. STRAUBE: I think I support getting rid of this, also, for reasons that I stated before. But also, when we are looking at economic value, if there is a business case to be made, it is often made by the people who will benefit from it. In the absence of the business case being there, it is often because there isn't a business case.

So this would be something that I would think that folks who were touting pharmacogenomics as being a cost-effective, positive thing, will likely have that information and be able to make it available.

The second thing, just as an aside to remind people, when we recommend to the Secretary that he do something, he can of course delegate that to any number of entities, including back to this Committee.

DR. FITZGERALD: Oh, sure. We have been there.

[Laughter.]

DR. FITZGERALD: Joe.

DR. TELFAIR: I guess that last note is what I was going to look at, sort of a middle ground thing. I think that eliminating this is not unreasonable, but I would say that the intent of it can be encompassed with some of the recommendations made earlier about other studies.

It seems to me that [we should add it] to the list of other studies. Given that there is a choice to either accept it or not, I think the add-on is not only delegated but also to accept or not accept. [That] is my understanding of recommendations.

This is more of a compromise thing here. Eliminate the whole one but keep the fact that you really do need to have some kind of cost effectiveness study done, and add it to the list of other studies from earlier recommendations.

DR. FITZGERALD: Then you have to pick which one you want to put that in.

DR. TELFAIR: Then I would say we already covered it.

DR. FITZGERALD: You are happy with what was said earlier. I just want to be sure.

DR. TELFAIR: Yes.

DR. FITZGERALD: I have Scott now. Go ahead.

LT. COL. McLEAN: I just want to concur that I think it can be folded into some of the other recommendations. But from the way I read the Personalized Health Care Initiative, cost savings is a fundamental tenet. If it is not addressed intrinsically, there will be plenty of critics and members of the loyal opposition that will address it for the Secretary.

DR. FITZGERALD: Steve.

DR. TEUTSCH: I will only point out that this was basically to look in a broader context rather than what is in there earlier, which is specific studies of cost effectiveness and specific technologies which are not in any particular context.

DR. FITZGERALD: Joe, go ahead.

DR. TELFAIR: I understand what was just said, but I think that there is still the option to expand it beyond just that. Even though it is made a specific recommendation, there is still the option. Cost effectiveness studies, by their very nature, can either be very specific or also broad, and they cover areas that are relevant to the assessment itself.

So I would still argue to eliminate it but to highlight that it is encompassed in an earlier recommendation.

DR. FITZGERALD: There does seem to be a little clarification required here. When you look at 5B, 5B is under that general rubric of establishing an evidence base for pharmacogenomic technology. That is not exactly necessarily the same as this. It is also in the first section of the report, which is the basic research, translational, clinical section of the report.

Now, we could say that this research is part of that basic research for pharmacogenomic technology. I don't think most people would conceptualize it that way, but I think if we do do that, and of course the Committee can decide to do that, we would have to clarify in the larger report that that is indeed what we are doing. I'm not sure people would naturally fit with that.

So I would say that is an option that we can take. It seems right now we have the option of keeping this recommendation and reworking it however we wish, getting rid of the recommendation, or getting rid of the recommendation and then in an earlier recommendation mentioning this and then in the report explicating what exactly we mean by having that in one of the earlier recommendations.

DR. TELFAIR: Make clear it is another piece of the evidence.

DR. FITZGERALD: I think when people talk about the evidence, as we were talking about before, we were thinking more the biological evidence rather than the economic and financial. But we can make that clear. That is a possibility. All these things are possibilities.

What I need now is a sense of where people wish to go. Are we going to rework this? Let's just do it this way. People who are generally in favor of still trying to hang on to this recommendation and rework it in some way, indicate by standing up or raising your hand. If anybody wants to try and fight this one.

[Show of hands.]

DR. FITZGERALD: Three, okay. Four, Michael.

Let me think of it this way. How many people would like to move this idea to an earlier recommendation and then explicate it clearly in the text that that was what was done and this is part of the evidence of establishing pharmacogenomic technologies?

[Show of hands.]

DR. FITZGERALD: We have 10. That is a much larger group.

The third is just drop it. Reed, Martin. What did you do, slip him a twenty, Reed, to make him vote?

It looks like we are moving toward the compromise sort of thing, if one wants to look at it that way, of dropping this one where it is and mentioning the need to do this in an earlier way. So we will probably have to go back to 5B, if that looks like the best place to put it. What is A?

Everybody quickly look at 5A, which is Slide 42. We talk about "HHS should provide resources to identify and address evidence gaps in the analytic validity, clinical validity, clinical utility, and

cost effectiveness and value of pharmacogenomics." We could then have to explicate in probably the executive summary as well as the text what we mean by "value" in that it would include this.

People are happy? I see generally people are happy with that. Done. No. 13 is gone. No. 5A, "value," we will include that. Thank you.

No. 14, which is on page 113 of your report. This is ethical, legal, and social implications research.

"NIH, in collaboration with other agencies, should continue to encourage and fund research on the ethical, legal, and social implications of pharmacogenomics. This research should include studies of whether integration of pharmacogenomics into clinical and public health practice exacerbates health and healthcare disparities, limits access to or decreases the quality of health care, increases medical liability, or results in genetic discrimination."

This is building on what is already there. I have Michael.

DR. AMOS: Does this not say the same thing as the economic value? This is part of the value equation.

DR. FITZGERALD: Paul?

DR. BILLINGS: It struck me as a little peculiar that in the text it is talking about disparities that exist and are widening in our society and the recommendation is for NIH to study it. Is there no stronger commitment that we could make in this document to the reduction or the anticipation of disparities widening without more directed policy and action on the Secretary's part?

DR. FITZGERALD: I'm trying to get to both questions at the same time. One could, in a really broad conceptualization of value, pull in ethics and legal issues and all that sort of thing. But due to exactly what Paul was just mentioning, the significance of these issues, this was seen as important to highlight.

Now, in that highlighting, what can we get at. In looking at the literature and discussions of this sort of thing, as you may well know, there are arguments back and forth whether or not pharmacogenomics actually will reduce healthcare disparities or exacerbate them. That is something that is still ongoing. So the idea was that perhaps study is not enough. There was a sense of, also, a continual review of what is going on to make sure that it doesn't in fact create greater healthcare disparities. I'm not sure we captured that in here.

Paul, go ahead.

DR. BILLINGS: Could you say, "should continue to encourage and fund research to avoid adverse social, ethical, and legal implications of PGx, to include, or including, an exacerbation of healthcare disparities, limits of access, and genetic discrimination," period?

DR. FITZGERALD: I think the idea was definitely to avoid. Go ahead, Paul.

DR. WISE: I like that. This is still about research that is going to come on line in five or 10 years, more likely, with this kind of research. Is there nothing in the document that is going to say that the Secretary should help develop policies that will facilitate access to advances in pharmacogenetics?

In other words, we already know differentials in access are profound. We also know that that will affect who in fact utilizes these advances, as opposed to doing research about it, which I think is fine. But, is this the only place where disparity reduction is going to be addressed?

DR. FITZGERALD: As far as a specific recommendation, yes. But we could put it in, if you would like to suggest some language. We will hear from Marc.

DR. WILLIAMS: I think the one other recommendation that we have talked about that does address this, at least peripherally, is the idea that we do have federally funded health care provision, Medicare, Medicaid, SCHIP, where we are essentially giving direction to say we think there may be some problems in terms of how we could actually fund this which will have an impact on being able to actually provide the services.

If that can be studied in a relatively short turnaround time to direct policies relating to coverage and reimbursement, that would impact disparity. So there is one other thing that at least indirectly impacts what I think you are talking about.

DR. FITZGERALD: Paul, did you have that language that you wanted?

DR. BILLINGS: I changed it to slightly more active. "Should continue to encourage and fund research to avoid adverse social." We could actually add, "And the Secretary should develop policies based on the likelihood of that outcome," or something like that.

DR. FITZGERALD: Let's go back up here. "Encourage and fund research to avoid adverse ethical, legal, and social implications of pharmacogenomics"? Does that capture what you had?

DR. BILLINGS: Yes, yes.

DR. FITZGERALD: Then, "This research should include studies," and then in the end, "adverse ethical, legal, and social implications," right. Then, "HHS should develop policies."

MS. AU: Kevin, I think at the beginning it should be "The Secretary or HHS should direct its agencies to develop policies and support activities that would discourage health disparity surrounding PGx," something like that. "HHS should direct its agencies." Or, "The Secretary should direct its agencies," "the HHS agencies" -- I don't know how that works -- "to develop policies and support activities."

DR. FITZGERALD: Marc?

DR. WILLIAMS: Steve and I were just chatting. I guess maybe the thing we need to narrow down here is that the research doesn't need to be overall. We all know that there are tons of healthcare disparities. So in some sense, it is an exceptionalism argument. Is this going to be different than all the other disparities that are already out there.

Maybe what we need to say is, are there specific issues related to pharmacogenomics. That is what we need to study, the things that pharmacogenomics would specifically increase disparities over and above all the other disparities that we already have.

DR. FITZGERALD: Also, my sense is that we want to be more proactive in addressing the use of pharmacogenomics to reduce disparities currently, right?

DR. WILLIAMS: Yes.

DR. FITZGERALD: That is what we are trying to capture. Robinsue, yes.

DR. FROHBOESE: I have some language that might accomplish that. How about, "HHS activities should support integration of PGx into clinical and public health practices that reduce health and healthcare disparities, increase access to and quality of health care, decrease medical liability," although I'm not sure whether we really need to include medical liability, "and reduce or eliminate genetic discrimination."

DR. FITZGERALD: Hang on. It is going to take us a little while here to get all this.

DR. FOX: Rather than focusing on studies, focusing on the impact, which is just picking up on the comments of others.

MS. GOODWIN: I don't know if you can see it, but let me know if I'm typing what you said correctly.

DR. FITZGERALD: We have "HHS activities should support integration of pharmacogenomics into clinical and public health practices in ways that reduce health and healthcare disparities, increase access to" -- what happened to "health"? You cut something out. Put something back. "Increase access to and quality of health care, and reduce genetic discrimination."

Is that close, Robinsue?

DR. FROHBOESE: Yes.

DR. FITZGERALD: Now, comments? Paul.

MR. MILLER: I was just listening to it and I was just thinking, if this really changes anything, adds anything new, or is a restatement of what, presumably, is already being done. To the extent that it isn't really directing HHS to do anything different, I wonder whether it is necessary or whether it can be folded in, or whether in fact there are political reasons why you want an ELSI recommendation. I just put those thoughts on the table.

DR. FITZGERALD: Yes, Robinsue.

DR. FROHBOESE: Paul, I think, just as we have the recommendation about privacy and confidentiality because it is such an important principle that underscores the basis of the Committee's recommendations, so too I think this [belongs here.]

MR. MILLER: I think that's fair and appropriate, but I just wonder, if we are going to have an ELSI recommendation, and I don't necessarily know what it should be, but whether there should be something that really is a little meatier, maybe goes a little further or says something a little different other than just supporting ELSI issues. I mean, let's spend some money.

[Laughter.]

DR. WILLIAMS: To me, that is actually a justification for including it, because there are specifically designated ELSI funds. What we are really talking about is reordering the priorities

where the Secretary could say, I would like a certain amount of these ELSI funds to be designated around issues of pharmacogenomics specifically. So there may be a practical reason.

DR. FITZGERALD: Right. Jim and then Paul.

DR. EVANS: I just want to remind people that I think the genesis, or at least one of the starting points for this was, again, the idea that is out there among many that pharmacogenomics may be less problematic from an ELSI standpoint than many other aspects of genetics. Thus, I would be in favor, if we are going to keep an ELSI bullet, that we emphasize studying that. Is pharmacogenomics indeed less problematic than other genetic technologies, and something to the effect that is obviously of great importance to minimize problems that are found.

I just want to remind people that there is a specific pharmacogenomic ELSI question.

DR. FITZGERALD: Paul.

DR. WISE: This is an ELSI question which can be addressed in a well-worded research statement that I think would be helpful and appropriate. But, there is a broader context. Just like there was the focus on race and ethnicity, you have this new arena of technical innovation. At some point, is this Committee going to recommend that the Secretary facilitate access of these new advances to all people in need, period.

In other words, it is not a research question alone. There needs to be attention to this research question, but at some point the decision might have to be made whether the Committee is going to recommend that this is such an important arena of technical innovation and health care that this Committee states clearly and sharply that the HHS needs to facilitate access to these advances to all people in need.

DR. FITZGERALD: Anyone else? Paul, one follow-up question to that, and to everybody else, I suppose, too. What we had initially was focused more on the research. What we have now is the more active. Do we want to take what we have now and support it with further research? In other words, are we going to say, in order to do this, whatever research needs to be done in order to guide, or do we want to just stick with what we have here? That is, I guess, my question. Paul and then Gurvaneet.

DR. WISE: I'm still a rookie on the club here, but my sense would be, if it is allowable, to go back to the original language for the research question. Except, maybe to expand beyond NIH because there are other agencies doing research in these areas. Maybe shorten it, as Paul was suggesting, or change it, because that was still focused on the research. I thought that was good language.

But then to have a second sentence area or even a second recommendation that merely states that "HHS should develop policies that facilitate access to pharmacogenetic interventions of value to all people in need."

DR. BILLINGS: I would only support Paul the Wise by saying that that statement should come first.

DR. FITZGERALD: Which we have right now.

DR. BILLINGS: Right. Then the research.

DR. FITZGERALD: The research can be in support of that.

DR. BILLINGS: Supportive of that.

DR. FITZGERALD: Gurvaneet.

DR. RANDHAWA: I was thinking about this because I think there is a bit of a disconnect here. I understand the sentiment. We don't want to do research for research's sake and keep on doing research. But I'm not sure we always know what policies will actually reduce or exacerbate disparities with intended or unintended consequences.

So I think the missing link is that, apart from research on the factors that can cause disparities, what we are lacking is research on interventions that have been shown to reduce disparities and then acting on that. I didn't quite see that being made in the recommendation.

DR. FITZGERALD: That is what we are going to try and do right now, I think, is try to also put in, perhaps second, the fact that more research is going to be required in order to perhaps develop the sort of activities that you were saying should be there to support the integration of pharmacogenomic technologies. So whatever research is necessary or useful in that regard we will also have in this language. Is that getting to the two Pauls' [comments]?

What we want to do is we want to wordsmith the second paragraph to fit better with the first, once Suzanne gets it all in there.

This is what we had originally in the research language. What we would like to do is, if we can, fix that to fit better with the first paragraph we have now, because we are going to keep that first. So, recommendations in that regard? How about we start off the second paragraph, "To this end," because that would refer to what we have in the beginning.

Yes, Paul.

DR. WISE: I apologize, but that first paragraph also seems like we are still talking about practice guidelines. In other words, integrating pharmacogenetics into clinical public health practices. We are really talking about broad access policies as well, in fact far more importantly. So it might be something like "should support policies that afford access to and then the integration of."

In other words, integration into -- I'm trying to follow as it is moving here -- clinical public health practice is not really what I was getting at. I think that is great. It is an important area. But, "should support policies that afford access to pharmacogenetic advances" or "advances of value" or something. Just "advances" would be fine with me.

DR. FITZGERALD: Is "technologies" okay?

DR. WISE: Sure.

DR. FITZGERALD: "Pharmacogenomic technologies." Just that in and of itself. "Should support policies that afford access to pharmacogenomic technologies"?

DR. WISE: No, and then the other parts.

DR. FITZGERALD: "In ways that reduce health and healthcare disparities, increase access to and quality." We have "access" twice.

DR. WISE: Get the "access," too. Just go right to "quality of."

DR. FITZGERALD: "Increase quality of health care and prevent genetic discrimination." Is that what you had in mind?

DR. WISE: Yes.

DR. FITZGERALD: Paul? Also, Paul?

DR. BILLINGS: Yes.

DR. FITZGERALD: We have the Pauls happy. Now we are in good shape.

Then, "To this end, HHS should continue to encourage and fund research."

DR. WILLIAMS: Can you just say "that supports this goal"?

DR. FITZGERALD: Yes, fine. "Research," after that, "in support of this goal." Yes, Michael.

DR. AMOS: That would mean actually funding the development of better, faster, cheaper technologies because that is really the rate-limiting factor in getting it out to everyone, to have the technology cheap enough so that it can be accessible by everyone. That is a part of it.

So, do we say anywhere in here that HHS should fund the development of new technologies? Or is that appropriate? Because that is part of the equation.

DR. FITZGERALD: Emily, go ahead.

DR. WINN-DEEN: We had that in one of the earlier recommendations and I think we ended up taking out the specific reference to genotyping technologies. I think we left it more broad in the end.

DR. FITZGERALD: Right. But I think we had in those earlier ones about the value, which we are putting as a large concept now. So if, obviously, better, cheaper, faster would be valuable, then that would be the way that it would be pursued.

DR. WINN-DEEN: I'm not sure that you can make a broad statement that the cost of a test is always the gating factor.

DR. AMOS: That is not what I'm saying. I'm saying that within certain contexts, if it costs $100 to conduct a test, some people aren't going to have access to that, as opposed to $1 a test.

DR. WINN-DEEN: If a therapy costs $10,000 to administer, some people aren't going to have access to it. So I think it is both things.

DR. AMOS: That is part of the ELSI. That is part of the discrimination.

DR. WINN-DEEN: It is cost-effective medicine, basically. We were trying to talk about that in more general terms, I think.

DR. FITZGERALD: This is where we are. Let's read it. "HHS should support policies that afford access to pharmacogenomic technologies in ways that reduce health and healthcare disparities, improve quality of health care, and prevent genetic discrimination. To this end, HHS should continue to encourage and fund research in support of this goal."

Did we capture it? Yes. Great. Fantastic. Moving on, we have two more recommendations to do. They are more related to structural issues. This is coordination of pharmacogenomics activities. No. 15A is that "An interdepartmental workgroup should be established to review these recommendations, assess whether and how to implement them, monitor HHS progress, and report back to SACGHS." This gets back to whatever we recommend could come back to bite us, as it often does. "The workgroup also could serve as a forum for discussion of other PGx activities."

Yes. Paul, Marc, and Joe.

DR. BILLINGS: I'm curious about whether this would have outside representation on it. You talk about "interdepartmental," which sounds like intergovernmental. Did you mean for that to be, or would you want, for instance, public-private partnership to be involved in this activity as well?

DR. FITZGERALD: Yes. Again, it is a recommendation to the Secretary of HHS, so I presume

DR. BILLINGS: Are we talking about better coordination intergovernmentally or are we talking about something that has an outside component?

DR. FITZGERALD: Steve, go ahead.

DR. TEUTSCH: This is an intergovernmental thing.

DR. FITZGERALD: Fine. Marc and then I had Joe, right? Right. Marc.

DR. WILLIAMS: There is one concept I think we need to represent, and this actually gets at what Reed has been talking about. I think we have to have prioritization in here. Some of these recommendations are going to be easier to implement, some of them are going to be more important to implement.

DR. FITZGERALD: Right. Now, on that note, there is that possibility, but here is the logistical issue. If we have time and we decide to do it, we can certainly then give the Committee the opportunity to prioritize the recommendations.

DR. WILLIAMS: No, no, no. I'm saying in this recommendation, "An interdepartmental workgroup should be established to review recommendations, prioritize those recommendations, assess whether and how to implement them."

DR. FITZGERALD: Oh, I see. Okay. That's fine. That's good. That's even better than us doing it.

I have Joe and then Andrea. No? Just Joe.

DR. TELFAIR: I guess mine would be, given what we just said, a point of information. If I'm wrong on this, maybe Reed can correct me. But, if it is intergovernmental or interdepartmental, isn't that something we are going to do anyway, apart from this last piece of prioritization? Isn't that something that is going to happen anyway?

DR. FITZGERALD: No, that was not our understanding. That was not understanding, that it would happen anyway.

DR. TELFAIR: A point of information. If we understand that that is not going to happen anyway.

DR. FITZGERALD: No. Again, this was what we heard from our representatives of the various departments of HHS. At least some people there said they wanted this as a recommendation to make sure that it happened. I'm representing that accurately, I do believe, but that was what we heard.

DR. FERREIRA-GONZALEZ: I don't think it costs any money.

[Laughter.]

DR. FITZGERALD: Just for your information. Thank you. Yes, Ellen.

DR. FOX: Do you mean "interdepartmental" or "intra"? Do you mean within HHS?

DR. FITZGERALD: Within HHS.

DR. FOX: Not other departments?

DR. FITZGERALD: Yes, yes. Other departments, yes. Right. This is government. Yes, Robinsue.

DR. FROHBOESE: I'm just trying to think of [about our] other reports. Have we been this prescriptive about actually forming a separate group to monitor, track, report back?

DR. FITZGERALD: My understanding is no. Has it happened before?

MS. CARR: Yes, sort of.

DR. FITZGERALD: This was in response to a request, again, from members of different agencies. They wanted this. Now we have it, I guess, in the LPS study, and that is probably also represented by their desires.

DR. FROHBOESE: I'm just thinking, in keeping with Reed's admonition about proliferation of workgroups and money, money, money, should this be the function of the ex officios of SACGHS?

MS. CARR: It may very well involve them. One would expect them to.

DR. FITZGERALD: I think they wanted, in fact, or some anyway, wanted that to be the case.

MS. CARR: I think it is maybe the Committee's recognition that this is a complex set of recommendations that would require a lot of thinking and deliberation on the part of HHS and the other agencies. I think it is the Committee's way of acknowledging that it is not just something that can just be taken up by the Secretary's Office perhaps by itself. So I think that is part of what you are getting at.

DR. FITZGERALD: Go ahead, Reed.

DR. TUCKSON: I will soften what I was going to say because the ex officios suggested it. It just seems to me that -- maybe because I'm from the private sector -- this is a priority. Figure out the best way to get it done and just get it done. I don't think you need to tell the Secretary how to run his business, that he has to create an interagency taskforce, which means somebody has to staff it. It gets very complex. Just get it done.

MS. CARR: Remember that we have a recommendation a little bit like this in the Oversight draft report, too, don't we?

DR. TUCKSON: Which is, again, reason for my point. All of a sudden, this Committee is suggesting that the Secretary establish four oversight committees. Come on. He can't do this. One committee will do it all.

MS. CARR: No, no. It could be the same.

DR. FITZGERALD: Go ahead and give them all the work. They have nothing else to do.

As far as the language of this recommendation, any suggestions? Ellen.

DR. FOX: If it is the ex officios that recommended this, I'm wondering if the ex officios in this room think this is a good idea. I'm not understanding how this would work or how it would relate to this Committee. I don't know if others share my view.

DR. FITZGERALD: Right. I can only try to represent what was said, but the idea was that there were members who thought it would be a useful recommendation because it would give them the impetus to pull together people from various silos.

DR. TUCKSON: Can I try language? "The Secretary is requested to take all necessary steps."

DR. FITZGERALD: Keep going.

DR. TUCKSON: I'm letting her type. "Is requested to take all necessary steps to establish and review and prioritize," whatever it was.

DR. FITZGERALD: So we have, "The Secretary is requested to take all necessary steps to review and prioritize these recommendations, assess whether and how to implement them, monitor HHS's progress, and report back to SACGHS. The workgroup also" -- no? Oh, you have to get rid of that, then.

This is going to be interesting because, if we accept this, it is going to be interesting to see what we think about the next recommendation. Yes, James.

DR. EVANS: Which brings me to my suggestion that we don't need that next recommendation.

DR. FITZGERALD: That is what I think we are probably going to get to. We just basically made this over again. Anyway, let's just see if everybody is happy with this as it is. It looks like we have a general -- no, yes? Good. All right.

No. 15A, which may be just No. 15 in a minute. We move now to No. 15, our last recommendation, which is that "HHS should assess the level and adequacy of resources being devoted to support the integration of pharmacogenomics into clinical and public health practice," we have already touched on that a little, "to be sure that gaps and opportunities identified in this report are addressed."

DR. BILLINGS: I would recommend this being removed since it is implied by the first one.

DR. FITZGERALD: I think I get a general sense of that. So as the person directing this discussion, I think we should just turn this into volumes and volumes. No.

[Laughter.]

DR. FITZGERALD: No. 15B is about to be gone. One, two?

[No response.]

DR. FITZGERALD: All right. No. 15B is out of here. We are just 15.

Now, before we move on to the next, Reed is going to interject.

DR. TUCKSON: First of all, that was extraordinary. Kevin is extraordinary. Let's applaud Kevin.

[Applause.]

DR. FITZGERALD: We are not done yet.

DR. TUCKSON: That is why you are getting your applause now. Take it while you can get it, my friend.

[Laughter.]