48th MEETING

NATIONAL BIOETHICS ADVISORY COMMISSION

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I N D E X

P R O C E E D I N G S

OPENING REMARKS

R. ALTA CHARO, J.D.

PROFESSOR CHARO: Okay. We are going to get started. For the members of the public who are observing, just to clarify, my name is Alta Charo and I am not the chair of the Commission but I will be opening up the meeting for Harold Shapiro, who will be here by approximately 9:15 or 9:30.

And so we would like to welcome everybody to what is now the 48th meeting of the National Bioethics Advisory Commission.

There are some small changes to the draft agenda that I should let you know about.

We are going to begin with some opening remarks from Eric Meslin and an Executive Director's report, and that will be followed then by a series of discussions of certain points that Dr. Shapiro has asked that we consider because they will affect the discussion that will follow of the text and recommendations that we are hoping to finalize at this meeting.

So at this time, I will turn the microphone over to Dr. Meslin.

EXECUTIVE DIRECTOR'S REPORT

ERIC M. MESLIN, Ph.D.

DR. MESLIN: Thanks very much and good morning, everyone. I will keep this report relatively short but I do have a piece of information that was not in the handout.

Our reports to you, both from me and the more lengthy legislative report that Ellen Gadbois from our staff prepared, are, as always, open for discussion.

The only item that I wanted to bring to your attention from the report that I have distributed with respect to our international project is that report is now up on the web. This is the report on the Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries. Both volumes of that report are now on NBAC's website at www.bioethics.gov in both HTML and PDF versions for those of you who follow such things.

We know that it has been difficult for some to download these so you simply have to call our office and you may get copies.

The final published version from the GPO will likely be available towards the end of this month and into early June, so as you are keeping track of NBAC reports, please feel free to stay in touch with the NBAC office.

And today the executive summary of the

international report should have been posted in the Federal Register so that is another place for you to get materials.

The other item I wanted to bring to your attention, which I only learned of yesterday, is that Commissioner Laurie Flynn has tendered her resignation from the Commission and although she is not here I know Dr. Shapiro would extend his thanks and appreciation to her for her work on behalf of NBAC and all the hard work that she has put in over the years. So she will obviously not be at this meeting, having written to us just a few days ago.

I do not have any other major items to bring to your attention that are not already listed on my report but I do again want to offer you the opportunity to ask questions either of me or of Ellen Gadbois, who produced, I think, as she always does, not only an excellent summary but in the case of this past legislative update is an extremely comprehensive one that should demonstrate without any difficulty whatsoever that there is an awful lot of interest on behalf of Congress and others in a wide range of topics relating to human research.

So that is my report. I am happy to answer any questions that commissioners may have before we move on to the meat of the business.

PROFESSOR CHARO: Well, if there are no questions then let me go back then to the revised order of discussion that Dr. Shapiro has asked us to pursue. There is going to be an opportunity to make general comments about the report when he begins the discussion about the text and all of the recommendations but he has asked that we actually go over five items that have kind of substantive content that will affect the kinds of recommendation language that will finally be adopted today. So, if I can, I would like to just move through them sequentially in order to clarify the commission's position and make it possible for staff to finalize the language here.

The first that he has asked us to turn our attention to was some possible confusion about the final views of the commission concerning IRB membership. This comes up in Recommendation 5.9, which talks about the need to have a quarter of the IRB include--a quarter of the IRB's membership reflect people who represent the prospective or potential participants who are unaffiliated with the institution conducting the research and who are not primarily identified as researchers themselves.

There was some confusion about whether the view was that there needed to be representation from each of these different classes of people or--that is

each of these classes of people had to have a certain set number of percentage of the IRB membership or whether as a whole a quarter of the membership had to be made up of people like this and any one person might actually fulfill both of those roles. So, for example, any one person might represent the prospective potential participants and be unaffiliated with the institution.

We had had some discussion about this at the last meeting. It appeared that there was a general comfort with the idea that one person can fill multiple roles, that overall the notion was that a quarter of the IRB membership is not affiliated, not scientists, and--or represent patient perspectives. I do recall Tom Murray making some comments by telephone about his wish for us to be perhaps even more aggressive on this and wanted to open this up for a kind of final discussion and conclusion.

Maybe I can suggest the following, although I had not actually intended to: Distributed at the table were some suggested revisions to the recommendations and it had not been my intent to ask everybody to go through them now because we may not need to go through them at all since some of them are based on substantive views that we have not agreed upon but in this case maybe it will help focus the discussion.

There is--under suggested revisions to Recommendations 5.9 there is a slight changing in the word--a slight change in the wording, which is designed to try to clarify that we simply need to be sure that a quarter of the IRB membership consists of people who have one or another of these characteristics that make them somehow separate from the usual membership.

If you can take a look at that and see whether you are comfortable with that language as opposed to the original language which might be read to require something a little bit more extensive, 5.9 of the original recommendations versus the suggested revisions.

Bette? And you will need to hit this thing.

MS. KRAMER: Excuse me. Is there any material in the text prior to this recommendation that discusses how these people ought to be enrolled for the IRB?

PROFESSOR CHARO: I wish I could tell you but Chapter 5 had run out in the back so I do not have the full text but if somebody has got it.

DR. SPEERS: What the text says is that--the text defines three types of members, those that are unaffiliated--otherwise unaffiliated with the institution, those who are nonscientists, and those who can represent the perspectives of participants, and in each of the cases it suggests that at least 25 percent

of the membership be comprised of those types of individuals. It says in the text that if an individual can fulfill more than one of those categories--so if a person can be both unaffiliated and a nonscientist that person can fulfill both of those membership categories.

PROFESSOR BACKLAR: And representative--

PROFESSOR CHARO: Trish?

PROFESSOR BACKLAR: Excuse me. And representative of the participant.

DR. SPEERS: Sure. I mean if a person met all three of those categories then a person could meet--you know, fulfill all those requirements. If a person meets two of the three then they would fulfill two of those three.

PROFESSOR BACKLAR: Could you tell us what page on the text--in the text? No, I brought the recommendation--but in the text--I was looking for the explanation in the text.

DR. SPEERS: Yes. It starts--the text--the relevant text on this starts on page 30 and continues over to page 34.

PROFESSOR CHARO: In the second to last paragraph of 33, Trish, I think you will find the introduction of the 25 percent number.

Bette?

MS. KRAMER: Well, the reason I asked the

question--I am not sure we have ever had any discussion on the subject--is my impression is from different IRB people that I have spoken to that it is not easy to enlist people who fall into this category. That is why I wondered if we had any discussion in the text as good suggestions as to how it might be done or--the 25 percent, I think, is a substantially higher number than has generally been requested in the past. Is it not? So is it--I guess I am talking--questioning whether--the feasibility of it and how it is supposed to happen.

DR. SPEERS: Right. The current regulations that state that an IRB should be comprised of at least five members says that one of those five should be unaffiliated, one of them should be a nonscientist. So there is an implied percentage of about 20 percent.

When this recommendation was written and included in the public draft version of the report, we had 50 percent as the recommended percentage for unaffiliated and for nonscientists. What we received in the public comments was that 50 percent seemed to be too high and what was recommended was 20 or 25 percent.

DR. MURRAY: I still--

PROFESSOR CHARO: Larry?

DR. MURRAY: --believe--oh, I am sorry.

PROFESSOR CHARO: That is all right. Tom, and then Larry.

DR. MURRAY: I still believe that 50 percent is the right number but I am willing to compromise on this. I think 25 percent is at least--it would be an improvement because you could have--in fact, the interpretation of the rule is that if an IRB consisted of 15 or 20 members you still only needed on that was unaffiliated, et cetera. So I would be willing to vote for this resolution.

I like the original language rather than the revised language. For one thing, the original language says that this accounts not only for the membership but also for determining a quorum because it would be one thing to have community members but then if they never showed up it would effectively gut the meaning of the resolution.

And I have worked in institutions, I now run an institution, it is difficult to get community members. I understand that. It would be--you know, it is much easier to call on your own folks in-house but--so, you know, I understand why administrators would balk at this kind of challenge but my view is that it ought to be done. They can be creative. They can accomplish it.

PROFESSOR CHARO: Larry?

DR. MIIKE: If I remember the original opening statement on this, the issue was whether people can

serve more than one category. Neither of these address it so why don't we just say it in there. There is just not language in there. So just add a sentence.

PROFESSOR CHARO: Arturo?

DR. BRITO: Well, the original recommendation does say that someone is permitted to fulfill more than one membership requirement and I think the issue here is that it gives the--no?

DR. MIIKE: Arturo, I am just looking at the current recommendations and Alta's recommendations.

DR. BRITO: Oh, I am sorry. I have the previous one. I have the one in the text and then I have the one from Atlanta where it did say an individual should be permitted to fulfill more than one membership requirement. And there I am not sure why we--it should be in there, right? Yes.

PROFESSOR CHARO: Other comments? Rhetaugh?

DR. DUMAS: As I understand this recommendation, as the recommendation reads, the 25 percent is--says at least a quarter so that does not mean that we--some groups could not get a higher percent, a proportion. And the other thing it says who are affiliated with the institution, so forth and so--or who are not primarily identified as researchers and I read that to mean that it can be people who either represent the participant or who are unaffiliated with

the institution or who are not primarily identified. So that means that if you got some in any one of those categories you would have fulfilled this recommendation the way it is written. And is that the way we mean it, that a participant who represents--a person who represents potential participants could satisfy the other two?

PROFESSOR CHARO: Diane?

DR. SCOTT-JONES: In the text on page 35 there is an "and"; in Alta's recommendation for changes there is an "are". So it is Alta's recommendation that changes the meaning of it and as it is written on page 35 you would interpret that to mean that the person had to meet all three of those because they are joined by "and" not "or".

DR. DUMAS: That is right.

DR. SCOTT-JONES: So you would have to be not affiliated, not primarily a scientist and representing the perspective of the participant. You would need to be all three of those.

DR. MURRAY: You would need to be all three to be counted for all three categories. You could have members who are counted for one of those categories, two of those categories or three of those categories.

DR. SCOTT-JONES: Then that should be explicitly in recommendation 5.9. What you are saying

should be written back in here.

PROFESSOR CHARO: I am sorry. Can you clarify what is it that you would like to have written back in exactly?

DR. SCOTT-JONES: What was already discussed to clarify whether a person could serve all three of those because the way 5.9 is written I would interpret that to mean that the person needed to be all of those. Then the last sentence says for each category IRB membership should be at least 25 percent, which could be interpreted to mean that if those are nonoverlapping in the persons you choose that could be 75 percent of the IRB.

PROFESSOR CHARO: And that, in fact, is exactly the reason for the proposed revision because of the way in which the mathematics worked out that it could be read to require that the IRB membership be more than 25 percent made up of these people because of the way the characteristics are laid out.

It seems to me that we have got a couple of very distinct things that we should probably just decide very cleanly and then go back and try to write the recommendation in a way that reflects them. Okay.

The first is Tom's suggestion that we move this number up to 50 percent, which is where it had been. The comments that came in showed a great deal of

resistance, partly for the reasons Bette outlined but it is an opportunity for us to decide again because it was put on the table whether we would like to go to 50 percent. So let me--

DR. MURRAY: I am sorry. I did not reintroduce 50 percent. I said--I mentioned it because I had made that proposal--

PROFESSOR CHARO: So you would rather not have anybody address it?

DR. MURRAY: No, I am not putting it up for-

PROFESSOR CHARO: Fine. Okay.

DR. MURRAY: If we move to the alternative language then I would feel differently but if we stick with the language in the formal draft of 5.9 adding a clarifying sentence that people may--a single individual may fulfill--

PROFESSOR CHARO: I suspect that we are not going to wind up with either the existing or the proposed revision because both of them seem to have identified problems so we are going to wind up with new language regardless.

Marjorie?

DR. SPEERS: I was just going to actually suggest language that could be added to this if you would like a possibility. It could be an individual should be permitted to fulfill more than one membership

requirement.

PROFESSOR CHARO: Yes, but that still does not handle the problem of the final sentence of the existing recommendation, which could have worked out to requiring virtually half to three-quarters of the membership of the IRB to represent these categories rather than the scientific disciplines.

Why don't we--I--let me just ask to clarify the point to be made here and then we can go back and try to get the writing down in the background and come back with it. Okay?

Is it correct that it is people's view that certainly an individual can fulfill one or more of these categories? Okay.

Is it correct that it is people's view that the goal here is that there should be a minimum membership of 25 percent that represents people who have any--at least one of these characteristics? Is that correct.

DR. DUMAS: That is confused in my mind and I am ambivalent about it. If it is important to have people who are not participants and if it is important to have people who are not researchers and if it is important to have people who are not primarily identified--well, we said researchers--from the institution, then I think we have to word it such that

those three categories are represented if that is what we are aiming to do.

PROFESSOR CHARO: So that what you would like it to say is that all three categories must be represented and in toto a quarter of the membership should represent all three of these?

DR. DUMAS: Right.

PROFESSOR CHARO: Tom is shaking his head no. Tom?

DR. MURRAY: Alta, you seem to be driving us towards your alternative language and I am not sure that--I am not ready to go to your alternative language.

PROFESSOR CHARO: I am not because my alternative language would not accomplish what I just said to Rhetaugh.

DR. MURRAY: Well, I think it would be very close to that.

PROFESSOR CHARO: What would you--what--substantively what would you--

DR. MURRAY: I think the current language of 5.9 is fine with the addition of a sentence along the line that Marjorie proposed.

PROFESSOR CHARO: Larry?

DR. MIIKE: If I recall correctly our past discussions, the initial issue was whether half should

be from outside the institution versus inside the institution, then we got into subcategories and subcategories. I think that is still a sense if I read the group correctly but it is a little confusing now when you look at that because you say 25, 25, 25. We have lost that separation between either scientists or nonscientists or institution versus noninstitution so I think that needs to be recaptured. And I think we got lost in that when we--when some of us got concerned about the 50 percent and then we went to the 25 percent.

PROFESSOR CHARO: Let me direct your attention to the final sentence of 5.9 because the language we are going to be redrafting may look a lot like 5.9 but the last sentence is the one that creates the arithmetic issue--I forget exactly who raised it now--for each category IRB membership should be at least 25 percent, which would suggest--I think it was Diane who said that if there is not perfect overlap it would mean that in the end you are requiring more than 25 percent of the membership to represent people from each--you know, in toto from these various categories.

Is that what people want or would they like to keep the overall requirement for this group--this category of people at the at least 25 percent level and not higher for the required minimum?

Diane?

DR. SCOTT-JONES: Couldn't we solve the problem by adding some of Marjorie's proposed language to the last sentence joined by "and". For each category IRB membership should be at least 25 percent and individuals may serve one or more of these functions, or whatever it was that Marjorie said. Then we have solved the problem. But I think one thing to avoid is having members who fit 5.9 being all from number one not affiliated and say being all from another institution down the road. You certainly do not want that.

PROFESSOR CHARO: Which is certainly what Rhetaugh was noting but the language that you are--I think we probably do need to go back and do the language in the background because saying that they can represent all three does not mean that they all necessarily will so you still can find yourself in a situation where people do not have overlapping credentials and you still have wound up with a required minimum that would functionally be 35 or 40 or 45 percent. So the question is whether or not you want that.

DR. DUMAS: Could I ask a question? Would we be satisfied to have an IRB that would be composed of people who are all from within the same institution?

No. Then I think that in the revised--in the next revision we need to be very clear about the affiliation with the institution and then state the other characteristics because the way it is now a person can be--can represent perspective participants and be from the same institution.

PROFESSOR CHARO: Diane?

DR. SCOTT-JONES: Then why don't we say--why don't we just remove number one and just say for members who are not otherwise affiliated with the institution and then let the conditions be two and three. They could be nonscientists or representing the perspective of the participant and all of them would be nonaffiliated.

DR. DUMAS: That takes care of my concern.

DR. SCOTT-JONES: Just remove number one.

PROFESSOR CHARO: Would it make sense at this point to try and allow people to go back and redraft it in time for the discussion later on when we get to Chapter 5 and when the recommendation comes up and test out language and see if it matches what was just discussed and allow--

DR. SPEERS: That is fine.

PROFESSOR CHARO: Okay. At this point I would like to defer to Dr. Shapiro. We are up to the second item that you wanted to have us discuss, which was--I

have lost my notes already. Which would be the definition of research.

DR. GREIDER: Could I ask a question? Is there a list of these items that we are supposed to be discussing? Okay.

PROFESSOR CHARO: I received it on e-mail last night at 6:00 p.m.

DR. MURRAY: I got my e-mail but AOL would not let me open the document so some of us are--

PROFESSOR CHARO: All right. I will continue for a moment while Dr. Shapiro is getting himself organized. At certain points in the text and in the recommendations particularly around Recommendation 3.4 there is the discussion about what is going to be covered by the oversight system and what is not. And it revolves around the definition of research and the existing recommendation for 3.4 did not clarify with much precision the way in which the decision should be made about what should be covered and what should not.

There had been some e-mail discussion surrounding the questions about social science research that had yielded some observations about things that sometimes reduce concerns about research that might yield the conclusion that oversight is not necessary.

And so one of the questions we were asked to

answer was whether we would like to say something a tad more specific, not that necessarily invites large areas of research to be moved outside the oversight system but, in fact, rather to identify kind of the limits of the things that should be moved outside the oversight system and mention some of the factors that had been discussed on e-mail.

If we were to do that, Recommendation 3.4 could be supplemented by some language within the recommendation that follows its suggestion that the federal system should identify the research activities that are not subject to oversight with something more specific that says things like such activities should be generally limited to situations in which there is no physical intervention, little or no risk to participants, and a clear and easy opportunity for people to refuse to participate. In other words, it sets the limits on what could be considered to be outside the system but also send some signals as to the kinds of factors that might be used for the determination that would be made by the appropriate officials.

So the question here was whether people wanted to have this kind of specificity added at this point and, if so, whether these would represent the right kinds of things to use as limiting factors which would

limit the universe of things that could be excluded from oversight.

Arturo?

DR. BRITO: Yes. I definitely favor more specificity in this recommendation and I really like the old recommendation--what used to be Recommendation 2.4 where we outlined at least three key features. And I mentioned this in an e-mail because I think here we lose a lot by not being more specific and I do not think those three key features are any more than the minimum of what should define the kind of research we are most concerned about in this report.

So I really--I have not had a chance to think about the one you just proposed now but I would like more specificity than what is currently in the text.

PROFESSOR CHARO: Can you remind us of the three key features?

DR. BRITO: Yes. Number one, the intent of the activity is to generate knowledge, facts, et cetera. The second one is anticipated results would have validity. And then the third is that it is a systematic collection or analysis of data. I do not think that that should be very controversial for anybody that is defining what research is but I cannot recall what the arguments against that were right now but--and I know that we had a general concern abut too

much specificity in the recommendations and I agree with that overall because I think that this proposed federal office that takes place, I think that they should have some room there to work with but I do not think this is much more than setting some minimum guidelines.

DISCUSSION OF DRAFT REPORT:

PROLOGUE, CHAPTER 1, CHAPTER 2

DR. SHAPIRO: Thank you. Any other comments now? We will come back to this when we look at the specific recommendations.

Yes, Larry?

DR. MIIKE: I assume 3.4 and 3.5 are--we originally started with a definition of research and a definition of human subjects, and I assume that these are the latest attempts at that.

DR. SHAPIRO: Right.

DR. MIIKE: I sort of agree with Arturo on 4. I have no problems with 5. I think 4 is a little bit too vague.

DR. SHAPIRO: Okay. Well, let's come back to this again as we go through the recommendations systematically. There are then a number of items that we need--wanted to discuss just in general to help our discussions I think as we go through the recommendations because if you recall the--for those of

you who got my e-mail yesterday, I do not know who was traveling and who was able to get the e-mail or not but I just want to go back to that for a moment.

How many of you got my e-mail from yesterday? Everyone? Who did not? Everybody has got it.

Well, as you say, the--my minimum objective today is to complete all these recommendations. I just think we cannot leave here without having done that and so I am just trying to clear a little bit of discussion away at the beginning and I am going to limit this discussion for the next 20 minutes or so and then I want to get back to the recommendations and go ahead. If we do not discipline ourselves in that way we can be talking a long time and I think we have to face up to just deciding on the recommendations and getting them out.

As I said in the e-mail yesterday, my current intention is, if the commission does not object, is to actually complete the recommendations today, put them up on the web tomorrow, and to be followed pretty quickly with a prologue and executive summary, which we will talk about a little later on, and then the full report will be somewhat later. It seems to me that that is a schedule which we more or less have to stick to if we are going to complete this report.

So the purpose of this initial discussion--I

want to thank Alta for getting it started this morning--and for a number of other things which we will talk about later but I just want to get this settled. There is only a few more and they are really in the neighborhood of tone and tactical issues as opposed to fundamental issues so let me just address two of them together and then one separately.

One is a question of as we go through the recommendations how often we should specify regulation as opposed to guidance or whether we should make those kinds of distinctions as often as we do and whether we want to leave somehow more leeway or we want to point out that some of these things in our judgment require regulation as opposed to guidance. It is really a question of tone and I do not think we really have to resolve that right now but as we go through the recommendations I think we should be conscious of the issue as to whether in any particular recommendation we are requiring regulations or simply, as Alta would put it, having an aspirational view of this and whether they accomplish it by regulation and the guidance does not really matter to us. It is a matter of whether it gets accomplished or not. So we ought to just think about that as we go through the recommendations.

There is a similar kind of issue when it comes to whether we are talking about legislation versus

government, that is whether you want the government to do something or you want legislation to do something. It is really the very same issue, that is it is a question of tone and how broad or how specific we want to be as we go through the recommendations.

We may want to say it requires legislation or we may want to--that is we may recommend legislation, excuse me--or we may want to say the government should accomplish this and whether they do it by legislation or executive order or any other way does not really matter to us. It is a question again of how we visualize this and how important it is for us to be narrower in the sense when we require legislation as opposed to when you say government meaning however you do it, get it done, that is what this report is speaking to.

So I just want you to keep those issues in mind as we go through the recommendations and I think we should strive--unless we have specific reasons--for some kind of consistency in this area, that is if we decide for the broader approach, namely the government should--we recommend the government to do this, however they do it, we should sort of stick to that approach except where there is a specific reason that we want legislation. Alternatively, if we go for the narrower one, we ought to stick consistent with that. So it

is really a question of tone. It is not an aspirational versus a specific, I guess is the way Alta has talked about it, and I think we ought to just keep that in mind as we go ahead. That will be true both for regulation versus guidance. It is the same issue in a different guise and with regulation being narrower and guidance being broader or less rigid, I suppose, easier to change, and the same thing in legislation versus government.

Finally, there is the issue--what I call the NOHRO issue or NOHRO issue, N-O-H-R-O, that is whether we specifically want--again it is really in the same notion whether we specifically want to identify an independent office of the type that is described in the report right now and that is what we want or that we want the government to accomplish those objectives, however they decide to do it, whether as an independent office this way, that way, part of HHS, independent and so on. Those arguments are laid out.

In that particular case, as you know from e-mail of a few weeks ago, even months ago now, I rather preferred the NOHRO version and my reason for that was really not very profound. It was simply that as I was talking to people around the country about this, having a name helped them focus their attention. So it was really not any substantive issue that I had in mind

that it had to be this way or had to be that way but it was an easy way to talk to people about it and they grasped--I could judge from the response of public comments we got that they really could grasp it that way.

However, I have to say it is not a fundamental issue. I think there we will have the choice and perhaps we could discuss this right now. I am saying--going along with the current text roughly speaking, setting up this office and then say in the text, by the way, if you do not set up an independent office there are other ways to accomplish this or we could go the reverse way around. We could state it in a more general form and say in the text we think it is our feeling that you might want to really give most careful consideration to this to some--to a specific alternative but do not have that in the recommendations. I do not think in my own mind that it is a fundamental issue whether we go one way or another on that but I think maybe we should discuss it.

We have gone back and forth on it. Different commissioners have had different ideas about that so why don't we just try to solve that. That will help us an awful lot when we get to the recommendations vis-a-vis the text.

Larry?

DR. MIIKE: Well, I voiced my vote for returning back to objectives because, for example, if you look at 3.4 this thing that says we should issue regulations and then issue guidance through the regulations, and it seems to me if we make it more generic and say this is what we need to accomplish the text will cover that in a particular situation there is already an office, you do not have to do regulations, you do not have to do guidance. I think to just be clear. Otherwise, we will--if we do something like Recommendation 3.4, every time we look at another recommendation we have got to be careful that we are going to say a regulation versus guidance, et cetera, et cetera.

DR. LO: This is Bernie on conference call. Can I put my hand up?

DR. SHAPIRO: Who is this?

DR. MURRAY: Bernie.

DR. SHAPIRO: Bernie, yes.

I will be back to you in a second, Bernie.

DR. LO: Okay.

PROFESSOR OLDAKER: If our intent here is to get the government to act in some way, and that would be my intent, looking at the government is a very amorphous thing. You have to be fairly specific if you want to get anyone's attention to do anything and so if

we do not specify either an organization that we think should be created, it will not be created as we state but at least will center people's minds to think about it and to debate it. Similarly, if we do not encourage people to think about legislation, the government, as this amorphous entity, will not really hear it as well. I think you have to be fairly specific in what we want done if we really want to get something done here.

I realize, you know, by doing that we are setting up, you know, the report not to be fulfilled entirely because it is impossible ever to get anything if, you know, suggesting and then work through the complicated process that it has to go through.

So I would feel fairly strongly because I would like to see ultimately whatever we put down here put forward in some way that we be as specific as possible and also to put forth where we think it should be regulations because that will center people's mind also on the issue.

DR. SHAPIRO: Bernie?

DR. LO: I would actually like to sort of argue the opposite, Bill, from what--the opposite position from what I think Bill just said. I am concerned that there is not really an office sort of waiting to receive the report--do the report in the way we would like and that if we look at what we are doing

as basically enunciating, you know, principles and ideas, I think there is a very good likelihood that most of the implementation of the report will be done probably through Greg Koski's office and possibly through some organizations internally at NIH.

I mean, that is the way a lot of our recommendations have already been sort of picked up from previous reports. So I think that although we may have a goal ultimately of having a single federal office in charge of everything, I just think that it is fairly unrealistic of the risk I think we take of writing it as if we really have as a primary purpose the establishment of this other new office, as I have tried to argue before, is that there are people who balk at the idea of creating yet another federal office and I think it is not just sort of political reasons but a lot of the scientists I talk to are already--and IRB members as well are already so concerned about what they see as a proliferation of directives from OHRP and previously from OPRR that they are very leery of any more sort of government oversight because they think it could make things worse. So I think our strongest way to reach those people who are sort of the end users of the report in some respects is to try to bring them back to the big picture principles which I think have a lot of agreement--on which we can forge a lot of

agreement even among people who are not quite agreed on how to implement those principles.

Can I make one procedural request? I am having trouble hearing. I am wondering if someone could try and turn up the volume on the speaker phone coming towards me?

DR. SHAPIRO: We will try to do our best, Bernie. I am sorry it is difficult. We will try to turn it up.

Alta?

PROFESSOR CHARO: I always get nervous if I am disagreeing with Harold Shapiro but in this case I do and I would like to add some comments that will follow on Bernie's because I share his view. I have several reasons for preferring what has come to be called on some conversations the de-NOHRO-fication of the report.

The first is that I think that this is a topic that will be handled in a series of consecutively more and more focused efforts and that this effort starts at the broadest base at an effort to make some comments about certain kinds of ethical obligations to people who are participants in research but not yet protected by any system and also some ethical arguments about the kind of protection they deserve in terms of how we think about risks and how we think about benefits and

how we think about vulnerability, et cetera.

And that it is important to keep the focus at that level and not to conflate this task with what I would think of as being a tact that is more associated with a law reform commission or an administrative law group that is now going to take that and make closer determinations about which things are best done through administrative action, which are done through legislation, which are done through a specific office versus another office.

So part of it had to do with my instincts about what the role of the commission should be on a topic as broad as this one as opposed to some of the narrower topics we have taken on where we quite appropriately delved into a fair amount of detail at the regulatory level.

The second was my instinct that in terms of the way we present those arguments that the obligation to protect subjects through various or participants through various mechanisms is not an obligation that is held by a particular office. To say that NOHRO must do this and NOHRO must do that as part of a recommendation that is really about how we think about risk or how we think about vulnerability, I thought missed the opportunity to make the point that it is not an obligation of the office, it is an obligation of the

entire government.

There is a government obligation to provide protection to citizens, even non-citizens who are enrolled in research, and that that obligation cannot be delegated. It is always held by the entire government no matter how it chooses to fulfill it.

The third is that with regard to catching the attention of people, I thought that the strong recommendation at the very beginning that we think that the best way to fulfill this obligation is to create a single office and better yet to create a single office that is independent like the Office of Government Ethics allows us to continually say for all the other recommendations that simply say the federal government should do this or such and such a thing should be done in the passive tense because we do not have a particular actor allows us to continually drum beat in the accompanying text the notion that we think the best way to do that is by following our very first recommendation, which is to create this office, but it does not tie up the actual recommendation language, which is about what we are supposed to be aiming for with the means of implementation. These things stand separate and they can constantly be used in tandem.

Finally, dropping the language of NOHRO allows in the rewriting of the recommendation because that, of

course, always requires some minor editing of the language, it allows one to appropriately use the passive tense sometimes and other times to just make it a little more general and that, in turn, allows one to get away from the need to be very specific about NOHRO does what. Does it issue a reg? Does it issue guidance? Does it convene a group?

And I shared Larry's instinct rather than Bill Oldaker's about the wisdom of trying to determine on each of these recommendations whether we should be looking for regulation or not.

First, one of the points I thought of the report was to get away from the top down regulatory approach to this area and by introducing the notion of accreditation and certification and an emphasis on education to allow for some easing of top down regulation because we would have strengthened the grassroots bottom up level of protection by virtue of the capabilities of the researchers and the IRBs to handle problems without microdirection from a distant regulator whose ability to reform the regs is limited by the slowness of the administrative procedures necessary.

And, second, because there are times that things do not need to be done by regulation but really can be done by guidance but I do not feel like our

discussions have necessarily tended towards analyzing each of these topics with an eye to that question so I am wary of making that judgment at the last minute and more comfortable with general language saying, you know, risks should be analyzed this way and leave it to the next stage of detailing whether or not that is best done through regulation or through a set of guidance documents that would be used in conjunction with accreditation and certification programs.

Finally, although I know that there is a great deal of congressional activity, you know, it is probably impossible to ever be accurate in one's predictions about what one will and will not happen in any session of Congress. Any number of events can skew the focus of the Congress and I would want our recommendations to make sense even if there were no NOHRO to implement them. I would want very much for anybody who is in any position in any number of agencies to implement as many of them as possible and in that sense would like them to be standing on their own.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, I do not think that the two views are mutually exclusive. I think that if you want something done in this, I am with Bill Oldaker, you have to say exactly what you think ought to be

done. No one has given this more thought than we have so when we come out with a conclusion about what we specifically think it is after a long time of deliberation and we cannot expect that that is going to happen at every stage.

On the other hand, there are the larger reasons why we are doing this, which we lay out in more abstract terms so I think that I happen to like NOHRO but the specific thing--I like it for the same reason. When you tell persons about this then they are focused on something and then they can act on it but I think that we ought want to make specific recommendations and back them up with the more general reasons why we feel that way.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I will join the de-NOHRO-fication group today and for the reasons that Alta and some others have mentioned so I respectfully disagree with my colleagues across the table.

DR. SHAPIRO: Thank you very much.

Diane?

DR. SCOTT-JONES: I agree with what Jim just said but I also think that we could put some of this language in an appendix for those people who want all of these details about NOHRO because it just seems to me that reading through these pages the report just

sounds so bureaucratic. There is page after page of acronym after acronym and I think our report should not be focused in this manner. I think it would be fine to have an appendix with some of this detail in it and let the text remain at a more general level.

DR. SHAPIRO: Thank you.

Carol?

DR. GREIDER: So if I understood Alta correctly, you were not suggesting that we do away with the recommendation that there be such an office or some description of the office but rather just take the constant referrals back to NOHRO out of the other recommendations so if that is, you know, sort of your idea then I support that idea but I really think there should be a description of the office and a suggestion.

DR. SHAPIRO: Okay. Let me make a--Rhetaugh, I am sorry. I apologize.

DR. DUMAS: I just wanted to agree with Carol's point. I like that.

DR. SHAPIRO: Okay. Let me then suggest the following by way of proceeding. We will turn our attention probably in 15 minutes or so directly to the recommendations and that comes up really in the second recommendation, that is Recommendation 3.2 where the issue comes up. We can look at some alternative language here and decide what we agree and we will just

have to proceed through these recommendations.

I think that we should not talk ourselves into making this a huge issue of principle here because if we decide to take NOHRO out of the recommendation it will be referred to in text as a possibility which many of us, perhaps not all of us, they ought to consider in any case and it will be a reverse way around if we let it in so let's not think of it as huge principle here but we will make our choices as we go through the recommendations.

My proposal now is we take a--probably no more than 15 or 20 minutes to take any observations, comments people want to make on the prologue and chapters 1 and 2. We do not get to recommendations until chapter 3. In general, I do not want to spend a lot of time today worrying about text itself, although, as always, we are extremely appreciative of any marked up text that you can give us because it will certainly improve the report as we get down to it.

So while I would like to consider more general issues here and advice as to how we would structure them, restructure them and so on, and we will take maybe at the most a half an hour on this and then we will go to the recommendations themselves and see where that discussion takes us.

Jim?

DR. CHILDRESS: Okay. So we are starting with the prologue then?

DR. SHAPIRO: Yes, starting with the prologue.

DR. CHILDRESS: Okay. It is great having this material and I understand it will be incorporated into the executive summary, and I think it will make an important contribution to the report.

There were a few conceptual issues I thought might merit a little attention today and I guess maybe the overall one is it seems to me that the prologue is oriented almost exclusively to harm with little attention to other rights that are important, that we do not--informed consent, dignity and all those things are really subordinate to the question of harm. I think that actually would distort the report as a whole and I would like to see more balance in this prologue in relation to basically what our mandate asked us to cover, namely the rights, protection of rights and welfare of research subjects.

So let me be a little more specific now and I will just run through it in order, and so that is my overall point and I will elaborate that.

Where we do have informed consent on page 5 I just think we have not stated it the way we want it to be stated. When we say no one should be used in research without his or her voluntary informed consent,

and that is not what we affirm in this report or any other. There are cases in which we believe that research subjects or participants can be used without their consent and I think we need to say that. We need to say that--something like no one should be used in research without his or her voluntary informed consent or the authorization of an appropriate surrogate or whoever if that is what we believe, and I think we could not defend our other reports if we did not believe something like that.

On page 8 is where we get into--begin to get into the issues in the bold area that suggest again the focus on harm almost to the exclusion of the other kinds of concerns where we say a comprehensive and effective oversight system is essential to uniformly protect participants from unnecessary harm.

I think it will be a lot better to say to uniformly protect rights and welfare of participants because we are concerned about both. We are concerned about dignity, respect, informed consent and the like as well as protection from harm and I think we ought to say that.

Then I guess I would ask for clarification about the language of unnecessary harm. I am really not sure what that means. If we ask what the opposite would be we might go in the direction of necessary and

that does not seem to work; inevitable, well that might be possible; or unavoidable might be possible. But if--whatever we decide there we ought to go back and say what it is, is it protecting participants from avoidable harm or excessive risk. But I just--I would appreciate some clarification.

I was not at the Atlanta meeting where this may well have been discussed but I just--I have trouble making sense of the notion of unnecessary harm.

DR. SHAPIRO: You know, I think you have made a good point. I think unnecessary harm is hard to understand and not the right word. I agree with that. As I recall the discussion, it was--and I may be responsible for it although I cannot remember that for certain--my only notion was there are--there is unavoidably some harms occurring here. The only way not to have any harms is to not have any experiments so I was trying--stretching and not very effectively obviously for something which signals to people that it was not zero harm that is in here but something--another way of describing it and you make a very good point, I think, and this is not the right way to do it but I would be interested in what might be some appropriate language here.

Larry, and then Diane?

DR. MIIKE: Well, I think the language is

right before the bold because we are really talking about extending the protection of the system to the private sector so we are really talking about participants should be protected. People are afforded the same protection that we currently have in the federal side. So I think it is a simple solution as to this is a substitute protection for the harm issue.

DR. SHAPIRO: Diane, and then Steve.

DR. SCOTT-JONES: Okay. Commenting on unnecessary harm. I think it is fine to eliminate unnecessary because the focus is on protecting participants from harm. That does not suggest that there will never be any harm but that you are protecting participants and I think eliminating unnecessary is fine. I have a comment about another issue on pages 3 and 5, the text in bold.

In each instance, page 3 and 5, we state no one should be used in research and I would suggest that we change that to no one should participate in research because the phrase being used suggests an improper role of the researcher--that the researcher is using people. So I would strongly say "participate" is more reflective of how we see the whole process.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Could I come back to Jim's point and instead of hanging up on unnecessary versus

necessary harm, I think Jim was talking about shifting from a notion of the locus being protecting against harm to safeguarding--

DR. SHAPIRO: Rights and welfare.

MR. HOLTZMAN: --rights and welfare.

DR. SHAPIRO: Well, that is the key point here.

MR. HOLTZMAN: And I really think that that is a very important and usable change and we could go back and just--

DR. SHAPIRO: I agree with that.

Tom?

DR. MURRAY: Thank you. It is good to be back. You may not agree after I am finished today but thank you.

(Laughter.)

DR. MURRAY: I have lots of small things but I am going to ignore all those and submit those independently and instead I need guidance on three things.

The first, I believe, occurs on page 7 where there is a full paragraph there that runs from lines 9 to 23. Now perhaps this was thoroughly discussed but here we are--I think we are trying to do something worthwhile but I think it does not work because what I wrote was this makes--this is the notion about we

should not categorize groups as vulnerable. Okay. It sounds very nice.

The fact is children who cannot give consent are vulnerable for that reason alone and people who for mental illness or retardation cannot give meaningful consent. There are some people whose ability to consent is impaired because of those conditions and, yes, you can create circumstances where, you know, avoid exploitation of those people but what I wrote was "this makes hash out of the sensible observation that while at times the circumstances create the vulnerability, at other times it is also the characteristics of the person, the children, et cetera." And I just felt like we were dancing around that in this paragraph. I am not sure what this paragraph was intended to accomplish. That is point number one.

Point number two is page 8, lines 13 and 14. We assert in the United States the general principles of the Belmont Report were preserved over two decades. I do not think we want the word "years" there. Two decades ago in the form of government regulations and professional guidelines. It may be correct. I think that may be a misreading of history. I mean, I think the IRB system preexisted the Belmont Report. The Belmont Report was the last thing to come out of that

commission and, you know, that is amply demonstrated in the record. I think we could simply revise that so as not to misrepresent history.

And the third comment if I can find--well, let me come back to the third one.

DR. SHAPIRO: Okay. Bette? We will come back to the issue Tom had.

MS. KRAMER: I also had a couple of comments. On page--

DR. SHAPIRO: Bette, press your mic.

MS. KRAMER: Sorry. I have a couple of places that I wanted to ask some questions. Page 7, lines 6, 7, 8, I was not exactly sure what that was. Am I the only one for whom that was not clear?

DR. CHILDRESS: I thought it was unclear also.

DR. SHAPIRO: This is page 7, lines 6--

MS. KRAMER: Yes. It is particularly line 7.

DR. SHAPIRO: Research--the bold type?

MS. KRAMER: Right. Just take that whole sentence beginning on 6.

DR. CHILDRESS: Could I add something to that?

MS. KRAMER: Please.

DR. CHILDRESS: Part of my confusion comes--I mean, I am not sure why we want to say here in which autonomous competent adults become unusually

susceptible to harm, manipulation and exploitation, why not all people--it is what is being captured here and so I guess I really miss the intent, as Bette does, of this particular bold section.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I think I might be able to tell you a little bit about the intent so that maybe some language can be offered up. This was about the tension between trying to include all segments of society while not creating an endless series of situations in which people are used in ways or in settings where they are, in fact, more susceptible to manipulation or exploitation, et cetera.

And so--and the reason for the phrase about autonomous competent adults was simply to exclude the categories of children, embryos and fetuses, and those persons with mental disorders that impair decision making because they are all kind of special issues, special categories.

So it was an attempt to somehow capture the tension and the point of the report, which is that research should be inclusive but also avoid the situations that create these susceptibilities. So if you think about it, there has been a conversation over years following Tuskegee about whether to think of ethnic minorities and racial minorities as

intrinsically vulnerable and the point here would be, no, they are not intrinsically vulnerable but there are situations in which they are more likely to be exploited and that what we should be doing is avoiding those situations rather than avoiding the enrollment of these populations.

So with that goal in mind what might be the language that would best express it?

DR. SHAPIRO: Trish?

PROFESSOR BACKLAR: It seems to me actually I could read this as meaning guarding against therapeutic misconception. You cannot hear me?

DR. SHAPIRO: Just bring the microphone a little closer to you.

PROFESSOR BACKLAR: All right. I actually did understand this sentence and I read it--I am looking at this and thinking of ACHR (sic). I am thinking of research protocols that bring people in who are very ill and very desirous of getting help because they are so anxious for care that they fall into the therapeutic misconception.

DR. SHAPIRO: Okay. Eric?

PROFESSOR BACKLAR: It does not mean we cannot--

DR. CASSELL: Well, the intent--I think--

PROFESSOR CHARO: Your microphone.

DR. CASSELL: The intent it seems to me is excellent but I think that the--we could do it by saying--getting rid of the first sentence and saying, "Wherever possible, research should be designed to encourage the participation of all groups of people while protecting their rights and welfare," and then we are just reiterating what the rest of the report is about.

DR. DUMAS: I like that one.

DR. SHAPIRO: Okay. Diane?

DR. SCOTT-JONES: Eric just made a good suggestion for the comment that I was going to make. This statement reads, "Research should be designed to meet the needs of all groups of people when research does not meet the needs of people." So I think Eric is saying encourage participation of all groups of people is far better than the language that is here now.

DR. SHAPIRO: Thank you.

Larry?

DR. MIIKE: I think Eric solved it because the sentence as read protects the wrong people if we are going to include everybody. This sentence says we should protect the autonomous and it should be the opposite. We should be dealing with the vulnerable. So I think what Eric has said solves it.

DR. SHAPIRO: Tom?

DR. MURRAY: I just--this is not language I am proposing. I just want to understand if this is the right concept you want. Do not exploit, do not exclude, do invite participation. Is that what we are after? Okay.

I remembered my other point. If--as I read this, I think--as I read the intent behind this, the idea is to have a really resonant statement that not only introduces people to this report but also tries to give a sense of what this commission has been about in so far as it concerns human subjects research. In which case, the prose needs to soar and I am wondering if it would be inconsistent with the drafter's intent to reform the beginning.

It seems to me really we should start with something like line 23 that today's system of research protections is a patchwork arrangement and so on. Just right up front. And then explain that, you know, our intent is to--if not a patchwork, at least make some beautiful quilt out of the current arrangement but something--is that--because we sort of go with this semi-apologetic language about, oh, science is wonderful. It is a typical writer's way of working up to when you want to hit somebody with something.

Why don't we hit them with it first? Then we can say we also think it is wonderful. Is that

consistent with--

DR. SHAPIRO: It is a useful suggestion. A very useful suggestion.

Steve?

MR. HOLTZMAN: So are we going to come back to Tom's first point and discuss it?

DR. SHAPIRO: Yes. I want to come back to that in a moment.

MR. HOLTZMAN: Okay.

DR. SHAPIRO: Because that has implications later on, major kinds of implications later on. That is why I was postponing that.

Bette?

MS. KRAMER: Okay. I had--there are some other questions. Page 8, lines--beginning at line 3, talking about the President's Commission call having called for pilot studies of compensation programs, a recommendation worth revisiting. It is left hanging. Did those programs--do the studies never take place?

DR. SHAPIRO: Never take place.

MS. KRAMER: Well, I think that just needs to be clarified.

DR. SHAPIRO: Yes.

MS. KRAMER: That they never took place and--

DR. SHAPIRO: We do put it here. It is in the text further on.

MS. KRAMER: Okay.

DR. SHAPIRO: But, yes, I understand the point.

MS. KRAMER: Okay. Let me see. And I think there was one other. Page 12, line 17. I know. Page 12, line 17. I objected to the--I think it was a mistake to include that term "secondary research participants" because--Eric is smiling. He knew I was going to catch it. That is that great area of contention and I do not think that we need to cooperate in it.

DR. SHAPIRO: That is fine.

MS. KRAMER: Okay.

DR. SHAPIRO: Other comments before we go back to Tom's point?

Okay. The point that Tom raises, I am trying to remember right now. Tom, which page is it on?

DR. MURRAY: 7.

DR. SHAPIRO: 7. It really has to do with our--with some suggestions that come up later regarding a different way to look at vulnerability as opposed to saying children and various categories, is to look at it in a different kind of analytic frame. One does not exclude the other. Children are going to fall into this frame no matter what, whether we go at it the first way we go at it or the second way.

And let's--I think we should discuss it for a few minutes now if anybody has any views on it but we will get to that also in the chapter itself and if that turns out that we are--for whatever reason--not happy with it, we will have to come back and look at this but I think your comment is absolutely correct that children are children in the sense that you meant it and it would get caught here but it would get caught in other schemes also.

But, Steve, did you have something you wanted to raise in this?

Okay. Arturo?

DR. BRITO: Yes. I think what happens here in the prologue is that what does not come across is the fact that the analytical model is more of a dynamic model than the categorical model and I think what we are trying to do here in this section is two part. We are trying too hard to get too much in here and I think all we need to really say here is that basically it is difficult and there are some problems with categorizing individuals into certain groups that are vulnerable because then it leads to certain stigma, et cetera.

But I really think that the discussion in the text on the analytical model really shows--and does not say that children are not vulnerable or people with mental difficulties or cognitive difficulties are not

going to be vulnerable. We are saying in certain situations they may be more vulnerable than others and it specifies how dynamic the situation is.

So I think what we need to do here--I do not think, Tom, were you suggesting that we--I do not think you were suggesting we do not use the analytical model. I think what you are saying here is in the prologue--if I am not mistaken, you were saying in the prologue that it really implies that certain categories of individuals are not vulnerable when, in fact, that is not true. Is that correct?

DR. MURRAY: Yes.

DR. BRITO: So I think what we need to do is reword this in a way that talks more about the general difficulties that one has with categorical groups.

DR. SHAPIRO: Tom?

DR. MURRAY: Actually Arturo's suggestion may go most if not all the way towards meeting my concern, which is simply acknowledge that there are some groups that are by virtue of their circumstances, mainly having to do with, you know, cognitive capacities, to understand and consent are in their nature vulnerable but then there are other groups that are called vulnerable but that is really more a matter of this dynamic model and I think that probably handles--I have to look at the new text but that may handle all of my

concerns.

DR. SHAPIRO: Okay. Alta, and then I want to move on, or Diane, and then we will move on, and we will come back to this later as I have said before.

PROFESSOR CHARO: First, I wanted to thank you for the request to make the language soar. One of the problems everybody recognizes is that when you have got 18 people editing a document it blandisizes quickly.

Would the following language--

DR. SHAPIRO: De-NOHRO-tise or something.

PROFESSOR CHARO: Blandisize is an official word closely associated with government document writing.

DR. SHAPIRO: In which language?

PROFESSOR CHARO: It is government--it is the language of government.

MR. HOLTZMAN: Is de-NOHRO-fication a species?

PROFESSOR CHARO: De-NOHRO-fication.

(Laughter.)

PROFESSOR CHARO: Tom, I wanted to know if this captures the meaning of what you and Arturo are suggesting that on page 7, line 9, it should say instead that we recommend that rather than focusing exclusively on categorizing groups as vulnerable, investigators and IRBs should also recognize and avoid situations that create susceptibility, da, da, da?

Does that capture it or is that still not quite there?

DR. MURRAY: It is in the right direction. I would probably say instead we acknowledge that some groups are by their nature because--and I do not--it is always a bad idea to compose on the fly but--

PROFESSOR CHARO: Right, right, right.

DR. MURRAY: --I want to--you know, the idea is that by their nature, by their--because of a lack of cognitive maturity or inability are going to be sort of vulnerable. But, however, there are other groups who have also been classified as vulnerable who--and then basically pick up everything else.

PROFESSOR CHARO: It is just spelling it out more explicitly.

DR. MURRAY: Yes.

PROFESSOR CHARO: The whole business about autonomous, competent adults was--it is actually quite--

DR. MURRAY: An effort to do that.

PROFESSOR CHARO: --it was an attempt to do that implicitly.

DR. MURRAY: Okay.

PROFESSOR CHARO: But explicitly is clearer.

DR. MURRAY: It soared right over my head in this case so I think we probably just need to say it right.

PROFESSOR CHARO: Yes.

DR. SHAPIRO: Thank you.

Steve?

MR. HOLTZMAN: So on this--with the spirit of soaring, right, if you go to 6, we try to wind into this with denoting that calling certain groups vulnerable can be intrinsically insulting or it is not politically correct or whatever is the politically correct term for not being politically correct.

I think what we are trying to say is the system embodied a certain view of the world, all right, which we have come to learn is not necessarily the best way to look at the world and that in a certain time and place a group will be categorized as vulnerable, e.g. pregnant women, when, in fact, they are not. And, therefore, what we would like to move is to a model that is not politically correct but rather recognizes, okay, that there is intrinsic and situationally caused vulnerabilities.

DR. SHAPIRO: Okay. Any other topic in the prologue anyone would like to raise at this time? Diane?

DR. SCOTT-JONES: On page 12, the section labeled "clarifying the scope of oversight" lacks clarity and there are places where we need to be more specific because it reads as if we have a hidden agenda

here. For example, line 10, certain types of surveys and interviews are certainly considered research but I think we need to come right out and be more specific about what is meant here on line 20 where research poses real risk. We need to be more specific, what is a real risk as opposed to a risk that is not real. And if the subtext here is that social science research is not quite research then I think we need to do something here to fix this.

DR. SHAPIRO: There is always--first of all, let's try to avoid writing the report in the prologue because that is the problem we had before.

Second of all, we do fall into some linguistic problems here with not distinguishing carefully between research and research that needs oversight, and that is what you point to in the second point that you made and we do have to be very careful, and we will as we draft this because almost always in this report research really means research requiring oversight, and that is, I think, the distinction that is not made here very carefully and I think your point is well taken. As we go through redrafting it we have got to be very careful on that issue. It comes up in a number of points throughout the report.

Larry?

DR. MIIKE: You just made a comment which has

been bugging me all this time, which is that, you know, when we--when the group, not me, decided that we would do a prologue versus a summary, and then now you have just said what I think this is becoming, this is becoming a summary, so I am sort of--because it was because it was becoming a summary I then said we should not have to bother with an executive summary. You can just stick the recommendations in at the end of this and we would have our executive summary. So I guess I need to reopen the issue is that what exactly are we doing with this prologue?

DR. SHAPIRO: My own view is that what we are trying to do with this prologue is give people a very--I do not know whether it is a--I do not know what to call it. I want to avoid getting into an argument of calling it prologue or summary--is to give people an opportunity to really pick up the key issues as we see them and the recommendations that will follow them. And with--that is the point of it and if they are interested, really interested in detail, they will go to the report and read it.

DR. MIIKE: If that is the case then our prologue really should signal why we were doing this and the kinds of issues that were crying out to be addressed rather than--then we got into the mess of trying to summarize everything that is in the report

and I think that is part of the problem I continue to have.

DR. SHAPIRO: Okay. Any other issues here?

Okay. We will redraft this as quickly as we can, that does not mean today but it means pretty shortly, and then send it out one more time for commissioners to review.

It really would be extremely helpful for those who have read it and have particular comments to leave them with us here today if at all possible because otherwise if we rely on back and forth given everybody's schedule and so on, it is not likely that we can capture some of the very good ideas that you have. So perhaps either leave with Eric or Marjorie a copy with your initials on it so they will know who it is so if they have questions they can call you and ask you about it.

Okay. We are running a little bit but not too far behind time here. Let's go to Chapter 1. As I say, Chapter 1 and Chapter 2 do not have recommendations in them but nevertheless we ought to consider if there are some general comments people would like to make. Once again, specific editorial suggestions we will take up separately. You can let Eric and Marjorie know directly about those.

Jim?

Let's go to Chapter 1 first by the way.

Jim?

DR. CHILDRESS: Right. Just to pick up a point I made earlier, and it seems to me here again looking at page 2 and at other places the emphasis tends to fall on the harm point and I just urge that we reconsider that along the lines of the previous discussion.

DR. SHAPIRO: No, that is a very good point and certainly you have to do that.

Alta?

PROFESSOR CHARO: I think I might have made some of these points on e-mail but it came out very late because of my own dawdling in getting reactions. On a substantive level the one thing that concerned me a little bit about Chapter 1 was the recitation of examples that at times relied on press reports rather than primary documents. I know that in some circumstances there is nothing but a press report but there are other circumstances where there are primary sources.

For example, in the discussion of the Jesse Gelsinger case there are primary sources from the FDA that are cited but there are other parts of the description of events that come out of press reports and I wanted to know if other people shared my sense of

nervousness when you are issuing a government report that might be viewed as authoritative in and of itself at using secondary sources where there is an alternative available.

DR. SHAPIRO: Looking for hands. Yes, I agree. I agree with that. That has to be fixed up in here. I agree. It does not mean we should exclude the others if they are relevant.

PROFESSOR CHARO: My point simply being if there are primary sources available then they should be preferred consistently.

DR. SHAPIRO: Right, I agree with that. Other comments?

DR. MIIKE: I might as well.

DR. SHAPIRO: What the heck.

DR. MIIKE: I wrote lots of reports that had personal communication, some press reports, and it is a policy document. This is not a peer reviewed scientific journal type of article--report and so I agree with that only to the extent it does not delay.

DR. SHAPIRO: Right. I agree with that. We have these references. Delay is the one thing I will not accept here today. Everything else is acceptable.

Anything else on Chapter 1 anyone would like to raise at this time? Again, please send whatever comments and so on you have to Eric, Marjorie or

myself, whatever is easier for you.

Let's look next or at least consider any questions you might have regarding Chapter 2, which I am busy trying to locate here in my pile. Any comments with respect to Chapter 2?

Alta? Excuse me, Alta?

PROFESSOR CHARO: I know that it was--sorry. I know that there was some--a place for--academic literature, that is right. In the second on Chapter 2 that goes into--

DR. SHAPIRO: Page?

PROFESSOR CHARO: Page 17, et seq., that goes into academic literature, I was hoping to see what would become the beginning of a more extensive discussion in Chapter 3 about the identified difficulties in applying the current system to social science and humanities research since that has been the subject of great discussion.

DR. SHAPIRO: So you would like to see something added in that section that deals specifically with the issues that have come up. There are many, I agree. I think that is a very good suggestion.

Steve?

MR. HOLTZMAN: This is either a nit or a I do not understand, on the chart the FDA kind of just hangs out there. Is it supposed to be connected to anything

or have some sort of--just might think about everything else having--

DR. SHAPIRO: This chart here?

MR. HOLTZMAN: Yes.

DR. SPEERS: It is intended to hang out there.

MR. HOLTZMAN: Okay.

DR. SPEERS: Because it is not connected to the Common Rule. It is a separate set of regulations.

MR. HOLTZMAN: Okay.

DR. SHAPIRO: That is true but I had a similar reaction actually to Steve's because the big heading in this table is "Federal--Current Federal Regulatory Structure." It is not just the Common Rule. And, therefore, you are looking where the FDA plays a major part. So either we have to change the title or we have to deal with this issue. At least--perhaps I have an old copy but that is the one I have. So, I mean, I agree with Steve since so much of it does work through the FDA.

Other comments?

Okay. Thank you very much. Again I am not trying to close the possibility of comments. I am looking forward to receiving other written comments you might have, marked up copies and so on, and I do not like to repeat myself as much as I do but it would be very helpful to get that from you. Okay. Let's move

on now.

My suggestion is that we move on to Chapter 3 and in this case let's start dealing with the recommendations.

We will come back to text and other things afterwards except as they might directly impact on these recommendations.

Eric, could you tell me what everyone has at their places?

DISCUSSION OF DRAFT REPORT: CHAPTER 3

DR. MESLIN: You should have a document that says, "Summary of Chapter Recommendations," which are--it begins with 3.1 and goes on for five pages, six pages. These are the recommendations that were taken out of the chapters that you have received over the last week or ten days simply repeated for you.

You should also have another document that we just reproduced from Alta's e-mail that says, "Suggested Revisions to Recommendations" at the top. For purposes of public, this is just material that Alta had put together. We are not even sure we are going to go over each of them but you should all have a copy of the document that says, "Summary of Chapter Recommendations." I believe your copy at the header says, "Embargoed until 8:30 a.m., May 15, 2001." It is now open for discussion because we are past that time.

So those should be the two things that you have, including obviously the chapters themselves.

DR. SHAPIRO: All right. Let's begin by looking at these recommendations and alternative suggestions regarding these and let's just go at it one by one just to go through in a systematic way. We will know what is behind us. And many of the issues we discussed earlier this morning, some of which were discussed prior to my arrival, will come up in the context of these and, indeed, they will come up almost right away.

Eric, why don't you begin by taking us through each of these recommendations and do you have a--well, I prefer--why don't you take us through this and point out the differences as we go on and we can discuss what people's preferences are?

DR. MESLIN: Well, you have the materials. I will just direct you to 3.1. I apologize. We did not put the page numbers on as we often do for you so we will try and give you that fairly quickly at the same time.

DR. SHAPIRO: Perhaps you could point to the distinctions, if any, to bring people's attention to it between these recommendations.

DR. MESLIN: Right.

DR. SHAPIRO: Because we are going to have to choose one or other or some other language.

DR. MESLIN: Well, there is not a change in 3.1.

DR. SHAPIRO: Eric?

DR. CASSELL: This is a place to put Jim's general comment in. The rights and welfare of all human participants in research should be protected by so that it opens the recommendations.

DR. SHAPIRO: Very helpful. Thank you.

Any other comment on 3.1? 3.1 is the same in both versions you have in front of you. I think it is.

PROFESSOR CHARO: No.

DR. SHAPIRO: What is the difference then?

PROFESSOR CHARO: There is a slight stylistic change. It is just--there is only a very slight stylistic change.

DR. SHAPIRO: Which is?

PROFESSOR CHARO: Instead of saying "should be protected by federal oversight system with its requirements off..." it says "should be protected by an oversight system that requires..." It is just--

DR. SHAPIRO: It seems the more straight forward. Okay.

Then we are going to--the amendment that Eric provided regarding the rights and welfare, we will go

ahead with Recommendation 3.1 as--which really is in what is on your list as Alta's version because I think the grammar--the language does work a little better that way.

Okay. Eric, let's go to 3.2.

DR. MESLIN: Right. Well, here is where the first distinction between NOHRO and the Federal Government exists. The sense in both 3.2s are essentially the same with a couple of important distinctions. The first is the creation of NOHRO and its enactment of legislation and its lead responsibilities as contrasted with the Alta version that simply refers to the government creating a single independent office.

The other significant change or suggestion in the Charo proposal is the last sentence which describes the office's responsibility with respect to intervening to protect research participants. So this is your first opportunity to decide whether you want to allow NOHRO in or NOHRO out.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Well, can we split it up into three distinct issues? I think you have identified them. The first is do we want to say the government should or do we want to say legislation should be enacted? The second is do we want to name NOHRO or

not? And the third is do we want to explicitly talk about intervention? There are three distinct issues.

DR. SHAPIRO: Let's talk about the first, first.

MR. HOLTZMAN: So on the first since I do not know how the government goes about creating things, I do not know what I am signing up for if I specifically say legislation. If I fail to say legislation and I said something that is too--

DR. SHAPIRO: Well--

MR. HOLTZMAN: --meaningless.

DR. SHAPIRO: --we are--

MR. HOLTZMAN: That is the question.

DR. SHAPIRO: --we are now in the area of speculation. This is directly--I do not know how to answer your question in a convincing way. Maybe Alta or someone else does. I do not know. Someone who reads legislation can say I want to do it some other way, never mind legislation. Someone who reads the general could say let's have legislation.

Larry, and then Alta.

DR. MIIKE: Well, there is a simple solution. We do not have to say the Federal Government or the federal legislation since it is pretty obvious that it is going to lead to legislation so just say create a single federal office, and the text makes it clear what

implementation steps would be required for that. So I do not think we need to get hung up on this.

DR. SHAPIRO: I agree with that point. Alta?

PROFESSOR CHARO: Yes, just to respond to Steve. I actually have no problem with naming NOHRO to answer your second. The reason I had suggested avoiding the phrase "passing legislation" is simply that a lot, although not everything, could also be done by administrative action. If President Bush were to direct all the cabinet secretaries to defer to a single lead office that was located in one of the departments, President Bush has that prerogative and, therefore, I did not want--my instinct was not to write a recommendation that necessarily required congressional action if the President were inclined to use as much executive power as is at his disposal.

DR. MIIKE: Can I just comment on that?

DR. SHAPIRO: Rachel?

MS. LEVINSON: Just on this point. If there are multiple ways, as Alta has just pointed out, that something might be accomplished then you do not want to be so prescriptive that you rule out one or the other. But if you already know that something could not be accomplished without legislation then you are probably better off saying legislation because you are going to get a specific kind of attention to that

recommendation.

DR. SHAPIRO: Larry?

DR. MIIKE: Can I just make a comment on what Alta said? I mean, it seems to me that the President cannot do it because look at what happened with the Common Rule. I thought we heard from legislative council out of the White House that they could not force these agencies to do this and it would seem that it was a pretty common sense thing that he could but--

DR. SHAPIRO: Alta?

PROFESSOR CHARO: If the political will is present one can ask one's cabinet secretaries to do what you, the President, want done. It would surprise me if any one of these issues was considered a make or break issue that would yield a do this or resign but there is that capability so I guess now we are talking about whether we want to talk about theoretical possibilities or politically likely possibilities but at that point we might as well drop legislation as well since that is not likely either, at least successful legislation.

So, I mean, once we go down the road of what is politically likely, we definitely need a crystal ball and lower expectations.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I am leaning on the side of

statements about legislation because we want this to be an enduring initiative and if you do not establish the office through legislative mechanisms it can be abolished at the will of the President or anybody else.

DR. SHAPIRO: Tom?

DR. MURRAY: I am so out of my depth here that, you know, I am drowning but I cannot predict which course is going to be the most successful. I did spend some time, though, with members of the House of Representatives recently and there does seem to be a very strong, at least among certain members of the House, and this is not a partisan issue so far as I can tell, to take seriously the protection of human subjects. I believe that there is reason to think there is similar sentiment in the Senate.

I have no idea whether it is enough to get legislation passed but I am with Rhetaugh and the others who said it is probably worth putting it up there and making it as a firm recommendation. It may not succeed and maybe it will get accomplished another way but I do not know that there is going to be a better moment to try to get this passed legislatively. There is interest. There is still lingering concern over a variety of human subjects, failures, so I would vote to keep legislation in.

DR. SHAPIRO: Any other comments on this?

Larry?

DR. MIIKE: One last thing is that I am for it. It is just that--

DR. SHAPIRO: For it meaning?

DR. MIIKE: For it being specific about legislation. My only hesitation is that we not be seen as putting all our marbles into a single federal office legislative approach to this but what I think--as long as we cover very specifically in the other recommendations a lot of this stuff can be done even if we do not do this.

DR. SHAPIRO: Let me repeat what I said the first time. Following this recommendation, let's suppose we choose legislation just to take this particular issue. The text is going to have to point out that there are other ways to achieve that other than by legislation and there may be other ways and we would certainly support those as well, and the reverse is true if we end up on the other side. So the report as a whole is going to have both options before us even though the specific recommendation should include only one of these.

Yes?

DR. MESLIN: No, I was--

DR. SHAPIRO: Excuse me. So let's just--we really have to get on with this so let's just see how

many members of the commission prefer that we stick with creating legislation, the stronger of these two things?

(A show of hands.)

DR. SHAPIRO: Okay. So that is the way we are going to go. So on this particular recommendation we will talk about legislation to create this. The text will, of course, talk about the broader issue of this being able to be accomplished in other ways perhaps.

Let's go to the second issue, which Steve identified in here, namely the naming of this federal-- Steve?

MR. HOLTZMAN: So we do introduce the name in the text and we use an acronym for it and I have no problem with that. It is a useful shorthand. I do think there is a substantive recommendation we have to create such a thing. We have a substantive recommendation that go beyond that about all the things we would like done. It is a good way to do it. If it does not exist we still want them done. So I cannot answer the question about naming NOHRO here without going into the question of do I want NOHRO to occur in the rest of the recs because my sole purpose for naming it here is because in the rest of the recs I am going to use it. If I am not going to use it in the rest of the recs I ain't going to name it here.

I personally would not use it in the rest of the recs but I think that is the way one ought to decide it.

DR. SHAPIRO: Yes. What is already decided, Steve?

MR. HOLTZMAN: I think that would be the decision principle I would use that if you are going to use it in the rest, introduce it here. If you are not, do not, and just use it as a convention in your textual stuff.

DR. SHAPIRO: Okay. Alta?

PROFESSOR CHARO: Actually although I have been leading the de-NOHRO-ization charge here, this is a place where having called for the legislation I would actually say why not use it even though for every other recommendation that comes down the line I am going to raise my hand and say take out the name NOHRO. And the reason is that there is likely to be one or two paragraphs following many of these recommendations that spell out in further detail what the recommendation is about and they very well may use the phrase NOHRO and, therefore, it makes sense to introduce it in this rec even if it should not appear in any other recommendation's main bolded language.

DR. SHAPIRO: Arturo?

DR. BRITO: Yes. I agree that using the NOHRO

name here would be prudent because it does--I think the key here is what everybody agrees with is that there is a need for an independent office and by just stating independent single federal office I am not sure it comes out clear and by putting the name in here that makes it a little more clear and little stronger statements so I agree with Alta's comment.

DR. SHAPIRO: Okay. Rhetaugh?

DR. DUMAS: My sense would be that there is a difference between naming the office and referring to the office by this name. And I would go toward referring to the office by this name, which means that we would write it in small letters instead of caps but it would at least give an identifiable label for what we are talking about.

DR. SHAPIRO: Okay. I sense that the--most commissioners really want to keep this name here. We will have to work on it as we go along so we will go along with that.

Now, Steve, what was your third item? You had three. You had divide this into three parts and I have forgotten what the third--

MR. HOLTZMAN: Well, we should turn--

DR. SHAPIRO: --enforcement. Excuse me.

MR. HOLTZMAN: We had Alta raises this notion of intervention to protect from harm of undue risk and

did--let's turn to Alta. Did you intend something beyond that which is captured in the previous one about enforcement?

PROFESSOR CHARO: It is a little bit along the lines of the conversation that took place before with Tom when we talked about things that are implicit that occasionally go right past you and in the revision, which changed that sentence slightly here and there, you know, taking out rule making and things like that, I was of the opinion that it was worth highlighting the enforcement issue very specifically with regard to protection of subjects because that was the most controversial aspect of OPRR's existence in the last few years and I wanted to in my view highlight the notion that it was still an appropriate thing for a lead federal office to be doing.

DR. SHAPIRO: My sense of this is I actually liked--if you take the last two sentences of Alta's recommendation compared to the last sentence of the one that we had--those are really the two alternatives here, I actually prefer the language "should oversee policy development" rather than "responsible for policy development" because the policy development will be on many levels and we want this to be only at the highest level. So I like the notion of oversee policy development at regulatory forum because I do not want

to over indulge or just up and throw everything into this basket. There is going to be shared responsibility here so I actually like Alta's--what is her penultimate sentence in this recommendation.

And I also, for the same reason, like her last sentence, that is it gives to me at least the idea that this is a shared responsibility of oversight. Oversight occurs at the institution and various other levels and NORAD--NORAD is really not what we need--that is what we really need--NOHRO--

PROFESSOR CHARO: A new use for NOHRO.

(Laughter.)

DR. SHAPIRO: Yes. You wanted to go to the Colorado mountain, right?

So my sense is I like the flavor at least. I do not want to argue about the words of the second part of Alta's recommendation. It seemed to me more consistent with what we mean.

Steve?

MR. HOLTZMAN: Just a quick question. FDA has a monitoring and an enforcement role with respect to drug trials.

DR. SHAPIRO: Yes.

MR. HOLTZMAN: When we envisage NOHRO and say "when needed, this office should intervene to protect research," are we--would the "when needed" be in this

case a right, an authority if the FDA is not doing its job well enough in NOHRO's opinion? I am just asking what do we mean and what are we envisaging?

DR. SHAPIRO: That is what I mean because if it is a single independent thing which oversees this thing the FDA is part of it, and that was just my sense.

Jim, then Larry.

DR. CHILDRESS: I will leave it off. I guess at this one, also, I think we are interested in protecting rights and welfare and not simply protection from harm again.

DR. SHAPIRO: That is an excellent point and let's just assume that we are going to do that.

PROFESSOR CHARO: So we say "protect research participants from violations of their rights--of their rights and welfare."

DR. CHILDRESS: Rights and welfare.

PROFESSOR CHARO: Or to protect their rights and welfare, to protect the rights and welfare of research participants.

DR. SHAPIRO: Other comments on--yes, Larry?

DR. MIIKE: I guess I am going to stand alone in this. I am uncomfortable with such a visible spotlighting of a direct intervention by this office. I think that the way we envision it is that this is

sort of the overseer of a whole system of care and now all of a sudden they are also the policemen. That may be the case but I certainly do not want to--I would not agree to highlight it in the recommendation so far up front as a primary role of this office.

DR. SHAPIRO: Meaning you are worried about "should intervene to protect." Well, what--let's see. Yes, Tom?

DR. MURRAY: Consistent, I think, Harold, with your notion that the FDA would be a part of this system, really what we are asking NOHRO to do is should coordinate interventions to protect research participants if I understand correctly.

DR. SHAPIRO: I would not be unhappy with that. I have not thought it through but I would not be unhappy with it.

DR. MURRAY: Because that could mean that NOHRO does not do it. It could mean that the FDA does it.

DR. SHAPIRO: Right.

DR. MURRAY: As long as the FDA is doing its job NOHRO can stand back. There will be research not covered by the FDA where human subjects are at risk and it may have to coordinate other interventions.

DR. SHAPIRO: Right. Jim?

DR. CHILDRESS: I agree. I think it would be

useful actually to--I take your point about oversee again--this is just building on Tom's--and just go back then to the end of the previous version and include monitoring and enforcement.

DR. SHAPIRO: Coordinate monitoring and enforcement.

DR. CHILDRESS: So you start with--you use the oversee model that Alta has but then you just go back after you should oversee policy--and then go back to all the words that are in the previous recommendation with enforcement just coming in at the end as one of those but it is not highlighted.

DR. SHAPIRO: Rhetaugh, and then Arturo?

DR. DUMAS: That would please me because I think the term "coordinate" does not really capture the control that I think that this office ultimately has to have. The monitoring and enforcement would do that for me.

DR. SHAPIRO: Okay. Steve?

MR. HOLTZMAN: So to me the two verbs we want is "oversee" and what it is going to oversee is policy development and regulatory reform research and research review.

DR. SHAPIRO: Right.

MR. HOLTZMAN: What it is going to insure, not coordinate but insure is monitoring and enforcement to

protect the welfare and rights, the rights and welfare of participants.

DR. SHAPIRO: Very helpful. Yes.

DR. CHILDRESS: I agree.

DR. SHAPIRO: That is very helpful, Steve. Thank you very much.

Other comments on 3.2? We will try some time during the break maybe to redraft this because there are quite a few changes in here and try to get it in front of us before we leave.

Okay. Eric, let's go on to 3.3

DR. MESLIN: Here the difference is really one of emphasis where in the original--the new created office should revise current regulations in order to create a unified comprehensive set of policies in the form of regulations and guidance and guidance should be used as needed to explain or implement the regulations, et cetera.

And a substitute suggestion is not speaking directly to the office but referring to what those policies and regulations should be reformed to do wherein the--it is a simple sentence, "current research policies and regulations should be reformed to create a unified, comprehensive federal policy embodied in regulations and guidance as needed."

DR. SHAPIRO: Tom?

DR. MURRAY: If, as I think we have decided, we are going to leave NOHRO out of subsequent recommendations then I think we begin with Alta's revision, which I think is very good. I am just not sure about that last phrase "as needed." It could mean two things. One is to reform current ones to the extent that they need them today. It could mean a continuing--some continuing function where as needed in response to changes in research paradigms or whatever, you know--all the changes we are seeing in the clinical trials moving into community hospitals, it may need to be, you know, future.

So "as needed" to me means both and I think both are needed and I am just looking for--I did not know which Alta had suggested, wanted or if we can find language that (a) if we agree that that is what we want--

DR. SHAPIRO: What it meant to me was that it would do either regulations or guidance depending on what was needed. That is how I read it.

DR. MURRAY: A third reading that I had not gotten at all, okay.

DR. SHAPIRO: This is a wonderful phrase. I think we should leave it in.

(Laughter.)

DR. SHAPIRO: I mean that is how I read it. I

apologize. That is how I read it.

DR. MURRAY: Something that allows itself of three different interpretations--we probably need to be--

DR. SHAPIRO: Careful.

DR. MURRAY: Brief is good. No, I mean it is not good.

(Laughter.)

DR. MURRAY: It is great if you are writing poetry. It is not good if you are writing recommendations.

DR. SHAPIRO: I do not think the "as needed" is needed. Larry?

DR. MIIKE: Just a sequencing kind of a thing because we are going to say that this should be overseeing private as well as public research and that if you read it in this sequence here it seems to be just reforming the federal portion of it all.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Larry, I think recommendation 3.1 does cover private and public but you are right that in the recommendation it is not pulled out.

DR. MIIKE: I do not want to--

DR. SHAPIRO: Yes.

DR. MIIKE: --because the text is set up a

different way.

PROFESSOR CHARO: Yes. But, you know, in 3.1 it might not be too difficult to go back and pull it out a little bit more explicitly for this purpose. Right now, as I understand it, it has been rewritten as the rights and welfare of human participants in research, right, and we could simply--should be protected by federal oversight system, and we could write it as the rights and welfare of all human participants in research regardless of funding source, right, or all participants in any research in the United States, right, either way, and that way get at your point and it would be right there in the first sentence.

DR. SHAPIRO: You are talking about 3.1 now?

PROFESSOR CHARO: Yes.

DR. SHAPIRO: Well, the issue there is--I mean my view is that all is all and we could say whatever we want in the text that clarifies this but all is everyone and we do not need--I think it sort of suffers by trying to modify it or explain it in the recommendation itself, although in the text I think, if you recall, it works quite easily.

The question, I think, that Larry was raising and I think it is interesting is that when we talk about current research policies that is how it starts.

It brings to mind for many people the Common Rule and the FDA and you mean something a little bit more than that because we are covering some people who were not covered. And so as I understood Larry's question it was is 3.3 sufficiently clear that we mean that it also covers everyone?

I think, Larry, I do not want to speak for you.

DR. MIIKE: That is exactly what I meant. That is why I think we do not need to talk about the current situation--

DR. SHAPIRO: Right.

DR. MIIKE: --because we are suggesting something much larger.

DR. SHAPIRO: Right.

PROFESSOR CHARO: Just delete current--

DR. SHAPIRO: Yes. Well, you cannot say--I think we can delete current but then you have to change the reformed and so on and so I think there is language that is easy--Steve?

MR. HOLTZMAN: Yes, I think we are now nitpicking our recommendations and trying to get the text in. I can read into the rec the word "comprehensive" and current has to be reformed, that is changed to a comprehensive, unified system to cover all based on what we said in 3.1. So I am perfectly

comfortable with how it is as long as you get rid of "as needed".

DR. SHAPIRO: The "as needed" is gone.

DR. MIIKE: All I am saying is that any kind of a change--I mean obviously you are going to make current regulations obsolete if you are talking about some laws but it just--to me it introduces a sense of confusion for those who is going to read the recommendations. It seems like we are just talking about--

DR. SHAPIRO: Let's just rewrite 3.3 to be a direct statement of what we want done and I think that is easily done. We do not have to get the language exactly straight right now.

I hope after we get through the recommendations 3.4/5/6 we will take a break and then we can perhaps even redraft some of these and people take a look at them.

Okay. Let's go on. Eric, 3.4.

DR. MESLIN: Right. This is another NOHRO choice which I think you have already evidenced your desire to remove. In the first version NOHRO should issue regulations defining research activities covered by the system. I am just short-handing it for you because you have it in front of you. And then it gives a list of those activities. And the last sentence, the

last two sentences of this initial recommendation, they should also list research-like activities that are not covered by the oversight system and provide guidance on how the determination of whether something is or is not covered.

The alternative is that the federal policy, not the office, the policy should clearly define those research activities that are covered. Then there is a similar description of what would generally be included and identification of those activities that would not be subject to federal oversight.

The new piece that I think warrants some discussion is the proposed sentence, "such activities should generally be limited to situations in which there is no physical intervention, little or no risk to participants, and a clear and easy opportunity for people to refuse to participate." Again for the public I am reading this out loud. I know you do not have it in front of you so that when you hear comparisons you know what we are talking about.

That sentence that I just read--Alta may want to say more about it but that is a difference from what the original recommendation is because it will make clear to you whether or not some kinds of nonphysical interventions create situations of exempting certain kinds of research.

Alta, did you want to clarify any of that?

PROFESSOR CHARO: Yes, because I want to make sure that the tone that I intended is clear to people even if the language turns out not to be for them. The goal here correctly--the first one was to avoid the call specifically for regulation, just on the chance that this might be accomplished with something short of formal administrative rule making with regard to defining research that is covered and the research that is not covered.

Then because some research will not be covered, and I use the word "research" as opposed to "research-like" because sometimes it really is research, a lot of the polling stuff is real research but it has never been covered and I do not think it was our intent to start covering it. All right. So we know that there is going to be some research activities that are not subject to federal oversight and it says that just like the original one does but then in order to try to put some detail to the limits on the range of things that could be found to be outside the oversight system. I thought I would try to identify those factors that represent the outer limits of what could be considered outside the system so--and that was these things about no physical intervention and little risk and easy opportunity to refuse. That is not to suggest

that all things that meet those criteria would necessarily be outside the system. It is only that things that do not have those characteristics would necessarily be inside the system and subject to oversight.

DR. SHAPIRO: Thank you.

Comments, Larry?

DR. MIIKE: I just want to see if people agree with me in the sense that Alta stuck in the word "generally" and I think that was key for me because the way I read the original recommendation it seemed like it described such activities as being a small universe but when you stick in the word "generally" then it made it sort of comparable that that is what we meant. That was your intent, right? If it was--

PROFESSOR CHARO: It cannot have been because that was my original word but Eric suggested it yesterday and that is why it appears on the paper today so you better ask him.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: I like Alta's recommendation--form of the recommendation and, in general, I want to say that--and I view what Alta did is taking stuff that had been worked very, very hard and with a fresh set of eyes really in most instances improved it but it should not be--it is not to me Alta's versus the other ones.

It is really--there was the opportunity to take a step back and make them--really to make the gold shine. And so I think that we should take advantage of it.

DR. SHAPIRO: Tom?

DR. MURRAY: I also like it. I want to make one--at least one amendment to it, to the language and raise a question about a second phrase. When you list clauses like this, these are the factors you take into account, we have got to be very careful of those--that those are the ones we want, we do not want any other ones and we say this as clearly as possible.

I would eliminate the word "physical" because there are behavioral interventions. There are community interventions, community research projects that you really would want to capture. I think that the key thing here is that it is an intervention as opposed to say an observation.

Very intensive behavioral therapy would not count as a physical--would not be included here.

PROFESSOR CHARO: Can I just ask--

DR. MURRAY: Yes.

PROFESSOR CHARO: If I can just clarify, Tom, because this is not suggesting that anything that lacks a physical intervention would automatically be presumed to be outside the oversight system. It only says that if something has a physical intervention then it

necessarily is going to be within the oversight system and so if we were to take out physical intervention and say that the uncovered activities are limited to those that simply have little risk to participants--

DR. MURRAY: No, no, no. I only want to take out the word "physical."

PROFESSOR CHARO: But then--

DR. MURRAY: But there is no intervention.

PROFESSOR CHARO: But I am not sure then how-- I mean if I can get called by a pollster, is that not considered an intervention?

DR. MURRAY: It is not an intervention.

PROFESSOR CHARO: Well, then I have got a problem because then I have a problem with the way in which we use these words because they are not completely intuitive.

DR. MURRAY: Intervention, I think, has a pretty clear meaning. I mean, it means you change something, yes.

DR. DUMAS: To intervene.

DR. MURRAY: Yes. It is observational research or polling research or interview research versus research that imposes some intervention.

PROFESSOR CHARO: So an interview is not considered intervention?

DR. MURRAY: No. No, it is not an

intervention. I mean, as I understand it, and I guess we need to revisit the text and make certain that that is true. So I would just strike the word "physical".

DR. SHAPIRO: I want to understand first, Tom--you may be right, but I want to understand the concern here. What that sentence tries to describe as I read it is things which are not going to be covered by the oversight system.

DR. MURRAY: Right.

DR. SHAPIRO: Okay. So that--and we are saying that those should be limited to situations, that is those things which are not covered, will not be reviewed.

DR. MURRAY: Right.

DR. SHAPIRO: Should be limited to those cases where there is no physical intervention.

DR. MURRAY: And I would say such activities should generally be limited to situations which there is no intervention. That is how the language reads. Intensive behavioral therapy is an intervention.

DR. SHAPIRO: Oh, I understand that.

DR. MURRAY: And it should be reviewed and we should not even imply that it does--

DR. SHAPIRO: I agree. But we are talking about things that should not be reviewed here.

DR. MURRAY: Exactly. And by leaving the word

"physical" in, the current language, it at least implies that nonphysical interventions--well, they are okay. Okay.

DR. SHAPIRO: Okay. I understand.

DR. MURRAY: The second thing I wanted--the second thing--but we do need to--I mean, if other people do not share and if we do not clearly define what we mean by intervention as opposed to other things like polling, interviewing, et cetera, then we have a problem and we need to be clear. I think most scientists would immediately understand what we mean by intervention.

"Little or no risk to participants," now when we use that phrase--well, I just want to know how people will read that. What about privacy? Would most people assume that including risks to privacy would be incorporated into this?

DR. SHAPIRO: I did. I cannot answer for--

DR. MURRAY: Okay. I think actually taking the word "physical" out of the prior clause probably helps.

DR. SHAPIRO: Yes. No, we discussed--I mean that is in the text we discussed a lot about the risks of privacy and those kind of questions.

DR. MURRAY: Okay. As long as that--as long as people feel that that is well accounted for then I

am quite--I am content with it.

DR. SHAPIRO: Thank you.

Arturo?

DR. BRITO: Yes, because--because some of the issues that Tom is raising, I do not feel comfortable with this sentence about such activities, et cetera, in here. I think it leaves too much room for interpretation in the many different ways and I do not know why in the recommendation we cannot just simply state that--you know, that sentence that the policies should also identify those research activities that are not subject to federal oversight, period, and leave it at that and then in the text discuss what we would consider to be research and what we consider not to be research that we need oversight for.

I think in the recommendation we just need to be very clear and let the proposed federal office or legislation or what have you make those determinations. I do not feel comfortable with this because there is too much--it is too open to different ways to interpret this.

DR. SHAPIRO: So you would prefer stopping the--taking the last two sentences out and covering those issues in the text somewhere.

DR. BRITO: Well, let me talk about the last sentence. All right.

DR. SHAPIRO: I do not want to put words in your mouth.

DR. BRITO: I am not sure about the last sentence but definitely the second to the last one I would leave out.

DR. SHAPIRO: All right.

Alta, and then Steve.

PROFESSOR CHARO: Yes. I actually--I appreciate completely the point that Arturo is making because by saying that certain limitations are placed on what could be considered outside the system, it does certainly give a taste of those things that might make something eligible to be outside the system.

But I want to put a plea on the table here that is going to come up in some other settings as well when we go through the chapters on behalf of the social science and humanities researchers of the world because they have been asking since the very first meeting we have had on this topic for some overt attention to their dilemmas and their dilemmas include one that is very basic, which is a fundamental confusion about what things they do need to be subjected to oversight that is ultimately encompassed in this big regulatory machine that goes all the way to Washington and, secondarily, even if they understand that they are subject to it, a plea for why should we be subject to

it when so much of what is at issue is so completely benign precisely because of the factors that are laid out here. That is there is absolutely no confusion in anybody's mind about what is going on and absolutely no difficulty from the point of view of potential participants in deciding whether or not to participate.

So this has been something that has been coming to me maybe because I am in the social sciences division at my own university and so I have had not only people at my university but all their friends and colleagues lined up to give me their stories at what has now become a tediously common series of dinner parties featuring one research protocol after another that they have used to demonstrate their point. So I am here to speak for them and to beg for your indulgence to send a signal to them.

DR. SHAPIRO: Okay. Then there is others--quite a few people who want to speak.

DR. BRITO: Just very quickly and I appreciate that, Alta, and I think I understand that there is a lot of things that are--not necessarily reviewed by IRBs, et cetera, and subject to the oversight but my concern here is once again when I read this I had some of the same feelings that Tom expressed. My concern here is that people tend to under estimate psychological risks in research in certain

psychological research and I am afraid the way this is written maybe there is another rewording we can do this but there are psychological interventions that I feel would be interpreted as, oh, it does not account for this and it is okay, we do not need oversight for this.

DR. SHAPIRO: Okay. I have the following people ho want to speak and then we are going to have to decide what we want on this.

Steve, you are next.

MR. HOLTZMAN: So two questions. The first is does anyone here think that if something does not involve physical intervention, does not involve risk, and there is a clear and easy opportunity for that person to refuse to participate, that it should be considered research? Everyone agrees that if it meets those--what?

PROFESSOR CHARO: Covered research.

MR. HOLTZMAN: Covered research. Research which meets the following three things: No physical intervention, essentially no risk and clear opportunity--just take as is--no physical intervention--you see if it has all three of those criteria do you agree it is not research?

DR. SHAPIRO: Covered research.

MR. HOLTZMAN: Not covered research. Okay. I am sorry. Not covered research. Because you are all--

the logic of the way this is written, all right, is as an only if, not as an if, and you are all arguing about it as it is written as an if statement. It is written as an only if statement. Okay. So Alta is giving us something of a logical form. If no physical intervention and no risk and no whatever, right, or had an opportunity to refuse then no oversight. If it fails any of those, it does not say whether or not oversight is necessary and appropriate. So it is giving a paradigm case of when oversight will not be applicable. That is the logic of what is written there and I think everyone would agree that it is--anyway.

DR. SHAPIRO: Tom?

DR. MURRAY: That is useful, Steve. I think it will be read to be more than just a paradigm example. I think it will be read as a fairly generic guidance but if we said--I mean, let's do this. Such activities should generally be limited. The generally is a modifier to situations which there is no intervention, I really think we should--we have already decided it is little or no risk to participants, and a clear and easy opportunity for people to refuse to participate, that is going to exclude from coverage a lot of social science straight forward interviewing.

It is going to exclude from coverage a lot of polling research which is, you know, upright about its

purposes. I think that is going to be a benefit. It is not just going to be a benefit to the scientists. It is not just going to be a benefit to Alta who no longer will be harangued at dinner parties.

(Laughter.)

DR. MURRAY: But it will be a benefit to the IRBs because they just--you know, why do they--you know, we should be very sensitive to IRB work load and why pile more stuff on to them if it really, you know, is unobjectionable?

Now what will it capture? I would hope it would not exclude coverage of deception research where there may not be an intervention arguably. If there is an experimental paradigm there may not be--"I could see a scientist arguing it is not an intervention," and yet we ask for their informed consent. They say, "We just do not tell them what we are doing."

So I would not mind a slight alteration in the language for people to give a fully informed refusal to participate, something like that because I do not want to let some--there are certain subsets, small subsets of social science research which I could see them arguing strenuously would be excluded under these criteria. It would be a heroic interpretation but I could hear it happening.

So I would just want to put something like

informed--you know, well informed refusal and then I am content.

DR. SHAPIRO: Diane, and then Trish.

DR. SCOTT-JONES: I would like to just build on what Tom has just said. I agree with him. There are many categories or research that would slip by that could pose some risk and I will just give another example besides deception work from social psychology, sociometrics with children. Children are often asked to name other children in their classroom who are not popular or name their best friend, name who they would not choose to play with, and in some ways that does not carry risk but in other ways it carries a great deal of risk for the child being interviewed. It is not an intervention. I think some research like that needs to be reviewed in some way and I think this is written in a way that would suggest to people that that kind of research would not be subject to oversight so I have a lot of concerns with the manner in which this is written.

DR. SHAPIRO: Trish?

PROFESSOR BACKLAR: And following on Tom's suggestion I would like to take out the "little" or I would like to say "no risk to participants.

DR. SHAPIRO: Okay. Jim, then Alta and Larry.

DR. CHILDRESS: If I understood Arturo

correctly, his suggestion was to get rid of that sentence and I think the discussion indicates why we should and actually puts a much more elaborate statement in the text to give the kinds of examples. I think otherwise highlighting this in the recommendation is going to create difficulties in interpretation and actually probably misuse of this but in the text we can provide the kind of elaboration that we have here.

DR. SHAPIRO: I am going to try to make a decision here because we have to move on here. I think the only way for us to handle this right now is to take this sentence out and deal with it in the text. I actually read the sentence the way Steve did myself so I had no problem with it but nevertheless let's not argue that any more. Let's just take the sentence out and we will deal with this issue as best we can in the text and let's just move on.

Okay. Anything else on that particular one because I want to move on to some of the others? We just do not have time. Let's go on to Recommendation 3.5.

Eric?

DR. MESLIN: A couple of differences here. A minor difference in the first sentence of each, the first, the original one that everyone has, "the oversight system should cover human participants who

are exposed to manipulations or interventions or otherwise interact with investigators." I will come to the rest of that in a second.

The comparative sentence in Alta's suggestion is "the oversight system should protect participants who are subject to manipulation or physical intervention or otherwise interact with researchers."

So the first difference is "the system should cover" versus "the system should protect" using probably Jim's modification, I suspect, if you were to go that route.

The second--

DR. CHILDRESS: I might add "protect" captures both of the elements.

DR. MESLIN: The second part is a description of what could be included in that. In the original version you have "are identifiable from observations related to a research study or are identifiable from existing data collected, i.e. extractions of records are analyzed for purposes related to a research study." And Alta's somewhat simpler version, I suspect to say it should be--it should also protect people who are identifiable due to examination of biological tissues, medical and other records or data bases. There the distinction is between the--in a sense from the data and the people but you will see that in the first there

is one sentence that lists some of these items and in Alta's she divides it up into two.

One is more--well, this is where social science issues come up again.

There is another issue here that really relates to what is not included or what is included but both--neither of those two recommendations talk about this such as embryos or fetuses or anything else.

DR. SHAPIRO: Okay. Recommendation 3.5. Bette?

MS. KRAMER: Yes. Do you intend this language to capture family histories and that problem?

PROFESSOR CHARO: No. I was trying to have it capture the HBM report.

MS. KRAMER: Well, there remains a problem. There remains a problem of what we are going to say about family histories and if it is not--if it is not in 3.5, and I do not read 3.5 as encompassing that but then, you know, where is it? I do--I reiterate again that I think it is important for us to say something about it. It is a big issue on the table right now.

DR. SHAPIRO: And how would you think we ought to handle it? Just the substance.

MS. KRAMER: In substance?

DR. SHAPIRO: Yes.

MS. KRAMER: Well, I think I redrafted the

text, the part of the text that I think addresses it on page 38 beginning on line 17 and basically the problem, of course, occurs in that the information that is divulged, it belongs to the person who is divulging it but it has pronounced effect on the people about whom it is being divulged. So the suggestion that I would make is that the IRB should assess whether or not there is greater than minimal risk but it should take appropriate measures to protect the confidentiality of the data as opposed to requiring that the others about whom information is identified be required to be--made consent.

DR. SHAPIRO: Is that in the part of the text which deals with third parties essentially? That is one person talks to another.

MS. KRAMER: Right.

DR. SHAPIRO: I think we ought to--I mean you have raised this point before.

MS. KRAMER: I have, I know, and I still do not think it is clarified.

DR. SHAPIRO: Yes. No, I think you are right and it is a good point so we should--in that area of the text we should deal with it. I mean, I agree with you but it is not clear to me it should be a part of this recommendation.

MS. KRAMER: Well, no, that is why I am

raising--was raising the question whether Alta intended that that be captured in 3.5. I do not really see it captured there nor do I see it captured in 3.6 and yet the text discusses it in Chapter 3.

DR. SHAPIRO: All right. Let's come back to make sure. I mean, you have raised that more than once and we should get it in there and I apologize for not having done it so we will come back and deal with the family history thing directly.

Tom?

DR. MURRAY: I have two things that I think are very easy, small and nonsubstantive changes and one question. Again I would strike the word “physical" from the second line of Alta's revision for the same reasons as on the previous recommendation. I would change--instead of the word "tissues" I would use the word "materials". It is consistent with our report, arguably some people, for example, doing DNA identifications might say, "Well, I do not actually have intact tissue. I just have fragments," et cetera. So those--I hope those are uncontroversial.

The question I have is the "otherwise interact with researchers." Because of what I fear is that that would just rope back in all the people doing social science interviews, surveys and the like, and I do not--I do not think we want to do that so I am not--but I

am not sure how to--I do not know what the intent was and I am not sure how to fix it.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Let me--so are you suggesting that it should read participants who are subject or exposed to manipulation or intervention, period?

DR. MURRAY: I do not know about the period. What are we trying to capture with the "otherwise interact with researchers?" Because it is over inclusive. It is bringing back in more than we want to bring in.

PROFESSOR CHARO: Yes. It was supposed to include everything that you forgot to say when you said "manipulation and physical intervention."

DR. MURRAY: Yes, which is a noble thing to try to do but do you see the problem it creates for your dinner parties? Yes.

PROFESSOR CHARO: You have already tanked my dinner parties.

(Laughter.)

DR. SHAPIRO: Eric?

DR. CASSELL: Tom covered my question.

DR. SHAPIRO: Okay. Larry?

DR. MIIKE: Two things. One is that as far as Bette's issues are concerned, we do not consider them

research subjects and I think this recommendation is about who is a research subject covered by the system. So I do not think it should belong. I would not agree that anything along that line should be folded into this recommendation.

The other part is that maybe we should use these words consistently. I understand that 3.4 and 3.5 are sort of interrelated. That is why we are getting the discussion about exceptions at the same time we are defining them but, you know, now it gets confusing. It says manipulations or interventions or otherwise interact, whereas we talk about interactions and interventions, and we say manipulations is about the same as interventions. So we should stick consistently with the way we use the language. We should talk about interactions and interventions. This way it just gets confused and people--I begin to think that manipulation has some bad connotation about it when we--in the text we just simply use it as an intervention.

DR. MURRAY: Larry, just a technical point coming from my long ago history in the social sciences. You would refer to setting up various experimental conditions as manipulations even if there was no "intervention" and I can see that distinction. So I do not know quite how to--we talk about experimental

manipulations and they do not actually involve even behavioral intervention. Just changing the circumstances into which a--or the expectations into which a person enters the experiment.

DR. MIIKE: That is fine but what I am saying is that we are using it in a different sense here. We are saying manipulations or interventions or otherwise interact, and that is not quite the same as the way we define it in the other place.

DR. SHAPIRO: I understand that. We should make that consistent.

Diane?

DR. SCOTT-JONES: I just have a clarifying question.

DR. SHAPIRO: Yes.

DR. SCOTT-JONES: I got confused. I was doing fine. The otherwise interact, in part, was mainly to capture survey research, some types of survey research. Are you saying that you do not want that or you do want that covered or you want at least something that is reviewed or, you know, that a determination is made about that?

DR. SHAPIRO: I, myself, do not favor a complete exemption of survey research. There is all kinds of surveys with very sensitive, difficult issues and we certainly do not want to exclude it so it is a

matter of judgment. We do not--all of it is not in but all of it is not out.

DR. SCOTT-JONES: Right.

DR. SHAPIRO: And that is my sense of it.

DR. MURRAY: Since you directed the question to me that makes sense to me but what I would like to exclude are--you know, I am interviewing somebody because I am writing their biography and I am totally up front about it, that is what I am doing, or I am observing public behavior. I want those people to be able--and I interact with people. I want, you know, where it is straight forward. The sort of thing that Alta was trying to capture in that language in 3.4 which we are going to expand upon outside the language of the recommendation now. I do not want to bring it back in by virtue of this little phrase.

DR. SHAPIRO: Alta, and then Steve, and then Diane, and then we are going to move on.

PROFESSOR CHARO: There is an interplay between 3.4 and 3.5, and it may--Steve was going in the same direction. It may offer a way out of this because focusing on 3.5 alone we are getting tied up in trying to define the research subject. I think that it would be fair to say that many of these people are, in fact, research subjects but they are the subject--or research participants, I am sorry, but they are

participating in a form of research that is not covered by the federal oversight system. And, therefore, the fact that they are a research participant is of no interest to the system because the system is not examining their research.

And so although I am not sure exactly what language to use yet, I think that the way to handle the 3.5 problem is going to be throw something in that talks about otherwise interacting with researchers in a context that is subject to federal oversight. All right. That may be the way to get it. Maybe not because people are looking at me with their eyebrows going up. But basically say that the oversight system should protect participants, right--well, it does get kind of tautological, doesn't it? It should protect participants who are in research that is subject to the protections of the oversight system if they are also a research subject.

DR. MURRAY: I did not hear that part.

PROFESSOR CHARO: Whatever I said.

(Laughter.)

PROFESSOR CHARO: Okay. But Steve was going in the same way and maybe he can do better.

DR. MURRAY: But you cannot disagree with a tautology. That was a philosopher's joke.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Yes. You know, you are exactly right. In 3.4 we are defining what is covered research activity, certain classes of research ought to be covered, all right, and now we are going to effectively hone in further on, when is a human subject in play.

PROFESSOR CHARO: So maybe we should actually start by saying who is a subject and then say notwithstanding that, only some--who is a participant? Sorry. We start--we flip them. Who is a researcher? Who is a participant in research without defining the word "research" and letting people just kind of assume they know what it means, and the participant is da, da, da, da, da. And then the next one would be, all right, so participants in these kinds of research are protected by the federal system, participants in other kinds of research to be delineated by somebody in the future somehow will not be protected by the system because they do not need it, right?

MR. HOLTZMAN: Well, without looking at the text I do not know what we have just done because I am not sure that I can make it flow the opposite way as well so let's just focus in. Having defined covered research and giving paradigms of noncovered research, what are we trying to do in 3.5? What is the take home? The take home is people have to be in play and people sometimes get embodied not necessarily on foot.

PROFESSOR CHARO: And that it is not cadavers.

MR. HOLTZMAN: And it is not--right.

PROFESSOR CHARO: And, in fact, Bette's point is correct, and it is not the third parties.

MR. HOLTZMAN: Right.

PROFESSOR CHARO: So there is a kind of exclusion goal here as well.

DR. SHAPIRO: Larry?

DR. MIIKE: The simplest thing to do since an exclusion seems to be an important part of the recommendation, simply pull it out and make it a third recommendation. We are covering what is a subject, what is a research, and we are trying to do too much in these two. So I think that we should just do that in sequence. What is research? What is human subject in that research and then what are the circumstances in which we recommend excluding it?

DR. SHAPIRO: Okay. Unless there are other comments--Bernie?

DR. LO: Yes, I wanted to put my hand up.

DR. SHAPIRO: Go ahead.

DR. LO: Yes. This reminds me very much of those pretty tables that the staff drew up for us back with the Human Biological Materials Report where, you know, the kind of algorithm that someone--I am sorry,

it is hard for me to identify names over the phone--sort of defining what is research, who is the subject, and then are you covered by these--this system, this new proposed system of federal oversight.

I actually visualized it as a table with sort of a series of questions where you work from the top to the bottom and it sounds like that is what we are heading towards, this package of recommendations. I do not know if that helps sort of lay out the logic behind what these recommendations are doing.

DR. SHAPIRO: Okay. Other comments on this recommendation? Obviously we are going to have to redraft it. Diane?

DR. SCOTT-JONES: Pass.

DR. SHAPIRO: Thank you. Let's go on to 3.4 or 3.6, excuse me. 3.4 is not going on.

DR. MESLIN: So the last one focuses on standards and procedures for reviewing risk. In the original version a proposed office, federal office should create review standards and procedures commensurate with the nature and level of risk of the research, and the standards should distinguish between research causing no more than minimal risk, research posing more than minimal risk, and research involving novel or controversial ethical considerations.

The slightly different version is that federal

oversight should require research review that is commensurate with the nature and level of risk and the standards and procedures for review should distinguish between those three items that I have just mentioned.

So the distinction again is between the office creating standards and procedures and in the alternative, federal oversight should require research review that is commensurate with the nature and level of risk and with those standards and procedures for review distinguishing between three areas.

DR. SHAPIRO: Okay. Does anyone have a preference for these two? Let me suggest we start with the new 3.6, that is Alta's version, which seems slightly--I mean they are really substantially the same recommendation. I do not really know how to distinguish between them. So let's just take Alta's version and work with that if there is any comments or questions.

DR. SCOTT-JONES: (Not at microphone.) Could I--

DR. SHAPIRO: Yes.

PROFESSOR CHARO: Yes, because I was deleting the implicit reference to NOHRO rather than saying that that federal office had to do it. I did not really care how it was done but what I wanted to see done was da, da, da.

DR. MESLIN: This was de-NOHRO-ization with prejudice.

(Laughter.)

DR. SHAPIRO: The other one says the proposed federal office. It does not say NOHRO. It talks about proposed federal office, the original one. So we will go with 3.6.

Bette?

MS. KRAMER: Just a question. I could probably go back in the text and find it. What are novel controversial ethical considerations?

DR. SHAPIRO: I do not think we should try to define those frankly. There is something--I mean, other than what we say here. There are going to be issues that come up--in my own view. This is my own view--from time-to-time and people will just have to recognize them. I do not know how to define them.

MS. KRAMER: All right. So this is not something that is picking up on material we discussed?

DR. SHAPIRO: No. I was not intending it that way myself.

PROFESSOR CHARO: I am sorry. Actually it was supposed to pick up on the call in the text for facilitating special review bodies for things like the research with the mentally impaired, for the stem cell report.

DR. SHAPIRO: Those are examples.

PROFESSOR CHARO: Right. For the RAC and gene therapy.

DR. SHAPIRO: Okay. Let me make a suggestion. See if we are cognitively capable of taking a 12 minute break while--and we are going to try to get started on redrafting 3 but we will come back and we will go immediately to the recommendations in Chapter 4. Let's try and reassemble at twenty after 11:00.

(Whereupon, at 11:07 a.m., a break was taken.)

DISCUSSION OF DRAFT REPORT: CHAPTER 4

DR. SHAPIRO: Colleagues, could we assemble, please. Reassemble. I want to now go on to the recommendations that are a part of Chapter 4. We will have for you, hopefully before we break for lunch, redrafted recommendations for Chapter 3, which I would ask you to look over, over lunch, and provide back any further comments you have. So I do not intend--unless we have some unexpectedly large amount of time somewhere to go back to Chapter 3. We will, of course, get a look at the recommendations to approve in their final form but if you could look at those over lunch it would be very helpful.

Eric, am I correct?

DR. MESLIN: Yes, absolutely.

DR. SHAPIRO: So it will be here before lunch,

which is 12:30?

DR. MESLIN: Yes.

DR. SHAPIRO: Okay. Thank you.

Let's now go on to the recommendations that are a part of Chapter 4. Eric, why don't you take us through these. The difference is in the two sets of recommendations you have--at least in my judgment, though, don't raise any substantive issues. You might prefer one over the other but they do not raise substantive issues. They, of course, deal with how often you refer to the so-called de-NOHRO-ization.

PROFESSOR CHARO: And also regulations.

DR. SHAPIRO: And guidance regulation and so on so there are differences of that type which we discussed before. But, Eric, let's go to the recommendations starting with 4.1 and let's try to go as quickly as we can. We will work through to 12:30. We will have an hour for lunch and then we have public comments at 1:30.

DR. MESLIN: Okay. This recommendation concerns the so-called component analysis of risk and the difference between the original, which says the analysis of risks of harms and potential benefits should be consistent across all types of research, and then there is the NOHRO sentence that says NOHRO should consider adopting an approach to the assessment of

risks and potential benefits in the regulations such that procedures offering and the prospect of direct benefits are not used to justify procedures that solely answer the research question. That is the original.

The proposed revision takes NOHRO out of the recommendation and simply says the analysis of risks of harm and potential benefits should be consistent across all types of research, in general each aspect of a study should be evaluated separately, and its risks should be both reasonable and justified by the potential benefits to society for the participant. Potential benefits from one aspect of a study should not be used to justify risks posed by a separable aspect of the study.

DR. SHAPIRO: Does anyone have any concerns about Recommendation 4.1? I am looking now--I am specifically looking at the--what we will call Alta's version since we decided we would not refer again and again to the office in the other recommendations. And I think that is the only substantive difference here, is just the way it is phrased. At least that is how it appears to me.

Diane?

DR. SCOTT-JONES: I have a concern not so much about the specific language of this recommendation but about the general message from all the recommendations,

and it seems that this makes a broad statement about all types of research, yet some of the previous recommendations have been directed toward limiting what counts as research and it just seems that there is some amount of inconsistency.

DR. SHAPIRO: Again this is covered research if that helps.

DR. SCOTT-JONES: And maybe adding--

DR. SHAPIRO: Yes. We have to--this is an issue that comes up over and over again. We are going to have to resolve that issue. I agree. I think if that is your point I agree completely with it because there is some research that is not covered and this does not speak to that at all. It should not speak to that.

Steve?

MR. HOLTZMAN: I think I share Diane's concern but I do not think that is the concern.

DR. SHAPIRO: Okay.

MR. HOLTZMAN: It is--the second sentence forward in either recommendation is where you talk about the component analysis.

DR. SHAPIRO: Right.

MR. HOLTZMAN: It is the first sentence, which talks about consistency of evaluation of covered research across all types of research.

DR. SHAPIRO: I see.

MR. HOLTZMAN: And one can ask the question what does one mean by consistent? All right. I can be consistent from the sense of applying the same standards to biomedical research and social science--covered social science research and get it all wrong or I can be consistent in the level of principle and get it right so it is just a question of what does it mean to be--what are we trying to convey there?

DR. SHAPIRO: I speak only for myself. It was the principle that I was concerned with.

MR. HOLTZMAN: Right.

DR. SHAPIRO: Because obviously the context is completely different.

MR. HOLTZMAN: Right. So I would ask one question just in simplification.

DR. SHAPIRO: Yes.

MR. HOLTZMAN: And let me ask the author. Alta, in the second sentence, "in general, each aspect of a study should be evaluated separately," if you just deleted the rest of that sentence and then just went to "potential benefits from one aspect should not be used to compensate," do you really--

PROFESSOR CHARO: Okay. First, there are parts I did author in the revision and there are parts that come from the original recommendation that I did

not author so that there will be things I am not really sure--

MR. HOLTZMAN: Okay. So to the authors.

PROFESSOR CHARO: So--but on that one I do think I actually did author that one and there was a reason for it and it is this: At the Atlanta meeting Alex Capron spoke at length about his view that there will be situations in which the benefit to society for doing particular research would be quite overwhelmingly--quite large potentially but that nonetheless the research should not be permitted because its risks were somehow intrinsically unreasonable. And it was an attempt to capture that comment that led to the second half of that sentence so that there is both the notion that the risks are reasonable in and of themselves. By some amorphous standard we all understand that the word "reasonable" is hard to handle outside of context plus then specifically comparing it to potential benefits.

DR. SHAPIRO: My idea here--my interpretation of this, and maybe there is better language, I took this to refer to a component analysis as I went through this saying that the component analysis applied to all. So another way to start this is to say the component analysis of risks and harms and potential benefits should be applied across all types of covered research

or something like that.

PROFESSOR CHARO: That works.

DR. SHAPIRO: So it would refer simply to the--

PROFESSOR CHARO: That works.

DR. SHAPIRO: --that is what I had in mind, put it that way. That is what I had in my head when this was written down because I also--I agree with anyone who says that this sentence as currently written is hard to understand what it means what it is supposed to refer to. So if we could start it that way would that be all right? The component analysis of risks and harms?

PROFESSOR CHARO: Or risks and potential benefits?

DR. SHAPIRO: Yes, of harms and potential benefits, yes. Something like that should be applied across all types of covered research.

Larry?

DR. MIIKE: Rather than referring to covered research and then having to do that every time in our recommendation, we should just drop the reference to the research. We know what we are all talking about.

DR. SHAPIRO: Yes. This has to be thought about as an interesting suggestion but we just have to straighten it out so it is clear when we are reading

it.

Eric?

DR. CASSELL: Well, I am a little confused because I can think of many situations in which the patient's disease is so dangerous that the chance of any success justifies presenting the opportunity to participate to the patient even though the risk may be also considerable and we generally accept that but this implies that you cannot do that. It says that potential benefits of one aspect of a study should not be used to justify risks posed by a separable aspect so I do not understand that. I thought that is always the case. You are always balancing risk against benefit in this.

MR. HOLTZMAN: No, but in your example the intervention itself is that--is the aspect which poses both the risk and the benefit, and it is a reasonable trade off is your contention as opposed to--

DR. CASSELL: Well, maybe you can give me an example from this so I could understand clearly the separation of these things.

MR. HOLTZMAN: I subject you to a risk, you personally, all right, which is very, very high, okay, and the benefit is to knowledge to society, which is very, very high so that would be two--and are they independently separable aspects.

DR. CASSELL: Well, could you give me an example? I mean that is just another way of saying the same thing that is on this paper.

DR. SHAPIRO: The intent of this originally as I understood it, Eric--I cannot give you a good example but I think I remember the intent. The intent was to take certain components, which may have no therapeutic--even potential therapeutic benefit but nevertheless may be very risky and not try to justify that by saying, well, there is another component of the research which may give you a benefit. And that is--we were trying not to justify all the risks in the non--sort of nontherapeutic area by themselves.

DR. CASSELL: Well--

MR. HOLTZMAN: I have an example. Okay.

DR. SHAPIRO: Yes.

MR. HOLTZMAN: You are a cancer patient with a hematological cancer, all right. I am going to give you a therapeutic regime so there is a risk return which is reasonable under the circumstances. And while I am in there I am going to subject you to several additional tests, lumbar punctures, et cetera, et cetera, to give me additional knowledge that can be useful for the study of the disease or for others, all right, and that if I do a noncomponent analysis overall the whole procedure, including those additional

experimental interventions, are justified in terms of the potential benefit to you but there is no reason why I have to do those and they have their own intrinsic risks. And if I separate them I would say do the first, give you the drug, and do the necessary experimentation associated with it but do not do these other procedures.

DR. CASSELL: I understand that. I accept that.

MR. HOLTZMAN: That is the example.

DR. CASSELL: I just find most of us would look at that research and say but that--those things you are doing have nothing to do with the--your intervention. They do not belong in this research, and that is what this is supposed to say. Fine.

(Laughter.)

DR. SHAPIRO: And if you have alternate language that would be great.

DR. CASSELL: It is just bad--it is just bad research. It is not--has nothing to do with this.

DR. SHAPIRO: It may not even be bad research. It may be research that should not be done but it may not be bad.

DR. BRITO: But I think Eric has a point here because the way this reads it almost implies that the whole research--is this not what you are saying, Eric,

is that the whole research project should not be done. Not just the other aspects, that is the way--

DR. CASSELL: That is exactly right. I mean, research is of a piece but I do not want to get into that again. I do understand now at least what you are all saying. I think it is not--I mean, I just do not think it adds anything but it is not that big a thing for me.

DR. BRITO: But I think it is big here in the recommendation the way this last one is written, and I think when we add all of the phrase before about the component analysis should be used, I think it will help take care of that.

DR. SHAPIRO: We will change that first sentence.

Yes, Larry?

DR. MIIKE: Not to beat a dead horse but I think what the intent of this was to say is that you bring a research project--we are not saying it is bad research. Take this piece out and then we can pass it.

DR. SHAPIRO: Right. That is right.

Any other comments on this?

Let's go on to Recommendation 4.2.

Eric?

DR. MESLIN: Alta wanted to say something.

DR. SHAPIRO: Oh.

PROFESSOR CHARO: Just one small correction in the typing of this on the suggested revision it should not begin "the federal regulations" but rather "the federal policy" as part of the de-regulation-ization, as well de-NOHRO-ization.

DR. SHAPIRO: Okay.

DR. MESLIN: In that spirit, the only difference between these two besides policy is that in the original there is a last two sentences. There are two sentences that refer to IRB review, procedures other than full IRB review should be available to review research studies posing no more than minimal risk and all research studies involving greater than minimal risk should be reviewed by the full IRB.

In the other version those are taken out. I would submit to you that for parody purposes you should compare the two recommendations with--I will just call it Alta's and the original, taking out the last two sentences. The reason I think--correct me if I am wrong, Alta, you want to consider removing that last sentence is that this recommendation is about the definition of minimal risk. It is not about a definition of what IRBs are supposed to do that can culminate in a separate recommendation.

PROFESSOR CHARO: That was part of it and it does, in fact, come up separately and also because it

seemed like that was the kind of thing perfect for the nonbulleted paragraph that follows most recommendations that spell out some further detail.

DR. MESLIN: Yes.

PROFESSOR CHARO: But it is just a suggestion, that is all.

DR. MESLIN: There is only one other word change which is--I am sorry, Harold.

DR. SHAPIRO: Go ahead.

DR. MESLIN: Which is in the second sentence. In the original when research involves individuals for whom the risks would be higher and the comparative sentences for whom these risks would be higher but that is at the level of wordsmithing.

DR. SHAPIRO: Yes, Tom?

DR. MURRAY: Maybe I am being dense but I actually do not understand that last sentence. For whom--when research involves participants for whom these risks would be higher in the risks of daily life. Such research should not be considered.

PROFESSOR CHARO: Personally I have got to say I agree with you that I was never completely satisfied with the clarity of this expression which we have been struggling with over many, many drafts. And I know that what we are trying to say is that when risks that would be comparable--when some people--when risks that

would be comparable to the risks of daily life for the general population, right, are experienced as higher than that absolute level by anybody by virtue of his or her own situation, all right, that those risks should not be considered minimal at least for that person. They may be minimal for other people but they are not minimal for this person.

DR. SHAPIRO: Eric?

DR. CASSELL: Alta, don't we--in other words, for a population that fits what you just said, their risk--their every day of life is the standards. It is their every day life.

PROFESSOR CHARO: No, you see because then what would happen is somebody who lives in a war zone, right, would presumably be eligible for minimal risk treatment for something that we would consider highly risky, those of us living in nice middle class backgrounds that are--

DR. CASSELL: But you picked a certain population, special population for whom every day life risk would already be above minimum.

PROFESSOR CHARO: Right. This was the dilemma. We wanted to make it very clear that people who live in crummy situations should not therefore somehow be eligible for exposure to even higher risks in research with minimal review on the theory that for

them it is comparable to what they experience every day.

MR. MURRAY: That is not what this says.

PROFESSOR CHARO: No, but that was the problem in the writing was that in certain forms of the writing we wind up saying that by accident. I think the goal here is to say that the level of risk that is comparable to every day life for the general population constitutes minimal risk and if for any individual research poses more than that level of risk, whether because of the research itself or because of the individual's own characteristics, it is no longer minimal risk. I have no idea what I just said.

DR. SHAPIRO: I know what you just said but I must say that the last sentence is the one that was bothering you, Eric, is that right?

MR. HOLTZMAN: Harold?

DR. SHAPIRO: Yes.

MR. HOLTZMAN: So, normal population, we define them in minimal risk. Are we trying to take care of one or two additional situations? I think where we hang up is there are two distinct situations. We say that a person who in their normal life is exposed to more risk, that should not be a justification for exposing them to more risk than the people who are not. That is one piece.

The other piece is the sensitivity to the people for whom a procedure, which for you and I would be minimal risk, for them would not be. Not because they live in a more hazardous situation but because they are more vulnerable in the situation or constituitively. Are we trying to deal with both of those here and maybe we just have to separate them?

DR. SHAPIRO: I was thinking of the latter myself in this recommendation. It was the latter that was in my mind as I thought about this recommendation. I understand the distinction.

MR. HOLTZMAN: Right.

DR. SHAPIRO: Tom?

DR. MURRAY: To try to capture with minimal disturbance in the draft here, the draft language, the point that Alta was making, which I think articulated well with what at least I understood this attempting to say, the problem is not with the word "these" as in "these risks," it is just too indefinite, ambiguous there. We need a phrase. We just need to insert a phrase that spells it out a little bit more for which the risks of daily life are perceived as much higher or, you know, something along that effect. And I think otherwise everything else in the--you know, the other language in the recommendation is good.

Trish is saying in my ear that we do not want

to use the word--I do not have any--I am not committed to any particular way of putting it but the problem is "these" is just--in the context it is way too ambiguous. We need a somewhat more precise phrase that delineates what we are trying to capture and then I think if we insert that the rest of the recommendation probably works as written.

DR. SHAPIRO: Let's go back then to what we are trying to capture to get this right.

Steve, you propose two different situations, one of which was that on a procedure specific basis some people for whom some procedure would be minimal risk would be greater than minimal risk for others. That is one and that is what I thought we were trying to deal with.

Now what was the other category you had, Steve?

MR. HOLTZMAN: If a participant encounters relatively higher risk in their daily life this fact should not be used to justify research of more than minimal risk for the standard population.

DR. SHAPIRO: Okay. Maybe you can write that out and we will find a way to incorporate it. Larry, do you have a question?

DR. MIIKE: Maybe we should define both of those so that it is clear, even though we are

concentrating on one it is clear what we mean.

DR. SHAPIRO: Yes. No, I agree. I agree and we will alter it.

Steve, would you help provide some language for that? Okay.

Anything else on 4.2? 4.3? Eric?

DR. MESLIN: Here again the difference between the role of NOHRO and not. This is the recommendation regarding vulnerability so I think Tom's points before need to be brought up here. In the original it begins "to protect while promoting the inclusion of all participants in research, NOHRO should eliminate the categorical listings of specific vulnerable groups as in subparts B to D, and instead adopt an analytic approach that describes different types of situations that render participants vulnerable to harm or coercion."

Let me give you the alternative to that because these are in a couple of parts in the so-called Alta alternative. "To protect participants while promoting the inclusion of all segments of society in research, the oversight system should avoid categorical listings of specific vulnerable groups and instead..." and the phrase is exactly the same thereafter.

So one is to specifically to direct that the subparts be eliminated and in the latter that the

system simply be constructed to avoid these categorical listings.

The second part of the recommendation is that guidance should be developed on how to identify such situations and how to design research that avoids the situations or that incorporate appropriate safeguards and that local IRBs should be permitted to review and approve such research when appropriate safeguards are incorporated. The comparison language is very, very similar except the word "research" is replaced with studies so guidance should be developed on how to identify such situations and how to design studies that avoid these situations. The rest is the same except adding into the study design at the end of the last sentence.

DR. SHAPIRO: Eric?

DR. CASSELL: Just a simple thing. I think we should take out to adopt an analytic approach and instead adopt an approach. The word "analytic" does not add anything to it.

DR. SHAPIRO: Now I take it from our discussion before we want to also acknowledge, as Tom suggested before when we were talking about the beginning of this, the prologue, that there are some categories. Children being the paradigm example here, which by virtue obviously are going to be included in.

So we need to have some language which incorporates the point that Tom made before, which I do not have in front of me right now but you probably have from our notes before so I take it we do want to incorporate that because it is to be consistent with what we decided before because despite my attempt to say we discovered--we would discuss it later, we actually discussed it at the time.

But are there other comments about this?

Okay. Well, subject to that--subject to including that we will have to find the right language.

Trish, yes?

PROFESSOR BACKLAR: Should we add in again "to protect participants rights and welfare" in there, Jim? Did you want to do that?

DR. CHILDRESS: My concern earlier was that when we were talking about it in specific terms we tended to do harm without attention to rights and protections. Given the way we understand it in the prologue now, it would cover this.

DR. SHAPIRO: Okay. Anything else on 4.3? Okay. 4.4, Eric?

DR. MESLIN: Here the difference is a de-NOHRO-ification difference only. In the original, "NOHRO should emphasize through regulations the process of insuring voluntary informed consent from competent

participants rather than the form of its documentation." I will just compare these to each other. And the proposed substitute, "Research oversight should emphasize ways to insure that people have given their voluntary informed consent to participant rather than emphasizing the ways to document that consent."

And the rest, correct me if I am wrong, Alta, is almost entirely identical that guidance should be provided to IRBs and investigators about how to provide appropriate information to prospective participants and essentially it is--I will not keep reading it but they are identical after that.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, I am happy with the de-NOHRO-ification but research oversight has a somewhat different meaning. When it is the Office for Research Oversight that is the whole process, including the oversight that is watching over research while it is going on, which we have not specifically discussed and this implies that in the process of watching the research in progress we should be doing this. And I am not sure we are ready to say that. I mean, it would be lovely if IRBs did, in fact, do that. They are supposed to but they never do. And this slightly shifts the verb.

DR. SHAPIRO: All right. Other comments? Jim?

DR. CHILDRESS: I notice that the original 4.4 has ensuring voluntary informed consent from competent participants and that is omitted from the original modifier before people, and I would suggest that we put in “ensure that competent people have given their voluntary informed consent”.

DR. SHAPIRO: Trish?

PROFESSOR BACKLAR: The one thing I do really like in the original 4.3 is the use of the word "process."

DR. CASSELL: Process, right.

PROFESSOR BACKLAR: Process is, I think, important somewhere to attach that to the informed consent process, which we make much of in the text and it is significant.

DR. SHAPIRO: I think that is a good point and we make that--we try to make that point over and over again, and it is one of the contributions of this approach of what we have got in here and so I think we should try to incorporate that and I appreciate that.

Other comments?

DR. MURRAY: I have what I thought was a useful comment and since I agree with Trish I do not know if it is useful anymore. I would have said--I do

not know if I would say federal policy or research oversight but something should emphasize ensuring that people have given--I mean ways to ensure seems to me a weak construction here. It is a little vague. I mean it is like you are going to lay out, you know, six different--you know, six ways to get informed consent and we are not proposing that. But how do we--I do not know how to put the process language in there.

PROFESSOR BACKLAR: One could emphasize the process of voluntary informed consent and ensure that people--I do not want to repeat that.

DR. MURRAY: Okay. This works. So the last part of that sentence it is "emphasizing the process rather than the means of documenting that consent."

DR. SHAPIRO: It is close to the original, the version here, but I think the process is the right focus to have here so I think that is where we ought to go.

Other comments on 4.4?

Okay. 4.5, Eric?

DR. MESLIN: Here there is very little difference between the original and the proposal except that the--I think Alta is proposing that the recommendation begin with a different first sentence and it should be--I will just read her first sentence, "Federal policy should permit research without the

informed consent of research participants in certain carefully limited situations if all of the following criteria are met..." and then I believe it is identical thereafter.

PROFESSOR CHARO: There was one other thing, Eric.

DR. MESLIN: I am sorry.

PROFESSOR CHARO: There was a misprint in the alteration which originally had dropped the final sentence about regulations and guidance on the view that it was implicit in this and all the other recommendations.

DR. MIIKE: Can I ask why--because the main thing is that you have now made it more general rather than to identifiable data. What was the point? The original one is specifically referenced to identifiable--

PROFESSOR CHARO: You know, this is about multiple editing. The first revision that I put out on e-mail on Sunday actually added back in the waiver of consent emergency research settings and that is why if you look at the opening sentence it broadens it and then it says there are two situations. There is emergency research. There is research on data and then in a subsequent conversation with Eric he asked that that be dropped because the report had not discussed

emergency research very much and so you are right that right now what we got was a mishmash.

DR. MIIKE: So are we sticking with--

PROFESSOR CHARO: So it might make sense to go back to the original 4.5, skip the revision that was suggested, go back to the original 4.5. I would still suggest that it would make sense to drop the last line as implicit already but other than that it would make--

DR. SHAPIRO: The last sentence in the recommendation.

PROFESSOR CHARO: In the original recommendation, 4.5.

DR. SHAPIRO: Yes. Thank you. Other comments on 4.5?

DR. BRITO: For clarification, which last sentence are we dropping because you have it on your--

PROFESSOR CHARO: Yes. It was not supposed to have been printed in the proposed revision but it got in there because of the cut and paste process.

DR. SHAPIRO: Other comments?

DR. MURRAY: (Not at microphone.)

DR. SHAPIRO: Right, that is correct. Okay. Excuse me. Any other questions? All right. Let's go on to 4.6. Eric?

DR. MESLIN: Here are the differences between what the federal regulations should require and what

researchers should do. In the original, "Federal regulations should require investigators to document that they have obtained voluntary informed consent from participants when appropriate but should be flexible with respect to the form of such documentation, signed written consent forms need not be the only form required document or documentation, especially when prospective participants can easily refuse to participate or discontinue participation or when signed forms might threaten confidentiality."

The revision is of virtue in its brevity in that there are two sentences, "Researchers should document that they have obtained voluntary informed consent of participants where required. Written signed consent documents need not be the only form of documentation."

I think the differences are self-evident.

DR. SHAPIRO: Thank you. Comments? Which does the--which 4.6? The original 4.6 we have is obviously longer and a little more detail. Does that help or hurt? Larry?

DR. MIIKE: I prefer the original. I think we need some explanation, otherwise it just sort of says you can do this way or you do not have to do it this way.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: This one seems to be addressed to researchers and I would suggest just inserting the words "be required to document." "Researchers should be required to document that they have obtained voluntary..."

DR. SHAPIRO: Excuse me.

PROFESSOR CHARO: I am sorry.

DR. SHAPIRO: Just one second, Rhetaugh.

DR. DUMAS: Okay.

DR. SHAPIRO: I am just trying to handle-- would you repeat it again? I apologize to you.

DR. DUMAS: All right. This is just for consistency. This has nothing to do with the content or what have you. In most of these recommendations we are talking about what the federal policies should include.

DR. SHAPIRO: Yes.

DR. DUMAS: And here we are addressing this one to the researchers so just word it so that researchers are required to do this or that the policy requires researchers to do this.

DR. SHAPIRO: Let me raise a point. I accept that point and agree with it.

DR. DUMAS: Okay.

DR. SHAPIRO: I had drafted my own version of this one which is really built on the original version

we have because I was--somebody made the point at our last meeting that being verified was important. Someone could verify the process if necessary. The one so-called vivid end of always having signed documents of all kinds leaves an audit trail that may not be worth all the rigidity that is in the system but that is a benefit.

So I wrote a thing which is really quite close to the first and let me just read it out. "The federal regulations should require investigators to document that they have obtained voluntary informed consent from participants when appropriate but should be flexible with respect to the form of such documentation. Signed written consent forms need not be the only form of required documentation especially when prospective participants..." I guess it should be 'the prospective participant.' "...can easily choose to participate or discontinue participation or when signed forms might threaten confidentiality and there is a means of verifying that informed consent was sought." It was really the last item I was trying to get in there. Let's not worry about the exact language. "Was obtained" is better than “sought”. Excuse me.

PROFESSOR CHARO: Would you accept a friendly amendment that you begin with the federal policy as opposed to the federal regulations?

DR. SHAPIRO: Sure. No, that is fine. That is an improvement.

DR. DUMAS: That takes care of my concern, too.

DR. MURRAY: Obtained.

DR. SHAPIRO: And obtained is also very important. Thank you, Tom. Sought is not much interest. Right.

MR. HOLTZMAN: So editorially can you move-- play with it a little and move your clause up to-- closer to "need not be the only form of required documentation"?

DR. SHAPIRO: Yes.

MR. HOLTZMAN: Your last clause, if you move it back up into there you offer it as the alternative and then you move to--

DR. SHAPIRO: That would be very helpful. Thank you very much. That does help. I will work this out. Yes, so that comes first up on top. Okay.

DR. DUMAS: So--

DR. SHAPIRO: Yes, Rhetaugh?

DR. DUMAS: So what we are really doing is taking the old 4.6--

DR. SHAPIRO: Right, that is right, and altering it in some small ways.

Okay. Somehow mine here skips to--what

happened to 4.7?

DR. MESLIN: Well, you will be pleased to know there was no proposed revision to 4.7.

DR. SHAPIRO: Okay.

DR. MESLIN: So you can assent to 4.7 as it is.

DR. SHAPIRO: No, I think we should propose revisions now.

(Laughter.)

DR. MESLIN: Or propose revisions.

DR. SHAPIRO: I do not think we should let anyone go off without any--all right. 4.7, which is--let's see if I have got that.

DR. MESLIN: Guidance should be developed and mechanisms provided to enable investigators and institutions to reduce threats to privacy or breaches of confidentiality.

DR. SHAPIRO: No, it was not--it was not a change. There was no alternative change. It is not eliminated.

MR. HOLTZMAN: I think the "or" should be an "and."

DR. SHAPIRO: Excuse me, Steve. I did not hear. I am sorry.

MR. HOLTZMAN: I think the "or" should be an "and."

DR. DUMAS: I agree.

DR. SHAPIRO: Yes. Right. It should be an "and."

MR. HOLTZMAN: That in a lot of records research, all right, the whole notion of how to protect confidentiality as a source of harm where privacy has not been very much focused on and so the suggestion is that it would be helpful to the institutions if there were some sources of authoritative guidance.

DR. SHAPIRO: Larry?

DR. MIIKE: If you look at 4.8 then, 4.8 is referring back to 4.7 when you talk about additional mechanisms.

DR. SHAPIRO: Yes.

DR. MIIKE: It is. Then I do not know whether we need to have two recommendations on mechanisms. The 7 seems to be pretty specific. Whereas the other one--the other one is more general but it is the additional mechanisms just in terms of the rationality of it all. I was just thinking maybe we might combine these.

DR. SHAPIRO: It might be an idea to combine 4.7 and 4.8 and take some of this into the text such as the certificates of confidentiality and so on. That last sentence in current 4.8 might just go in the text and then combine--I think it is a good idea to make one recommendation out of this and put something in the

text here on things as specific as the certificates. Does that seem reasonable to people?

Trish?

PROFESSOR BACKLAR: I think it is in the text. I think--

DR. SHAPIRO: Yes, that could be. I am not--that could be. It is just--we will pick up whatever is necessary there. Okay. So we will do that.

I hope you remember this moment, Larry, having always accused us of doing the opposite. How eagerly we accepted your recommendation this time.

Okay. We are now at 4.9. Eric?

DR. MESLIN: This is a very simple choice between NOHRO and not NOHRO. Somebody should convene interested parties to facilitate or interested parties should be convened to facilitate discussion about emerging research protection issues and to develop a research agenda.

DR. SHAPIRO: Yes, Tom?

DR. MURRAY: This is the first time having lost NOHRO I think the recommendation sort of goes off into never-never land because we should assign this--I did my doctoral--my masters thesis on diffusion of responsibility. This is a classic case. We got--

DR. SHAPIRO: This is a good--

DR. MURRAY: --we have got to tell somebody to

do this. I did it at Princeton. So we have got to tell somebody to do this.

DR. SHAPIRO: Right.

(Laughter.)

DR. SHAPIRO: Does that seem reasonable to everybody? Alta?

PROFESSOR CHARO: Yes, I completely agree with you as a distinct critic of the passive tense. This is--but my question as I was going over the recommendations was whether this should be solely the task of the new office or whether we wanted to be inviting PRIM&R and ARENA or other professional societies to potential be the convener, which is where the passive tense emerged from, was the lack of clarity as to whether we wanted to focus primarily on this federal office or to simply say that this is an important thing to be done. The federal office could do it. Somebody else could do it.

DR. SHAPIRO: Yes, I am sorry. Steve, I am sorry.

MR. HOLTZMAN: If you look quickly down to 5.2.

DR. SHAPIRO: Yes.

MR. HOLTZMAN: Doesn't something like 4.9--can't that get swallowed into there?

DR. SHAPIRO: It is--I mean, I do not have a

strong opinion about it, frankly, but this focuses on education and the development of innovative educational programs. I do not think--to me that is a little different. I do not want to make a big deal out of it but it is different enough it seems to me to keep Recommendation 4.9 but I agree with Tom that we ought to find some way to direct somebody to do it.

Tom, and then Eric?

DR. MURRAY: Tongue in cheek, we could say the Hastings Center should be lavishly funded to convene--

(Laughter.)

DR. MURRAY: --but we probably could not get that--

PROFESSOR CHARO: Which you have not had the conflict of interest discussion there, Tom?

DR. MURRAY: There is no conflict of interest here whatsoever.

MR. HOLTZMAN: And Art Caplan will be your special advisor, right?

DR. MURRAY: Right. But I do--I mean, I just reiterate I think we need to assign it to somebody.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, it really says NOHRO should stay up-to-date and I mean is that really a recommendation that NOHRO should stay up-to-date?

DR. SHAPIRO: I think--my own sense of what

this is, is there just has not been enough discussion mobilized on issues that come up all the time as new, you know, protocols are developed and new ideas--and new research--types of research protocols are developed. So I think somewhere there should be some ongoing conversation about this. Now it could be characterized as the let's keep up-to-date gang and that is all we are saying. I mean, I think it could be characterized that way but it is interesting it does not happen by itself.

But anyway, Diane, then Arturo, then Alta.

DR. SCOTT-JONES: The more I hear people talk, the more I like the suggestion Steve made about somehow folding it in with 5.2, which does name other entities, academic and professional societies that would also be involved in this, and then also the last clause, "develop a research agenda," is not that clear. Is it develop a research agenda about ethical issues? It just kind of stands out as it is without any clear meaning. So it seems that you need to name the academic and professional societies in 4.9 or somehow fold it into 5.2, which focuses on education. But they are very closely related.

DR. SHAPIRO: Let's see who we have got here. Arturo, Alta, then Larry.

DR. BRITO: They are closely related but I

think there is a value of having the recommendation 4.9 as is and including mentioning NOHRO because I think to bring back the issue of NOHRO or an independent federal office brings back--this has a very proactive tone to it. Much like the recommendation earlier that we decided--I think we made the decision to take out the word "intervene" or change the vocabulary because that is more reactionary and I think that there is a lot of value here to having it as is with the NOHRO mentioned.

DR. SHAPIRO: I think we can agree on two things. I propose we keep them separate but I think we do have to--I agree with Diane on a number of points. Namely that "develop a research agenda" is not clear what it means, that we have to bring in the professional societies and so on, and we have to name NOHRO. So this just needs some redrafting here. It is not satisfactory as it stands but let's see what other ideas there are.

Alta, and then Larry.

PROFESSOR CHARO: I think actually--I am sorry. I think it is possible, although it will not answer Arturo's specific point but the independent office--everybody else's points, I think, are answered by using 5.2 as a model but not folding it in and it could be redrafted to say the following: The federal government in partnership with academic and

professional societies should convene interested parties to facilitate discussion about emerging human research protection issues and to develop a research agenda about research ethics.

DR. SHAPIRO: Very good. Do you prefer federal government or do you prefer--do you want--you do not expect a recommendation from Alta to come with NOHRO in it.

PROFESSOR CHARO: Well, that is why I say it does not answer Arturo's specific comment but it does answer, I think, the other ones that had been put on so far.

DR. SHAPIRO: So that sounds very responsive to the comments I heard but just let me ask the question just so we do not go around. Is the federal government who we want here or do we want to ask NOHRO to do this, which is, I think, what you were suggesting, Arturo, if I understood? Go ahead.

DR. BRITO: Yes. I also--there are two different points here. We have NOHRO, we have federal government or another body or just a general statement, and that is the first one. The second point is do we--I do read 4.9 and 5.2. I know they overlap but I think there is a distinction here.

DR. SHAPIRO: I agree.

DR. BRITO: And I think what gets lost if you

combine the two is the--

PROFESSOR CHARO: This was a proposal to rewrite 4.9. The language was going to be parallel to the 5.2 language but the 4.9 would stand separately.

DR. BRITO: Okay.

DR. SHAPIRO: 5.2 remains.

DR. BRITO: So I would keep 4.9 with NOHRO, not the federal government, and I would do 5.2 more that general recommendation for the education because I think it was more interested--

DR. SHAPIRO: We will come to 5.2 in a second. We have agreed that 4.9 in one form or another will keep. I think--well, Jim, and then Diane, and then we are going to make a decision.

DR. CHILDRESS: Against Arturo's recommendation, I would prefer federal government here because it could well be that it could be convened by any area within the government. I would propose we not restrict it to NOHRO.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: Well, maybe Jim's suggestion would take care of my concern because unless NOHRO is going to fund or conduct research, developing a research agenda about research ethics does not seem quite right as a task for NOHRO.

DR. SHAPIRO: All right. I think the balance

of opinion here is that we should go as Alta phrased it in her revised statement orally here with federal government.

Okay. Thank you very much.

Now there was a suggestion--excuse me, Larry. I apologize.

DR. MIIKE: Actually it is still on 4.9.

DR. SHAPIRO: Okay. I apologize. You are on my list and I just forgot to call you.

DR. MIIKE: I think 4.9 is too weak. I would make an analogy to how health services research was slow in coming when we started funding services and I think what--the sense that I would like to see in here is really that a research agenda on human subjects protection is what we are after, not so much as convening a group to go develop a research agenda. So we need something here that is stronger and really should sort of tie to 6.1. 6.1 is sort of a general catch all thing that says we need the resources to do it.

DR. SHAPIRO: Right.

DR. MIIKE: So if I had my druthers I would rather say somebody has to provide the resources to not just develop a research agenda but to make sure that it goes forward. To just call for a meeting or something like that is not going to really cut it so I would ask

for something stronger on this.

DR. SHAPIRO: Okay. Let me make a--I am going to come back to that issue in a minute because we are going to have to reach--there is some redrafting, not a lot but there is some redrafting here for 4 just as there was under 3. But there was an additional recommendation, Eric, I think. Could you talk about that?

DR. MESLIN: I think this was Alta's suggestion that in the--in an earlier version of this chapter we had a recommendation 4.12 which read something like "the federal policy should require local IRBs to obtain additional expert reviews for certain studies that involve novel or controversial ethical issues. The U.S. Government should identify such studies and facilitate the creation of necessary expert review bodies." That was dropped in the version that you have in front of you but the issue really relates partly to the Recommendation 3.6 that we had with respect to vulnerable persons, groups or situations. So there are a number of things that you could do. One is it could stay absent. Secondly, it could be reconstituted as what would now, I guess, be a number for 10. Or you could amend 3.6 by referring to this issue in some way so you have a few options. I do not want to say more about this.

Alta, you may want to flush it out some more?

PROFESSOR CHARO: Yes. Actually just one minor correction. 3.6 did not deal with vulnerability. It dealt with the levels of research review being commensurate with risk.

Without being at all tied to the old language of 4.12, which is kind of awkward as such, the question in my mind was whether we wanted to highlight or not something that is nonetheless in the report. So this is not a huge big deal. It is in there. We have called in our previous reports on occasion for special review bodies. There are other special review bodies like the RAC for gene therapy that already exist. So we have fallen into a pattern of expecting that this is a useful model for some circumstances where local IRB review has--does not have the capability consistently to handle the research ethics questions.

My preference--but it was a preference was to highlight this and to say something about it in the recommendations and to find some way to take advantage of the old 4.12 but it is in the text regardless.

DR. SHAPIRO: How do commissioners feel? Do you want a recommendation developed that deals with this issue? It is actually a very difficult issue. It is difficult to define. It is difficult to operationalize. It is a very difficult--it is not--it

is a real issue. It is not a fake--you know, not a--
but Diane, then Bette.

DR. SCOTT-JONES: The issue is somewhat related to the composition of IRBs, isn't it? And could it be folded in somewhere with our statements about composition of IRBs to say that--something about special expertise for novel or controversial issues and somehow refer to supplementing IRBs, IRB members.

DR. SHAPIRO: We certainly could do that. Well, that will be coming up shortly. I mean that is coming up in the next chapter. That is possible. How do others feel about this? This is--I say I do not quite know how to come down on this myself. Bette?

MS. KRAMER: Mine was really a question. Was this intended to address--I think we talked about the problems of IRBs at particularly smaller than larger academic institutions that would not necessarily have the expertise to understand some of the issues involved? Was that--

DR. SHAPIRO: No.

MS. KRAMER: --it is not related to that.

DR. SHAPIRO: This--my take on this is related to novel, new and, you know, not fully understood situations. And where certain types of expertise might help, you know, to provide the appropriate protections and so on. But Diane and then Alta?

DR. SCOTT-JONES: Recommendation 5.4 refers to competency in core areas for IRB members and it seems that there might be a place to fold in something about competencies in areas that are not the core areas. It seems to me that 5.4 would be a good place to fold that in without adding--or to add the recommendation there with 5.4, to add another recommendation in that series.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Yes. One way that we could handle this that takes advantage of Diane's comment and also takes advantage of the observation that 3.6 is related to this would be to consider the following. You have all got the piece of paper that was distributed with Marjorie's redraft of the Chapter 3 recommendation.

DR. SHAPIRO: That is a single page which has been put at everybody's place.

PROFESSOR CHARO: Right. If you look at the redraft of 3.6, okay, there could be some slight alteration of that redraft and it would--it could go as follows now. "Federal oversight should require research review..." I guess that is a typo there "...should require research review that is commensurate with the nature and level of risk. Standards and procedures for review should distinguish between risk that poses no more than minimal risk and research that

poses more than minimal risk. In addition, the federal government should facilitate the creation of special supplementary review bodies for research that involves novel or controversial ethical considerations."

In that sense it talks about facilitating the creation of bodies without getting into whether they are required, whether IRBs are precluded, right, so it keeps that open enough for further development.

Then later when we get to 5.4 and we are talking about core competencies we can consider how we might think about adding either in the recommendation or the draft text right after it something about the core competencies for a general IRB versus the core competencies for a special supplementary review board that is being created for one of these purposes, which was something that had been discussed at the Utah meeting. I think Bernie talked a lot about having different kinds of accreditation for different kinds of boards.

DR. SHAPIRO: Well, it does seem like a good change for 3.6 I have to say. I am not quite sure about the second part of your recommendation but we could come to that when we get to 5.

Arturo?

DR. BRITO: In principle, I agree with the recommendation to make this change. The only question

I have is that--is there going to be any ambiguity in this recommendation by--with the addendum that research involving novel or controversial ethical considerations? What I mean by that is in the text we do describe some of these examples. We give some examples but when you put out in the recommendation it is going to be a little bit confusing--you know, what is a novel consideration or a novel research that has some different ethical implications and things like that. So it is just something that--

DR. SHAPIRO: That is always going to be a problem for interpretation, I agree. I do not know how to avoid it. It is a significant issue.

All right. Let me make a suggestion now since it is 12:30. We will draft a change in Recommendation 3.6 so that you will have a clean sheet in front of you when you return. In the meantime if you could during lunch look at the 3.1 through 3.5 and see if you have any further comments, that would be very helpful. We will also try to draft in the next little while the suggested changes in 4 and we will reconvene at 1:30.

(Whereupon, at 12:30 p.m., a luncheon break was taken.)

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A F T E R N O O N S E S S I O N

DR. SHAPIRO: Bernie, are you there?

DR. LO: Yes.

DR. SHAPIRO: Thank you for sticking with us. Okay.

DISCUSSION OF DRAFT REPORT: CHAPTER 5

DR. SHAPIRO: Let's now go on to the recommendations that come out of Chapter 5. We are trying to, as we speak, incorporate not only the comments you made on 4 but some of the written suggestions you handed in just before the lunch hour, and we will see just how far we get but I want to now move on to Chapter 5, and it is a series of recommendations.

Eric, do you want to take us through those?

DR. MESLIN: Yes. In Chapter 5, 5.1, there were no alternative suggestions for you but let me just remind you what the recommendation was.

"All institutions and sponsors engaged in research involving human participants should provide educational programs and research ethics pertaining to participant protection to appropriate institutional officials, investigators, IRB members and IRB staff. Colleges and universities should include research ethics in curricula relating to conducting research. Professional societies should encourage, as

appropriate, graduate and professional schools to include research ethics as part of the curriculum and should include research ethics in their programs of continuing education."

There was not a suggestion for revision but that is the one on offer at the moment.

DR. SHAPIRO: Let me ask a question, which I am always asking and I always forget the answer, does investigator--the word "investigator" is used in this context include research staff? It does. I am just asking. If it does, I am satisfied. Okay. Thank you. I will try to remember that. I have probably only asked this eight or nine times.

Any other comments just on 5.1?

DR. MURRAY: Just an alliterative mouthful pertaining to participant protection. It is problematic.

(Laughter.)

DR. MURRAY: But I mean it is accurate. It would just be nice if somebody could streamline it a little bit but I have no substantive objections.

DR. SHAPIRO: All right. We will try--we will find ways to streamline that if we can think of it. Any other comments on 5.1?

5.2, Eric?

DR. MESLIN: So this is a recommendation where

NOHRO is figuring prominently in the two versions but they are very close. NOHRO in partnership with academic and professional societies should enhance the teaching of research ethics related to protection of the human research participants and stimulate the development of innovative educational programs, relevant professional societies should be consulted so that educational programs are designed to meet the needs of all who conduct research. The difference is that the federal government in partnership with professional societies should enhance, et cetera.

DR. SHAPIRO: Again this is one of those issues where it is the federal government versus NOHRO--not versus but it is the alternative in this recommendation. How do people feel about it in this case?

Which one do you like, Arturo?

DR. BRITO: It is more appropriate here for the federal government. I think it should be a more general comment.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Just as a procedural question, should we just decide that NOHRO is not going to be in any of these once and for all so that Eric does not have to read them twice? And if there is only--if there is no substantive difference between the two

versions, and there is just a little bit of a wording, just take it back to staff to choose the best wording.

DR. SHAPIRO: That is fine with me. Okay. Anything else on 5.2?

DR. MURRAY: It does not--

DR. SHAPIRO: Tom?

DR. MURRAY: It does not say--well, there is a "the" that does not belong there. The second line says "should enhance research ethics education."

DR. SHAPIRO: Yes.

DR. MURRAY: It does not say education of whom. I mean, research ethics education in undergraduate courses in bioethics research--do we really mean--do we mean it broadly? That is fine. Or do we mean to really direct this towards people conducting research? And I do not know which we mean. Either would be acceptable to me.

DR. SHAPIRO: I think in the--if you read the text--my recollection of the text, I do not have it perfectly in my mind, is the broader group. It would do different things in different ways of course but I think it includes the broader group of the two that you suggested.

Yes, Steve?

MR. HOLTZMAN: Well, Tom, I think your question is answered in 5.1 and here we are saying that

the feds ought to put up some money and work with the institutions to develop and to devise those research programs that will be then taught under 5.1. DR. SHAPIRO: Okay. 5.3, any comments or questions? Eric?

DR. MESLIN: Using Steve's rule there is nothing substantive there except for the NOHRO issue.

DR. SHAPIRO: Any comments, questions, concerns on 5.3? Okay. 5.4? Eric?

DR. MESLIN: Ditto.

DR. SHAPIRO: Ditto. It is on file. Any-- let's see--quite aside from the ditto, is there any other comments or questions, concerns on 5.4?

PUBLIC COMMENT

DR. SHAPIRO: I want to be-- we need to stop our discussion for a second because I really should have started us off this afternoon to see if there were any public comments. We do not have anyone signed up for public comments but is there anyone in the audience who has something they wanted to say to the commission?

(No response.)

DR. SHAPIRO: Okay. Thank you. I apologize for the commissioners for forgetting that because we did have a public comment session set up. Okay. Let's go on then.

DISCUSSION OF DRAFT REPORT: CHAPTER 5 (cont)

DR. SHAPIRO: 5.5?

DR. MESLIN: In 5.5 the only difference really is the grammar, the assurance of compliance process should be modified to reduce unnecessary burden on institutions versus the process for assuring compliance with federal regulations should be modified to reduce unnecessary burdens on institutions.

DR. SHAPIRO: That is in Steve's category, I think.

DR. MESLIN: Yes.

DR. SHAPIRO: But let's see what comments there are on 5.5. Thank you.

5.6? I am sorry. I did not see your hand up. I apologize.

MR. HOLTZMAN: I hate to take us backwards but on 5.3, if I look at the last sentence, here we are talking about certification of individuals, and the last sentence says it sets standards for determining whether institutions and sponsors have an effective process for certification.

Is it--I do not think it is necessarily the institutions or sponsors who will be engaged in certification. If you look at the sentence immediately before it, we encourage organizations, et cetera, to develop certification programs and mechanisms. I am just--does that sentence add anything and does it add it right is my question?

DR. SHAPIRO: What I had interpreted that sentence to mean--I am not answering the last question, have we expressed it correctly--was that there should be some standards for these certification programs. It is not just enough that they have them. They should sort of fulfill some standards and someone has to, sort of, assure that. That was my--the way I interpreted it. Now I am not answering the second part of your question. I will have to think about that as to whether it is achieving--

MR. HOLTZMAN: Staff, when you look at that, just think of whether we have captured it.

DR. SHAPIRO: Yes. Okay. Is there anything you want to say on 5.6? Any comments on 5.6? 5.7, Eric?

DR. MESLIN: Just the NOHRO issue.

DR. SHAPIRO: Any comments? Yes, Larry?

DR. MIIKE: I have not really looked at the text on this lately but is it necessary to say the second part of that? Is that a separate and distinct issue aside from conflict of interest to insure that that does not harm or lead to an unnecessary risk? Those are two different thoughts all together. One is an issue per se. The other one is an impact of that issue.

DR. SHAPIRO: Right. Alta, I am sorry. I did

not see you.

PROFESSOR CHARO: Without asserting that this language accomplishes it, here is something that came out at a meeting I went to on conflicts of interest that I would like to see us be able to put out here somehow, that there are conflicts of interest that we need to worry about and that there are conflicts of interest that we do not really need to worry about because they do not have any consequences that pertain to the rights and welfare of the human participants. So one might want to define certain situations as a conflict of interest and then next state whether it is sufficient to simply reveal it or whether one needs to be recused, you know, to be excused from deliberation or whether some other means is necessary to handle the conflicts. They are slightly different thoughts and this was an attempt, I think, on both the original and on the revision to capture both of those thoughts.

DR. SHAPIRO: Let me go to Eric first. I have a question about that one. Eric?

DR. CASSELL: Just a simple thing. Is it self-evident in whom these conflicts of interests might occur that we are concerned about? If it is IRB members, we ought to say IRB members. If it is investigators, we ought to say that. But just blanket conflicts of interest it seems to me.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: But, Eric, I think if you look at the text associated with it, actually it is a nice recitation of the fact that it is not just--there are IRBs that could have conflicts, members could have conflicts, institutions could have conflicts.

DR. SHAPIRO: Well, that is--we ought to specify that.

MR. HOLTZMAN: But I think we do--

DR. SHAPIRO: Inside the recommendations.

DR. CASSELL: Yes. It is not--there is nothing wrong with just saying, no, there should be no conflicts of interest and if there are they should not have an impact on whatever, but we should make it clear that conflicts of interest in institutions and conflicts of interest in the IRB itself and all those are of issue.

DR. SHAPIRO: One could, if we desire, easily build this into this recommendation right after the words "conflict of interest" to deal with IRBs, institutions, et cetera, we have that listed in the text and that could be easily--I think that could be easily handled.

But there is this issue that Larry raised, which I would like to see how the commission feels about, that is whether we want to deal with their

impact if I understood what you said, Larry, in a separate recommendation or if we even need to deal with it.

DR. MIIKE: Yes. I mean, it basically has two thoughts here. I just wanted clarification about the common issue.

DR. SHAPIRO: Yes. Arturo?

DR. BRITO: Yes, I think this is related to what Larry's point is going at and it is related to something Jim has mentioned several times, particularly with the prologue but also here, is I want to throw out this general question. Is the concern with the conflict of interest always related to risk? Isn't it more related to individual rights and then would somehow writing this in a way that it does not interfere with individual participant rights kind of make it more general and then, therefore, we do not have to get into the area that Larry is really more concerned about?

DR. SHAPIRO: Steve, then Alta?

MR. HOLTZMAN: So I think we can broaden it from risks to the issues that Jim--the standard formulation, but there are two distinct things I believe we have asked the federal government or NOHRO to do. (A) Help people to identify when there is a conflict. That is the guidance on what are conflicts

to Eric's point. But the second thing is to provide guidance on how to deal with those conflicts, and to Alta's point what we are effectively going to say is there are certain species of the genus conflict which will be dealt with simply through disclosure. There are other ones where we believe they are of such a nature that disclosure will not be enough. Recusal or just--you cannot do it. And that we are asking, therefore--Larry, I think we are--we did say in the text that we did want guidance on both of those. And I almost think that you want to split it up into two sentences, define and furthermore.

DR. SHAPIRO: I think--excuse me, Rhetaugh.

DR. DUMAS: I would like to suggest altering that sentence to read "federal guidance should be issued for defining and handling conflicts of interest," and then list the IRBs, institutions, individuals, whatever.

DR. SHAPIRO: Okay. I understand what the commission would like in this respect is, first of all, to identify where these conflicts are, that is institutions, investigators and so on, where they could be, and also that it be clear that we want both to identify them, help identify them, and manage them or deal with them in some way. So we will try to--we will rewrite 5.7 along those lines. We will try out

something. I do not want to edit the whole thing right now but we will have to develop something new in 5.7 to provide some more detail.

Tom?

DR. MURRAY: As you are aware, there are many bodies concerned with conflicts of interest in research right now. Just yesterday I was here for the Association of American Medical Colleges Conflict of Interest Task Force and that organization is trying to come up with its own definitions and its own strategies for management, prohibitions, et cetera. So I have mixed feelings here. I do not want to, you know, duplicate the wheel. This is an area where consciousness has been raised, lots of ideas are going to be floating around in the near future. It is a moving target and I am not sure where to go with this.

I guess we do want to ask them to do something but we probably ought to keep it as, you know, nonspecific as possible.

DR. SHAPIRO: The staff--I think that is correct and the staff has, in fact--I thought I had it in front of me. It must be in my briefcase. -- developed an interesting analysis of all those initiatives that are underway right now, some of which have actual recommendations and some of which are just in process. But you are exactly right. There is a

tremendous amount of interest and movement in this area right now and I--but I agree with you completely that we ought to just be general and not specific here.

Okay. Anything else on 5.7?

5.8, Eric?

DR. MESLIN: Although there was not an alternative suggested, I only wanted to flag that the text reads, "Sponsors and institutions that sponsor or conduct human participant research..." and I think some of you have expressed the desire to change that to be "research involving human participants," but it is--other than that there were no other suggestions made.

DR. SHAPIRO: So that will be changed in that way.

DR. MESLIN: If you would like to do it.

DR. SHAPIRO: Unless there is an objection to that. Okay. Anything else on 5.8? Any issues dealing with 5.8?

PROFESSOR BACKLAR: (Not at microphone.)

DR. SHAPIRO: It may indeed. Trish made the point that 5.8 is really part of 5.7 and relates very much to the discussion we just had in 5.7 and as we redo it, it is not--we might even combine these two. Combining 5.7 and 5.8 might work. I do not know. We will have to try it out.

DR. MURRAY: The difference is in previous

reports we have somehow sorted recommendations out according to whom they are addressed.

DR. SHAPIRO: Right.

DR. MURRAY: And these are addressed to different parties.

DR. SHAPIRO: Correct.

DR. MURRAY: One is addressed to the federal government and this is addressed now to sponsors and institutions so it may be useful to keep them separate.

The first sentence--I am all in favor of it but it is rather limitless. It is identify and manage all types of conflicts of interest. We might want to add "relevant to research" or something to that effect because there are lots of conflicts of interest that are none of our business.

DR. SHAPIRO: Other comments or questions on 5.8? Rachel?

MS. LEVINSON: The second sentence refers to investigators' conflicts of interest and you probably want to be able to include conflicts of interest of institutions, sponsors, others who are involved in patient care and all aspects, not just investigators.

DR. SHAPIRO: Let me think about that a minute. I think, in general, that is right. Yes. Yes. That is--no, the issue is on the second sentence in 5.8 where it says "in particular, such policies,"

that is in addition to whatever is said under the first sentence. It says, "In particular, we should require disclosure of investigators' conflicts to both institutions, IRBs and participants." And the question is do you want that in particular--as I understand your question, Rachel--in particular to be broader than that. Is that correct?

MS. LEVINSON: Yes. It is just that you--as long as you read it with the “in particular”, otherwise it looks as if you are only focusing--that the only concern relates to the conflicts of investigators and not others where there also might be an issue with respect to the desire of the subject to know--participant to know about the conflicts.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I would like just to ask a question about the goal of the recommendation prior to getting the language down. Is the goal of the recommendation very much to pull out and highlight disclosure generally or to highlight disclosure of investigators specifically or is it neither of those, in which case that sentence “in particular” might be dropped and the last sentence somewhat altered to say that policies should describe--should describe at least the specific types of prohibited--any specific types of prohibited relationships and any mandated disclosures?

DR. SHAPIRO: What does mandated disclosures mean?

PROFESSOR CHARO: Well, it is the stuff that was in the “in particular”.

(Laughter.)

DR. SHAPIRO: At least it was defined here, whether right or wrong.

PROFESSOR CHARO: Well, I mean, I guess I was assuming that there was something in--I do not remember when the “in particular” language came in. I do not remember how far back it goes. I certainly do not remember the discussion around it, which is why I was asking what the goal of the recommendation was at this point.

DR. SHAPIRO: I think--I mean, I have not gotten language at my disposal--at my finger tips here for that. I think my own feeling is that, you know, significant conflicts in all these areas ought to be disclosed to participants. Otherwise, they do not really know what they are--what kind of context they are operating under, and how far their trust ought to go. And so I respond actually positively to Rachel's suggestion. I have not gotten language to put it in but the reason for this is to protect participants. Give them some information on which they can make a useful decision--that is my sense of it.

PROFESSOR CHARO: Well, in that case would it make sense then to start to take out that sentence and substitute something that says “in particular participants should receive disclosure of all relevant conflicts of interest”, and that does not limit it to investigators. It is any relevant conflict. And then the last sentence talks about prescription of certain relationships.

DR. SHAPIRO: Something like that would go along with my own thinking on it. I would be happy to--I have not thought through all those words but I mean it sounds correct to me.

Yes, Arturo?

DR. BRITO: Can we go back? Maybe somebody could refresh my memory here as to why we were most concerned--and I think I know why--we were most concerned about investigators when here we mean research staff, right, all research staff, because I think sometimes when you read and reread and reread these you forget that it involves anybody involved in research as opposed to, for instance, somebody on the IRB who may have a conflict of interest. And if I remember correctly, we went through this quite a bit, and I think our biggest concern was that when it is the investigator one on one with the individual, or somebody on the research staff, that is our largest

concern that the participant have a right to know that that investigator may have stock in whatever company may be involved in this research, or what have you. So I am afraid--while I agree with Rachel's suggestion, I am afraid that if we start wordsmithing here and reword it, we are going to lose that primary concern.

DR. SHAPIRO: It seems to me it is not clear whether--I understand the point you are making that the--very often it is the relationship between the investigator and the participant where the contact takes place and, therefore, you want to be especially sensitive to that, which I take to be the point that you are raising, which I understand. But it is hard to know where the biggest conflict is and whether the conflict really is at the institutional level. We do not know who holds the stock, just to take an example. You know, whether it is the individual or the institution or both or other issues. So, you know, I do not feel very strongly about it, but I think we are somewhat better off to make it more general in this case. It is my feeling. The text takes care of all this as you point out and it deals with all these in the text.

Other comments or questions on it?

DR. MIIKE: I agree with Arturo.

DR. SHAPIRO: Okay.

DR. MIIKE: I think we should make it a point to particularly focus on the investigators.

DR. SHAPIRO: In the way that it is here, that is not mention the others beyond this--

DR. MIIKE: Well, in particular--

DR. SHAPIRO: --you like the in particular.

DR. MIIKE: --if you mention everybody else then you are not “in particular”.

DR. SHAPIRO: That is right. All right. Okay.

DR. BRITO: We have to make sure the text matches. I cannot remember the exact wording in the text but I thought in the text--am I not correct that there was an emphasis on the investigators.

DR. SHAPIRO: I think the emphasis is on the investigator both in the text and in most general accounts of this, and the reason is the easy examples all refer to investigators. The harder examples are on the IRB and institutional, which therefore do not get well articulated in most cases, and my own view is that while these are all important, that it is the institutional and the IRB conflicts that get the least attention and are often quite important. So, you know, it is not a make or break deal as Larry said. It says “in particular”. It does not mean avoid the others. It just says “in particular”.

But how do people feel about that? Do you want to, just as a shorthand keep, it as the “in particular” in there or not? People are indifferent?

DR. MURRAY: No, I would go with Alta's previous suggestion to reframe it in a more general manner. I think institutional conflicts of interest just have not been on the radar screen, but as they get on the radar screen people are going to want to know more about them, about as much as they are going to want to know about the investigators' conflicts of interest, so I would--I would be reluctant to just focus on the investigators.

DR. SHAPIRO: How do others feel?

DR. MIIKE: Well, as I said, it is not focusing only on investigators. It is saying “in particular attention should be paid”. I guess it is just the way you rephrase it.

DR. SHAPIRO: Yes. Bette?

MS. KRAMER: I agree with Tom.

DR. SHAPIRO: With who? Tom. I did not hear the Tom part. It sounded like John some how. Carol?

DR. GREIDER: I also agree with Tom.

DR. SHAPIRO: Okay. Everyone else does not care who has not spoken. Arturo?

DR. BRITO: I am not disagreeing with what Tom is saying. I would like to go back and reread the text

before this recommendation and see what the--and I do not think it would take a lot of changes in the text, but somewhere in there emphasize that we are not just concerned about investigators who are going to go this way. That is my concern, just matching there.

DR. SHAPIRO: Okay. We will certainly match it either way. Steve, and then Trish.

MR. HOLTZMAN: Well, there is a substantive issue here about, so to speak, legacy of the commission. All right. And we can have a choice here between saying that what we really want to convey is that the previous focus on the investigators' conflicts and on financial conflicts, while not wrong, is too narrow and our legacy is one of broadening the focus of potential sources of conflict.

The other legacy we could say is we do want to broaden the focus but nevertheless the primacy of the relationship, particularly in the biomedical context of the investigator to the subject, okay, and not wanting to compromise that relationship of trust is something that retains the primacy. So I do not think it is an--I am sitting here struggling with which is the legacy we want to leave.

DR. SHAPIRO: Trish?

PROFESSOR BACKLAR: What I am concerned about is that someone will just look at our recommendations

and that if we leave out some of these rather key positions that we are taking that they may be missed and never found in the text.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: First, I completely agree with Steve's first statement about the thing that is new, relatively speaking here, is the notion that the conflicts of interest of concern are broader than those that focus on the investigator alone. So I am comfortable with the emphasis on the broader formulation.

And, second, as has happened repeatedly, including to my beloved effort to get something in there about social science research earlier on in 3.3 or whatever it was, this may be an example yet again of something that is difficult to capture in a sentence short enough to go into a recommendation but needs to be put in the unbolded text immediately following it in the published version of the recs that often have a little bit of text right after each one to explain it in some more detail.

DR. SHAPIRO: Other comments or questions here? This is again 5.8.

What about if we try to rewrite 5.8? Instead of saying “identify and manage all types of conflicts of interest”, which includes the universe of conflicts,

whatever they are, if we try to identify in that sentence the conflicts that deal with institutions, sponsors, et cetera, so in the first sentence it really captures everyone, and we could leave in the second sentence as just--you know, so we try to do both in here. How would that seem to people?

Larry?

DR. MIIKE: Let me throw out another suggestion is that we start off by saying that our recommendation expands beyond the current focus on investigators to include all parties that may be in conflict of interest. That may be one other way of looking at it.

DR. SHAPIRO: I think we could do that. I would prefer we do that in the text immediately before the recommendation it would seem to me. All right. We will try to rewrite it that way and you will get another look at it.

Let's go on to Recommendation 5.9. Eric?

DR. MESLIN: This is the recommendation that you all began discussing a little bit the very first thing this morning. So the recommendation as it stands is "Federal regulations should set minimum percentage requirements for IRB membership composition and a quorum determination for members: (1) who are not otherwise affiliated with the institution; (2) whose

primary concerns are in nonscientific areas; and (3) who represent the perspective of the participant. For each category IRB membership should be at least 25 percent." And you had a discussion about overlapping and nonoverlapping.

Alta had circulated a proposal but she has now just handed an even more articulate version which I will read to you for the first time.

"IRB membership should include members who represent the perspective of participants and members who are unaffiliated with the institution and members whose primary concerns are in nonscientific areas. A single member may represent one, two or all three of these characteristics. For the purposes of both overall membership and quorum determinations, these persons should collectively represent one-quarter of the IRB."

PROFESSOR CHARO: Because it is a little hard to see it when you are only listening, I just wanted to note that the rewrite takes the categories and puts an "and" before each of them so it is very clear that you have to have people from each of these categories. It is not enough to have any one category satisfy it. So you have to have people from each of these, although one person may satisfy two categories simultaneously so long as all of these characteristics are present on an

IRB and that together the complement of people representing these different characteristics has to be at least 25 percent for both membership and to pick up on a point Tom had made, a quorum.

DR. SHAPIRO: Okay. Larry, then Tom.

DR. MIIKE: Can you read the last sentence of that because it seemed to make a substantive change in the first part? Can you read the last sentence?

PROFESSOR CHARO: I mean there was an intent to make a change because the first one had an arithmetic caboodle.

DR. MIIKE: Well, in the sense that we talk about a quarter for about three categories and someone can satisfy one or more of that but then at the end for quorum purposes they could all collectively equal 25 percent and that is the quorum, and that to me is quite a different outlook than to talk about the first part where you have three. Do you understand what I am saying? Read the last sentence.

PROFESSOR CHARO: Okay. "A single member may represent one, two or all three of these characteristics. For the purposes of both overall membership and quorum determinations, these persons should collectively represent one-quarter of the IRB."

DR. SHAPIRO: At least it has got to be for the--

PROFESSOR CHARO: Collectively represent at least one quarter of the IRB.

DR. SHAPIRO: Let me try to just get myself updated on the discussion you had this morning. I missed that discussion, which I take it was focused on what the 25 percent meant, what it referred to. Whether there were three 25 percents or one 25 percent and so on. Would someone describe to me where that discussion went this morning?

No where. All right. We will start all over again.

DR. MURRAY: I will give it a try.

DR. SHAPIRO: All right.

DR. MURRAY: I mean, I propose that 150 percent of IRB members be from--

(Laughter.)

DR. MURRAY: Drop that. There was--we had originally--Alta's substitute versus, the one that was--that came from the commission.

DR. SHAPIRO: Right.

DR. MURRAY: One concern was that if there was an ambiguity in the commission's original 5.9, some IRBs might feel themselves compelled to have 75 percent of their members.

DR. SHAPIRO: Right.

DR. MURRAY: 25 percent independently from

each of those three categories specified. That is clearly--that is not the intent of it and one question is should we simply try to clarify that that is not our intent and that a single individual can account for as many as all three of those categories.

Alta substitute received some objections because of the "or" and so my objection would be, for example, imagine that you have got a 12 person IRB and you have three members who happen to be scientists at a neighboring institution. Right. So you would have met the criteria in the substitute and I do not think--that is not--that is not--I do not think Alta was aiming at that, but that is not what we wanted, so we wanted to try to get--in fact, if 25 percent of each--if it has got a 25 percent have got to be from each of these three specified groups, although again you could have--you could have three individuals on a 12 person IRB, all of them hitting off--you know, they are all three baggers--that is fine. That is fine. So 25 percent. Although many institutions may find it hard to do that and they may end up with more than 25 percent of the total membership being in one or the other of these categories.

So imagine a situation where you have got a 12 person IRB, a quorum is eight, if two of those people show up, you have made your quorum.

DR. SHAPIRO: Was that--okay. I find myself in agreement with what you have described. I just do not know if everyone else is in agreement with that.

Steve?

MR. HOLTZMAN: I am and I just think that we just have to find the right language that makes very clear a few things. Right. We are saying that there are three categories we want represented, that a person can represent more than one category, that 25 percent or more should be of people who represent those categories in terms of the overall composition, and that for a quorum to occur, 25 percent present must represent, one or more of those, not all have to be there.

DR. SHAPIRO: Right. Those are the elements. I just want to understand if--I am not referring to language now. If there is general agreement that that is our target here. Larry?

DR. MIIKE: Well, I tell you what I have a problem with. We started off with 50 percent and now we are down to 25 percent. And when you begin to read this it sounds as though like, oh, you know, it is 25 percent but collectively there are going to be more people or at least equal amounts of people that are not affiliated with the institution, et cetera, et cetera. But in reality we are still talking 25 percent of the

whole total and it does not somehow jive with me when we talk about two categories, each of 25 percent, and then you end up with something like it is just an absolute 25 percent.

DR. SHAPIRO: We did discuss, as Tom especially will remember, I think, whether it should be 25 or 50. We had a discussion of that. It was not at our last meeting. It was the meeting before. And we ended up with at least 25 percent, which is--that is where we ended up. And so we can always reconsider that and say, look, given this, it is not enough and we can certainly do that. I mean, I do not know how to get around the fact that it takes so many words to define this and you end up with only 25 percent of--that is true. I mean, I accept that and it is--

DR. MIIKE: The simple way is to say of these three categories a person can satisfy two and not three.

DR. SHAPIRO: There is all kinds of ways to do that, right. So I am just trying--Alta, sorry.

PROFESSOR CHARO: I do not know--I do not know how recently most of us have served on IRBs but I do want to have a plea for some degree of restraint here. In many of our recommendations we have decided not to get down to the kind of microscopic level of potential regulation precisely to avoid this. Now before I would

want to go into this any further, and to be honest, it was why I had originally dropped quorum out of my suggested revision, I would want to have testimony on what are the range of sizes of IRBs, what does this numerically mean. How many IRBs, especially in light of the recommendations about the expanded discipline set that needs to be represented, are now going to be at a minimum of a size of 18 members or more to which we are now adding additional nonspecialist, unaffiliated or participant prospective people? How likely is it that people will actually show up for what is usually an unfunded activity on top of their usual work lives? To what extent will we in the end wind up not approving protocols this week but have to wait to next week or next month to do it because a quorum did not make it? And to what extent is there going to be a net loss of value because of the kind of hoops and hurdles we are creating?

And I would much rather leave this to the people who have to write the Federal Register notice and avoid having to do it ourselves. I think that this is a level of detail and knowledge of the inner workings of IRBs that we could happily avoid, because the main point here was that we simply did not think a single voice, which is the current pattern, a single nonspecialist voice can adequately represent both study

participant, you know, perspectives and represent some check on conflict of interest.

The main thrust, the important thrust, is simply that we think there ought to be a bigger presence, and anything that gets too detailed, I think, is only going to hit a wall of resistance because it may not have been well thought out.

DR. SHAPIRO: Eric?

DR. CASSELL: In few words, I could not agree more. I just see this with my hat as an IRB chair trying to figure out how I would get a meeting going, much less get these people, and then we figure out how we do this stuff in the back room somehow so we can get around the regulation.

(Laughter.)

DR. SHAPIRO: Tom?

DR. MURRAY: I disagree with my colleagues on this. We are not a rule making body. We make recommendations. I think we should--I do not think this is an unrealistically ambitious target. And, Eric, if you had more resources you could, you know, get your--imagine a real administrator for your IRB and the kind of support that IRBs deserve.

DR. CASSELL: In a big institution but not in a smaller institution with a small IRB.

DR. MURRAY: I served on IRBs and the last one

a couple of years ago, I have not served since I moved to Hastings but I would favor what--the conditions, I think, Steve described probably most concisely. I think we should recommend that. I think we should vote for it. We have already had testimony apparently from groups that said that 50 percent was too high but 25 percent was okay. So we have had some of the relevant testimony. If you want to bury something, you can throw up a lot of objections to it. There are reasonable objections to this but I think we should vote for it.

DR. SHAPIRO: I agree with Tom on this one. We all--in fact, we are recommending things. You can be sure there will be many other powerful voices that will jump into the ring before anything really happens here and they will have their say and something will come out of it but I think if we back off of that just because we do not want to, sort of, anticipate all that, I do not--it does not sound right to me.

I think many of our recommendations will not work if IRBs are not better supported in the future than they are right now. I mean, just about most of our recommendations will not work. And so we have to assume that that is going to happen over time. Now that is not easy and there will be all kinds of static before we get there or before--but that does not mean

we should not have our say here. And I do not have the right language but I, myself, am very comfortable with the idea that these are the three categories, together they have to make up no less than 25 percent, with double counting and so on. It is not easy to put the language together and I do not propose to do it right this second.

But it seems to me like the right place to be and others will chime in before these rules are written down and enacted into some kind of regulations.

DR. LO: Could I put my hand up?

DR. SHAPIRO: Bernie?

DR. LO: Yes. Just to chime in on this. I want to go back to Alta's point that we should try to make our main points, which I think you just did, Harold, without getting down to the level of detail that we really would have a hard time working through, because we have not thought of all, the sort of, range of cases, unusual situations. So I think that it is fine to, sort of, have the 25 percent combination and be very clear on that but not to get down to levels of, sort of, you know, additional specialists and quorums. If we are going to do that, do it in the text and leave it open for other people to work out in more detail. I just would like us to present sort of the vague idea of the main heading in the blueprint and let

others sort of discuss how to fill it in.

DR. SHAPIRO: Bernie, do I understand your comment to mean that you are in favor of the recommendation on membership but things like quorums should be left for others to think through?

DR. LO: Right, because I think if you have 25 percent real membership then I think it can be worked out, sort of, who has to be there for which meeting. We just should not try and do everything in this set of recommendations.

DR. SHAPIRO: Larry, then Tom?

DR. MIIKE: My last comment was that I did not particularly like the last part of what Alta was saying because I think the point is to aim for diversity in the IRB and then if we say explicitly or--and you know actually someone can--we can say they have to come from these categories, you can fit more than one, but then to go on beyond that to say that sort of pushing toward people saying, oh, but, you know, a quarter of them--we just need a quarter of them and someone can satisfy all, that is to me pushing the edge a little bit too far.

You understand what I am saying, which is that when we state expressly in the recommendation that the minimum can be 25 percent even though we have these three categories, it is sort of like telling people go

ahead and do it that way and we really do not mean the diversity that the three categories is supposed to be addressing.

Because in some--I could make an argument that says we should be talking about the three categories of 25 percent so that they should collectively equal 75 percent rather than 25 percent, and if we get--we get so explicit in the recommendation it is just sort of telling people that, you know, we really mean all these people are just going to be 25 percent of the IRB. And that I cannot agree with.

DR. SHAPIRO: Alta, and then--Tom, excuse me. Tom, you were next, and then Alta.

DR. MURRAY: This is specifically to Bernie. Bernie, this recommendation is actually not more detailed than some others that we have already approved, which have, you know, four or five subclauses. So I think complexity--we have got to apply it consistently to recommendations and this one is not more complex.

I want to argue for the quorum a bit because, I mean, I can hear it now, imagine the--it is the headline in your local paper. Oh, IRB, you know, horrible study done. Yes, they had lay unaffiliated members but guess what? None of them were at the meeting and they never do show up at meetings and it is

window dressing. If we do not--I think I would stand pretty firmly on some quorum figure. I think voices--you know, the people who go to IRBs, the nonscientists, noninstitutional members who show up at these meetings, we have heard eloquently express that you cannot be alone. You need to have company and so that is why I would like to have that remain. The quorum piece remain.

DR. SHAPIRO: All right. Let's just see if we can decide where we are going. Let's not worry about language at the moment but the proposal that is in front of us is for--I am not going to repeat all the details but it is for a 25 percent requirement in membership for quorum purposes to be drawn from the groups that are identified here with overlap required or not required--allowed, overlap allowed. So without any further editorial comments, how many people would like to stick with that recommendation in some form?

(A show of hands.)

DR. SHAPIRO: Okay. I believe it. All right. That is going to go ahead. We will work out the language.

Okay. Let's go on. Excuse me, Bette.

MS. KRAMER: I know it is late in the day but I am just curious. What is--oh, shoot, where is it? What is "represents the perspective of potential

participants?"

DR. SHAPIRO: You mean who represents?

MS. KRAMER: Yes.

DR. SHAPIRO: I presume people from the--might be people from the community, for example, might be from whom the participants might be drawn. Community members, for example.

DR. MURRAY: It could also be somebody who works at the university.

DR. SHAPIRO: Right.

DR. MURRAY: Who happens to have a serious disease or a family member with a serious disease who understands from the subject's point of view.

MS. KRAMER: Okay.

DR. SHAPIRO: Okay. Let's go on to 5.10. Eric?

DR. MESLIN: There was no suggested revision to this that federal guidance should be issued related to the selection of members on IRBs, and the percent of IRB members with expertise and experience should be commensurate with the types of research reviewed by the IRB. There were no--

DR. SHAPIRO: Any comments on 5.10?

Yes, Diane?

DR. SCOTT-JONES: This is just very minor but I think expertise and experience needs some modifier

because it does not say very much without something else. With the relevant expertise and experience. It is just with expertise and experience and everyone would have some expertise and some experience.

DR. SHAPIRO: I agree with that. That is a good point. I think that is right. We will change the language there.

Any other comments on 5.10?

5.11, Eric?

DR. MESLIN: There is just a small grammar suggestion. "Federal guidance should be issued describing how ongoing research needs to be monitored by sponsors and by institutions carrying out research." I think this is a Holtzman “let staff do the grammar work” rather than you spending time but you should agree whether you like what it is saying anyway.

DR. SHAPIRO: This is 5.11. Any comments?

MR. HOLTZMAN: The staff other than you?

DR. MESLIN: Yes.

DR. SHAPIRO: Okay. 5.12, Eric?

DR. MESLIN: Here is principally a NOHRO issue so it is, "The oversight system should have clear requirements for continuing IRB research--"

DR. SHAPIRO: Review.

DR. MESLIN: "--continuing IRB review of ongoing research and continuing review should not be

required for research studies involving no more than minimal risk." The rest is principally the same as what was circulated except for NOHRO.

DR. SHAPIRO: This is 5.12.

DR. MESLIN: Right.

DR. SHAPIRO: Any comments on 5.12?

Okay. Oh, I am sorry, excuse me, Diane. I apologize.

DR. SCOTT-JONES: I have a little bit of a concern about the phrase "for research studies involving no more than minimal risk" because studies change over time and there should be some way--I am not sure what language could be put in there, but there needs to be some way to know whether from year to year the study has remained the same. A study that starts out with no more than minimal risk may not remain that way for the life of a study.

MR. HOLTZMAN: Read the last sentence, Diane.

DR. SCOTT-JONES: I am sorry.

DR. SHAPIRO: Does that satisfy your concern?

DR. SCOTT-JONES: Yes.

DR. SHAPIRO: Okay. Thank you.

Other comments or questions?

5.13, Eric?

DR. MESLIN: 27 down, six to go, just in case you are--five to go. Excuse me. Just in case you are-

-for those of you keeping score in the audience. The staff will do the arithmetic too.

(Laughter.)

DR. MESLIN: I am not going to tell you what is different in 5.13. You have to figure it out on your own. So there.

This actually is--it appears small and minor but I think there is a difference you need to make a decision on. In the original, "Guidance should be issued on three issues. Which types of changes to approved protocols must be reported to IRBs and which changes do not. Which types of protocol amendments must be reviewed by the full IRB and which may be reviewed by other procedures. And (3) which types of unanticipated problems must be reported and to whom?" And the suggestion which shortens that excludes the third of those three. "The federal policy should--" excuse me. Yes. "The federal policy should clarify when changes in research design require review and new approval by an IRB."

And I think, Alta, your question was you were not sure what was intended by the third clause, "types of unanticipated problems that must be reported and to whom." That was, I think, one of your concerns.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Well, the question, I think,

would be--is number three something different than what is addressed in the next recommendation. Right? If not, it should go. If there is something else intended, what was it?

DR. SHAPIRO: I had thought that it came up in the next recommendation. That is the way I interpreted it and, therefore, was not needed in 5.13, but I was not the author of that so I cannot say. Maybe Alta or someone else could say.

PROFESSOR CHARO: That is exactly what drove it for me.

Marjorie?

DR. SPEERS: All I would say is that 5.14 is dealing specifically with--

DR. SHAPIRO: Adverse events.

DR. SPEERS: --adverse events that generally occur in clinical research as we use that term. You can have in social science research unanticipated problems, things that can go wrong in the course of a study or occur that you do not expect that would not be called adverse events.

DR. SHAPIRO: In that case that should be in 5.14 the way I would think about it. In addition to adverse events you could have adverse or unanticipated if that is the issue.

DR. CASSELL: Well, how about it is suddenly

clear you need a much larger population than you originally described because interim data analysis shows that and you originally went to the IRB for 100 participants and now you need 500. You would normally have to go back for that and that is not an adverse--it is unanticipated.

DR. SHAPIRO: Protocol changes. A change in the protocol though.

DR. CASSELL: Yes.

DR. SHAPIRO: A significant change. It would have to go back.

I am sorry, Alta. I am sorry. I cannot see you over on my far left over there. I apologize.

PROFESSOR CHARO: You anticipate me. Anything that requires a change is handled in either version of the recommendation, the second--you know, the second revision just uses far fewer words. That is really the only change. So if there is something people have in mind that is not about a change in protocol or something that triggers a change in protocol but it is something separate from that, and is also not an adverse event, an example would be very helpful because it would focus my mind on what is being accomplished.

DR. SHAPIRO: Tom?

DR. MURRAY: Yes. In a social science study of a particular kind of drug using behavior, and in the

course of the--when the study--when the protocol is introduced it is not criminal behavior but New York State passes a law which criminalizes that particular behavior and so the risk to the subjects suddenly change dramatically. Rare, a rare sort of contingency but not impossible. So I just--it may be that Alta's revised language might--in 5.14 might work. I would not be keen on bootlegging it into 5.14 because 5.14 is so clearly about adverse events that I think it is probably not a good idea to load other stuff on to it.

DR. SHAPIRO: So the issue is whether 5.13, the shortened version of 5.13 really is broad enough to incorporate the kinds of example you gave, Tom. Eric?

DR. CASSELL: It certainly would be if you added the word "context." Research design or context.

DR. SHAPIRO: I think that is a good suggestion. Research design or context under 5.13. Yes. So just add it after the word "design." That is a very good suggestion. Okay. Anything else on 5.13? 5.14? Eric?

DR. MESLIN: 5.14 gives a list in four parts of the various roles and responsibilities of IRBs and DSMBs regarding adverse event reporting and the suggested revision is to make that less lexically ordered and to create text that just identifies those points in the following way: "The federal government

should create a uniform system for evaluating and reporting adverse events that is capable of integrating reports from multiple study sites. The reporting and data analysis responsibilities of investigators, sponsors, IRBs, DSMBs and federal agencies should be clear and efficient. The system should protect the confidentiality of proprietary information to the extent that this does not compromise protection of research participants."

DR. SHAPIRO: Comments on 5.14, either the original or the suggested change? Tom?

DR. MURRAY: Alta's shortened version is meritorious because it is short. It seems to capture most of what was in the longer version. A couple of questions. One is in the last piece about the confidentiality of proprietary information. This is very much a hot button issue in the world of gene transfer research right now and there is a big argument over whether--you know, whether adverse events are proprietary information or not. Exactly. So I do not know--I mean, I would not vote for a recommendation--I could not in good conscience vote for a recommendation that could be used to support the proposition that adverse events report are proprietary information and should not be made available to subjects or the public.

DR. SHAPIRO: Jim?

DR. CHILDRESS: Tom, there is a part at the end, to the extent that this does not compromise the protection of research participants, doesn't that take care of your concern?

DR. MURRAY: Jim, just reflecting on that, since I can imagine the advocates of treating adverse event reports of proprietary information, I would argue that, no, it does not compromise because the FDA will make a decision whether or not to, you know, stop a study. The FDA can stop a study and all studies of a family and not tell anybody why. They can just say, you know, we stopped it on the basis of evidence we have but it is proprietary.

And I will tell you that the participants in gene therapy research and people--members of the Council of Public Representatives at NIH more broadly would probably take umbridge at that interpretation.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: First, I think that Tom raises an important point that might be addressed both in the writing, whether we choose the original version or the shorter one because the difference is entirely stylistic. There is no substantive difference intended so it is a purely an aesthetic choice on the part of the commission. I think it can be addressed both in the recommendation and also in the text immediately

following it assuming we have those little paragraphs.

Let me start with the latter. I think if we have those little paragraphs, one of the things we need to put right in there is that the commission takes no position on this topic because we have never talked about it and, therefore, it would be hard to take a position on it. I will throw that in as a suggestion. And we do not want the recommendation to imply that a position has been taken. We are kind of neutral and other people will work it out.

The second, and it is a tiny little change and I do not know if it will convey the same tone to you that it kind of conveys to me, but at the end of mine and at the end of the original, the same spot on both, there is the phrase "the system should protect the confidentiality of proprietary information," which Tom was reading as raising a red flag. It kind of suggested that the adverse events are confidential proprietary information.

If we add in either one of them just the word of "any," in which it reads, "The system should protect the confidentiality of any proprietary information," it kind of suggests that some information may not be but other information might be and it helps to--to me, maybe not to you, opens up the tone of it--

DR. MURRAY: I have a more radical proposal that just occurred to me. Delete the sentence.

DR. SHAPIRO: I will have to see how everyone feels about it. It is an important issue and a small correction--we have discussed this. I do not know that we have discussed it at length or adequately. I will not make those claims but this was an issue that we have discussed before.

PROFESSOR CHARO: Whether the adverse events themselves as opposed to the information about the drug and such that are part of the adverse event reporting.

DR. SHAPIRO: Yes. I am not trying to defend the recommendation. I am just pointing out that this was discussed. Not that this is the right solution or the right recommendation. How do people feel? This is an important issue.

Carol?

DR. GREIDER: I agree with Tom that we should just delete the sentence. I think that takes care of a lot of the issues.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Well, on the substantive issue I think I do disagree with Tom about what should be required in adverse reporting--adverse event reporting but having said that I think there is a point maybe where we can find agreement and it may have to do with

converting the logic of the sentence such that one is saying that what comes first is the protection of research participants and any withholding of information that might be allowed to protect confidentiality ought not compromise that. The way we have done it is we are saying insure confidentiality of the adverse event reporting providing that it does not, and maybe if we turned it around that is something we would all agree on. Okay.

DR. MURRAY: I think that would be better than the current one, which I think was sensible to put in there. This is not a criticism of the drafting of the one that was in there. What would be lost in just deleting the sentence? I think it is equivalent to taking, you know, no particular position on the issue. I have no doubt that when this recommendation comes to be actually debated and put into policy that the voices on both sides will make sure that they are heard. So I am not worried that suddenly there will be, you know, a complete divulgence of all sensitive proprietary information. That will not--that is not going to happen in nobody's dream or nightmare, but I would just assume--I mean, I would either go with your rewritten sentence or I would delete it, and I am leaning towards deletion but I could be--

DR. SHAPIRO: Do you want to repeat it again,

Steve, because I did not--I do not think I got the whole thing in my head.

MR. HOLTZMAN: Yes, I am not sure I have the words, Harold, but it is really to say that if you read the way we have written it we say the reporting requirement should address the concerns of the private sector provided that you do not hurt the patients. I think what we want to say is the reporting should protect the patients.

DR. MURRAY: It would read something like this: Where the protection of research participants is paramount, when respecting the confidentiality of proprietary information does not endanger that protection the system should respect that confidentiality, or something like that.

DR. SHAPIRO: I understand the point.

Larry, you have a comment?

DR. MIIKE: I generally agree with Tom and if you look at the original, at the end of 3 is the word "appropriately." Now we can take that in two ways. One is why do we need to even say it because we are not going to report things inappropriately. But on the other hand if we are going to report it appropriately, that takes into consideration all of these multiple issues that one has to deal with, with a reporting system of which one is proprietary information. So

some spin on the word appropriately." But I agree with Tom. You know, we are suggesting a system. This just happens to be one issue that has risen to the point that it is included in the recommendation, but there are a lot of issues that are going to come up when you develop an appropriate reporting system and I would rather--it is already addressed in the text, so I do not see why we need to make that a point in our recommendation.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I do have the sense that there are different kinds of information that we are talking about here, and I think in my mind you can have a situation where some things need to be reported and other things really are not related to participant protection but nonetheless are proprietary. It might have to do with the process that is not yet patented that is being used to make something that in and of itself is the substance of interest.

DR. MURRAY: There are adverse events.

PROFESSOR CHARO: I understand. I understand. And part of it depends on how detailed your adverse event reports are and that depends upon exactly what you are testing. We have all looked at many of those sheets and know how variable they can be. I do in the end, I think, agree with what Tom was heading towards

and might suggest that we just try to say in a couple of sentences that all--you know, every--all events and information necessary to protect patient--protect participants must be reported--must be disclosed and reported. All right.

Any remaining proprietary information, right, may be held confidential provided that participant protections are in no way compromised, and maybe that will give it the emphasis you were looking for.

DR. MURRAY: That was Steve's proposal. I can live with that.

PROFESSOR CHARO: Okay.

DR. MURRAY: But I still have not heard the argument as to why we should not just delete it. Steve gave us an argument.

DR. SHAPIRO: Let me suggest a possibility here. Again I think it is--once we raise the issue of proprietary information it is very hard to deal with it except very explicitly and carefully. And so I have yet a third possibility. If you had in that sentence the reporting of data analysis--the second sentence of that 5.14 ends with "should be clear and efficient." I added a phrase, or one could add the phrase, "and take the protection of current and prospective participants as primary" because as I understand the issues here it is not simply the current participants which might be

protected by stopping the study. It is the future participants who might benefit from knowing some information regarding adverse events in some future study. I mean that is how I--I do not fully understand this issue so I am just posing this as a possibility.

That would not--that has the benefit or deficiency of not taking a stand in the proprietary information directly, all right. It does not raise that issue but it does say that it is always the participant protection, current and future, that is of primary concern.

DR. MURRAY: I like that. I mean, the context--and it is always a bad idea to make today's policy solve yesterday's tragedy, but we have got to bear in mind what led to the concern among the Council of Public Representatives, which led to the NIH appointed gene transfer research oversight task force and such, and one of the reasons was that there were serious adverse events in earlier stages of the Gelsinger trial and they did not tell Jesse. They did not incorporate that information. They did not tell the IRB apparently and they did not tell Jesse. So I think that is the sort of consciousness that animates the concern among research subjects and those representatives of research subjects to not give too much weight to the--and the eyebrows raised and the

actual palpable anger on the part of some individuals when they realized that, you know, companies were claiming adverse event reports as proprietary information, which is visible.

DR. SHAPIRO: I mean, I--Larry?

DR. MIIKE: Well, you know, maybe we are just getting too much into the detail because the basic point of this is a uniform system that--so maybe we should just sort of say that is what it is and we make observations. Instead of this being part of the system, these are really observations on the issues that have to be addressed when you put a uniform system together. Then we do not have to take sides.

DR. SHAPIRO: That would go along with Tom's suggestion of just dropping the last sentence and try to see what we can say in the text. How do people feel about that? How many people prefer to take that approach here?

(A show of hands.)

DR. SHAPIRO: Well, it is clearly a majority.

DR. SCOTT-JONES: I still like the phrase you added about the protection of research participants being paramount to be added to what will now be the last sentence if we drop the current last one. I thought that was just a nice addition.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I would support that also.

DR. SHAPIRO: I have it written down and will give it to you later. Okay.

Let's move on then to 5.15. Eric?

DR. MESLIN: These two recommendations are just being suggested. The two proposals are to clarify and make it a little simpler. I will just read you the substitute proposal for 5.15. "To reduce the burdens of duplicative IRB review of identical protocols for multisite research, federal policy should permit alternative models such as central or lead IRB review provided that participant protections are maintained." This just makes two sentences into one.

DR. SHAPIRO: Comments on 5.15?

DR. MURRAY: I think it is very good. I just wonder if--I am listening to some of the critics on the other side now and how they would respond to this and how they responded to our comments in the international report about, you know, trying to avoid duplicative IRB review. Should we add an adjective that vigorous participant protection? I do not know the right adjectives. I mean, we do not want minimal protections. We really want it to be--

DR. CASSELL: Full.

DR. MURRAY: Full would work for me. It does not change the meaning. It just punches up the desire

not to let anything slip.

DR. SHAPIRO: Other questions or comments on this?

DR. MIIKE: Just a comment. I do not think--no matter what language you put in there, as long as you provide an alternative to individual by individual institution review people are going to say it is not full review so it does not matter what language you put in here.

DR. SHAPIRO: Arturo?

DR. BRITO: Yes. I would just leave it as it is. I mean, the phrase at the end "provided participant protections are maintained," I think pretty much takes care of that. Just leave it.

DR. SHAPIRO: My own judgment is that the--I mean I am perfectly happy with the recommendation. I think the big barrier to actually getting it implemented will not be--will be institutional behavior which will get in the way of its being implemented. Liability, that will get in the way but nothing we can do about that. We cannot change that system.

Trish?

PROFESSOR BACKLAR: I think this might be a place to refer back to Jim's suggestion. Perhaps one would say “provided that participant's rights and welfare are protected and maintained” and that punches

it up in the way that we start off.

DR. SHAPIRO: I do not want to get into Jim's speech again. He thinks protections is all right. It is just harms. But anyhow we will--Diane?

DR. SCOTT-JONES: For recommendation 5.15 I prefer the language that begins with "permitting alternative models of review" because I think the first phrase is unnecessarily taking one side, "to reduce the burdens of duplicative IRB review of identical protocols." I think it would be more neutral for us to begin with something like “federal policies should permit alternative models such as central or lead IRB review” or returning to something more like the original language because I think that first phrase just marks us as taking one side when I would rather us appear more neutral in the language of the recommendation.

DR. SHAPIRO: I agree. Our recommendations should not be editorial. They should be as recommendations and I think you made a very good point. And I think we could use your suggestion. We could start with a multisite research as we did before so that you know where you are going, permitting--so we can marry the first part of the second--the first part of this one here and then go to the suggestion you made. I think that would be useful. Thank you. That

is a lot more appropriate.

Anything else on 5.15?

5.16?

DR. MESLIN: This is another reducing two sentences to one. It is noncontroversial changes regarding studying recompensation programs. You can read it as quickly as I can.

DR. SHAPIRO: You will recall from the text of the document that we do not know much about compensation and about what--the amount of research injuries that take place so it is hard to know how to design this system, so we are really recommending a study take place.

Steve, and then Jim?

MR. HOLTZMAN: So what does it mean to revisit? Can you visit and decide you do not want to do it and would be happy that that was the visit that they get paid or do we want them to do it? I think we want them to do it.

DR. SHAPIRO: That is easy. We want them to do it.

MR. HOLTZMAN: Right. So--and implement the 1982 recommendation, and I think that comes up in the prologue as well where we also talk about revisiting.

DR. SHAPIRO: Okay. That is a good point.

Alta?

PROFESSOR CHARO: Just because this is going to be like our last time through so I want to make sure we really mean what we mean, right. It starts by saying that the government should study research related injury in order to see if there is any need for a comprehensive program. Right. It could be that such a study reveals that, yes, you want compensation but you do not need a comprehensive program. The President's commission had suggested pilot studies to evaluate possible mechanisms for comprehensive programs but what if your study said you do not need a comprehensive program, would you really want them to have to go ahead and do the pilot study? Probably not. So you do want a two step process, don't you? Do we need a comprehensive program? If we do then let's do what they said in 1982, which is do some pilot programs.

DR. CASSELL: You would say you cannot determine whether you need a comprehensive without a pilot study.

PROFESSOR CHARO: I am not sure that is true. If you did a study of research injuries and you were to find that there really are very few, that of the injuries that do occur most, in fact, are handled quite adequately on an informal basis by the institutions where the injury took place or, if need be, are--you

know, wind up receiving substantial compensation fairly efficiently through some other mechanism. So you might determine you do not need a comprehensive program.

DR. CASSELL: Well, then you would have done the pilot study.

PROFESSOR CHARO: No, the pilot study--what the President's commission was calling for was stuff like do you want one of these administrative--arbitrator program--do you want an arbitrator program, mediator program? Do you want an insurance pool? Do you want a no fault tort system? I mean, they were really about mechanisms for comprehensive systems. They were not about whether or not you need a comprehensive system.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I think we could probably handle this by simply having two sentences and the first one at the end of after program, and if there is a need for a comprehensive--I am not--this wording is--I do not have it down for this, but if there is a need for such a program then they should conduct a pilot study to evaluate the mechanisms because I agree with Alta, the mechanism point is a different one from the need point.

DR. SPEERS: I think we might have the language here. We were working on it, which would be

to say that "the federal government should study research related injury to determine if there is a need for a comprehensive compensation program and, if needed, should implement the recommendation of the President's Commission to conduct a pilot study." I have not typed it all. "To evaluate possible program mechanisms."

DR. SHAPIRO: Larry?

DR. MIIKE: Actually I am not satisfied with--I am okay with just dealing with the issue of a compensation program but I am not satisfied with either of these because I think the step is that it is not that you take a look at the extent of injuries and decide whether a comprehensive program is needed because you are either--you are talking about two things. One is providing appropriate care for those who were injured with the nexus to the research and the other one is whether you should actually financially compensate them. So I think it is a two step process that says--and I think the first step is fairly easy. You can look at past research protocols and the adverse events and make a judgment on something like that.

But then the next step is if there is a problem here, it is not so much a comprehensive program or what is the appropriate response in terms of a continued treatment and financial compensation kind of

thing. So to me neither of these catches that.

PROFESSOR CHARO: Larry, you realize in the revision it does not talk only about number of research injuries. It actually tried to anticipate you a little bit by talking about studying the phenomenon of research injury.

DR. MIIKE: I know but it also says a comprehensive compensation program. I am saying that you do not know what the response will be until you have done the first part of the study, so you do not want to just sort of aim toward a comprehensive research program. It is what the appropriate care, treatment and financial compensation should be.

DR. SHAPIRO: Other comments? Okay. We will have to redraft this and pass it in front of you again. The main point being we need two steps here to determine what the nature of the problem is and then if there is a problem to make recommendations regarding ways to deal with it. Okay.

All right. Anything? That is the last of the recommendations in 5. Let's deal with the 6.1 and then we will take a break.

DISCUSSION OF DRAFT REPORT: CHAPTER 6

DR. MESLIN: So the difference between the original 6.1 and the proposed is just a shorter version and a more general description of what the federal

system should do. In the proposed version, "The federal system should have the resources needed to insure the protection of human participants in the promotion of ethically responsible research" as contrasted with the original recommendation that lists various ways and methods of funding and allowing for that support to occur in four points.

DR. SHAPIRO: Larry?

DR. MIIKE: I like the original. This one is too general. It just sort of says we should have money and it does not really--it just to me is just too general. I think we should keep some of the specific recommendations.

DR. SHAPIRO: Carol?

DR. GREIDER: I am usually for simplicity but I agree with Larry on this. I think that laying out the exact points solidifies it in a way that is needed.

DR. SHAPIRO: Other comments on 6.1 or do people generally agree that the original is more satisfactory? Steve?

MR. HOLTZMAN: I am inclined towards the original to get more specific but I am wondering here if we do not want to direct a recommendation to the Congress to start out with "money should be appropriated for the implementation of the system" and

then it is from that that you would get the points one, two and three, right, that creates the pot of money and that is how we will access the pot of money. DR. SHAPIRO: I think the only problem I have with that--I understand the point because only Congress can appropriate money here but we are asking for more--if I understand 6.1, it is not just Congress and my concept here all along is that everyone involved in here should be participating, right, sponsors of various kinds, institutions themselves, sponsors of course including the federal government, not restricted to the federal government. And so two, for example--let's see. Item two, yes, 6.1(2) says that directly and so I do not want to start with just Congress. That was my only--

MR. HOLTZMAN: You are right.

DR. SHAPIRO: Jim?

DR. CHILDRESS: Yes. I am going to have to slip out at the break and I just wonder if I can beg your indulgence and say a word about 3.1 if it would be all right before I go.

DR. SHAPIRO: Absolutely.

DR. CHILDRESS: And this is really verbal in nature but if people have 3.1 here is what I would propose: Again virtually every word is there but just reordered. "The federal oversight system should protect the rights and welfare of all human

participants in research by requiring independent review of risks and potential benefits to the research and informed consent from participants." And then the last sentence would remain the same. I think that captures it better.

DR. SHAPIRO: It does. Why don't you just make sure we have it so we can--free at last. Okay. I am going to propose that we take a break now to be able to reassess where we are. For those of you that are able to stay, we will try to get together in 15 minutes. Let's take a 15 minute break.

(Whereupon, a brief break was taken.)

DR. SHAPIRO: Colleagues, I did not want everyone necessarily to sit down again. We are just waiting for--you can stand up. We are waiting for a new version of the recommendations redrafting many of those that we had promised to do so to give us a chance to look over at least as many as we can today and see if they have met the suggestions adequately.

There are a number of recommendations, particularly 3.4, 3.5 and I think it is 5.9, which we have not rewritten yet so we will not be able to go over those but I would like to get your reaction to the ones we have rewritten, and then we will take your reactions into account and try to get an entirely new list out to you tomorrow morning. And then I would

like about a 24 hour turnaround time on any further suggestions you have on the recommendations only.

As I mentioned before, the prologue and executive summary will come after that and so on so this will be on the recommendations only.

So until they reappear from the business center, I think they are trying--we stand recessed.

(Whereupon, a break was taken.)

DR. SHAPIRO: Colleagues, you should have in front of you revised recommendations, and perhaps you could take just a few minutes to go over them quickly, and then I would like to go by them one by one to see if you feel they have met the sense of our discussions. That is certainly the intent but it is now a question of whether they have. If they have, we can consider these recommendations done. If they have not, we will go back and alter some.

So perhaps we could just take five or ten minutes just to look them over and then we will just go by them one by one.

(Whereupon, a break was taken.)

NEXT STEPS: FINALIZING THE OVERSIGHT REPORT

DR. SHAPIRO: Let's go over these and I will try--in order to expedite it and get a focus of attention on those which we still think need attention, let me just go through each one and see if there are--

there may be some recommendations here, which everyone feels are okay as they stand, and we will just put those aside and then focus on the ones where--so let me just ask as we go by this one by one if anyone has any concerns or recommendations besides minor typographical issues, which we do not have to deal with.

Recommendation 3.1? Yes, Larry?

DR. MIIKE: I think "all" should be on the research rather than--the emphasis of "all" should be--"in all research" rather than all human participants because that is what we really mean. All research. Anyway I think it needs to be fixed.

DR. SHAPIRO: Yes. Okay. Let me go at it this way so we will know--if there are--let me just find out if there are any recommendations in which there are no further comments right now. All right. So 3.1 there is a comment. Does somebody have a comment on 3.2? Typographical we will just--yes, things like that--please let us know what those are. So 3.2 is okay for the moment. 3.3? Tom?

DR. MURRAY: Minor?

DR. SHAPIRO: Yes.

DR. MURRAY: I would substitute the words "instead off--"in the second line "could be used for," I would say "should be created that could apply to--would apply to." So it would read "united

comprehensive--unified comprehensive federal policy embodied in regulations and guidance should be created that would apply to all types of research involving human participants." "Could be used for" sounds too optional.

DR. SHAPIRO: Okay. Any concerns of that? Okay. We will assume that is okay on 3.3 with that change that Tom has just proposed.

I will come back to 3.4 and 5 which are being--3.4 and 3.5, which are being written. What about 3.6? Any comments on 3.6?

Okay. 4--excuse me. I am sorry, Larry.

DR. MIIKE: Not specifically on that but 3.6 and 4.2 when you read them just like these seem to be sort of out of sync because they almost say the same thing in some of the sentences. No risk and minimal risk. I think it is just sort of hard to deal with that. But they are in separate chapters but they sound--

DR. SHAPIRO: All right. We will wait and see what 3.4 and 3.5 look like, which are being rewritten, and that may have an impact on that. 4.1? Tom?

DR. MURRAY: This is again just in the spirit of clarification. It is in the second sentence, which reads in general, "Each component of the study should be evaluated separately and its risks should be..." and

here is where I have a problem "...both reasonable and justified by the potential benefits to society or the participant." It is ambiguous about whether the reasonable is modified by the phrase "by the potential benefits." So I would just rewrite it to say, "These risks shall be both reasonable in themselves as well as justified by the..."

DR. SHAPIRO: Does anybody have any concern at all with that? It sounds like a useful change to me.

Okay. 4.2? Larry?

DR. MIIKE: The last sentence is kind of confusing so I would say change it to "if the risk of daily living poses a risk to an individual that is higher than would be experienced," et cetera. It is just that the way that it is written now does not to me capture what we mean.

DR. SHAPIRO: Let me suggest a--what I think is a similar change in that but also a change because I think there is a problem with that sentence. Would it meet our meaning if we said "if an individual participant is expected to experience..." and then go on with the sentence.

DR. CASSELL: Isn't that the same thing really as the definition before? Minimal risk should be defined as, and then in the next thing we say "more than minimal risk is more than that." Is that--I

thought we were trying to get to the idea that there are people for whom their daily ordinary risks are more than minimal risk because they are a particularly fragile population?

DR. SHAPIRO: That was--we are back to the same discussion we had before because there are two issues here as Steve pointed out. One is you have a study which only for certain participants is more than minimal risk because of their special characteristics they have and that is one thing. And then there is a second issue which has to do if they are in some particular--they experience greater risk as a normal part of their lives.

Steve?

MR. HOLTZMAN: It seems to me we accurately captured one of them and I provided language--distinct language for both of them on a piece of yellow paper over there.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: In one of my interim suggestions that eventually got rejected I had proposed that we might use the phrase "average people" or "average person" instead of general population and I went back from it when I was asked to but actually in some ways in the last sentence I think it may be clearer. If you were to say if an individual

participant would experience higher risk in the study than would be experienced by the average person, the research should not be considered to involve minimal risk, I think that actually that is clearer than when you use the phrase "general population" there and it would suggest that higher up where you talk about risks that are normally encountered in the daily lives, you would say normally encountered in the daily lives of average people. It is a different way of saying the same thing but I think it actually helps to clarify what we are trying to say.

DR. MIIKE: Can I comment on that? No, I do not think it captures it because correct me if I am wrong but I think what we are trying to say is that the risks of daily living to the average person is a risk that might be higher to another person. And that is what we are trying to capture.

DR. SHAPIRO: There are two--I am afraid there are two different aspects of this and we have to decide if we want to comment on both of them or either of them or none of them. But one is exactly what you said. It is people who are living in an environment or context where they experience much higher daily risks than others and how to deal with them and the other is someone who for some reason a particular protocol may be at higher risk for them than for the average

population, although they do not live in any general environment that is any different.

And I--well, let's--we will have to come back. We have not succeeded in 4.2 so we will have to come back to that.

4.3. It seems to me as it is currently written to not have what we said we would have in here. It really is an acknowledgement of the issue that Tom raised so we are going to have to build that in.

Tom, do you have a particular suggestion?

DR. MURRAY: No, unfortunately, but also I would add as the--under 4.3 to protect participants while promoting...just add the word.

DR. SHAPIRO: Okay. What about 4.4. because we have to come back and deal with 4.3? 4.4? Okay. 4.5? Alta, I am sorry. I cannot see through Eric and Marjorie.

PROFESSOR CHARO: Not a lay down in the road on this one but because I had been focused earlier on--

DR. SHAPIRO: That is a relief, yes.

PROFESSOR CHARO: --because I had been focused earlier on a wholesale edit, I never focused on the specific language of the existing rec, and I just wanted to say that I--with some minor stuff on the top, I find that the very first criterion is confusing to me because we have largely dropped out of the

recommendations the phrasing about components designed solely to answer a research question. It appears in the main text. I wondered if we might consider clarifying or simplifying that criterion by simply saying no component of the study involves greater than minimal risk without any prospect of personal benefit?

DR. SHAPIRO: Yes, that is fine. I think that works probably better as we have seen in the recommendation alone. I agree with that.

DR. MURRAY: And this is minor but 4.5--it should say "federal policy" and eliminate the "the." We have consistently just been referring to federal policy.

DR. SHAPIRO: Marjorie, did you get the wording that Alta suggested for sub (1)?

DR. SPEERS: Yes.

DR. SHAPIRO: Okay.

DR. SPEERS: Could I just raise a question here, and that would be this recommendation is really dealing with research that involves no interaction with individuals, and so I am wondering if one should just be rewritten to be the research study involves no greater than minimal risk.

PROFESSOR CHARO: You know, there are some studies on databases and on tissue samples that absolutely can offer personal benefit. You can be

doing that with an eye to bringing information back to people that they will be using in a diagnostic capacity, in a prophylactic capacity. We did make a distinction, I think, in the HBM report between research that offered some benefit and research that did not. We did not assume that all biological material research was by definition without any prospect of personal benefit and designed solely to answer research questions so I would not want to make that assumption here if we could avoid it.

DR. SHAPIRO: No, I think we can reword the--I think it does work better to reword one as you suggested. It just takes it from the other perspective and I think it reads a lot easier.

Anything else on 4.5?

DR. MURRAY: I am sorry about this but Alta just reminded me that it may be superficial, at least inconsistent with some of our recommendations in the Human Biological Materials Report if we just leave the phrase "using existing tissue samples" if it is using anonymous. If we are just giving examples there using anonymous tissue samples would work. Really existing can be fully identifiable and then you have got a human subject and you need the full review. So if we substitute--no?

MR. HOLTZMAN: No, this is what we are saying

is even if it is identifiable if the following conditions are met--right.

PROFESSOR CHARO: This is consistent with what we said in the HMB except for one thing, which--

MR. HOLTZMAN: We took out the practicability.

PROFESSOR CHARO: Well, there is that but we did something on presumptions narrowly and something else but I do not know if you want to go--we said that that business about these waivers for existing collections should operate only for collections that were existing as of the time we wrote our report. We then said now that we have written our report and everybody is on fair notice, these kinds of waivers should not be permitted because new collections now being made, which may be existing ten years from now when somebody is trying to apply this recommendation, were being made at a time when everybody was on fair warning and they should have gotten the proper prospective authorizations. And so to that extent this recommendation is slightly inconsistent with the HBM but, you know--

DR. MURRAY: We have improved with age. If we just--I really do not want this to be--you know, to delay us any further. What if we said “or certain research using existing tissue samples”? That would be fine. I mean, I just do not want it to sound like we

are making an unqualified claim. That is all. Let them then go to that report and interpret it and everything else. Is that all right? Inserting the word "certain?"

DR. SHAPIRO: Okay. 4.6? Steve?

MR. HOLTZMAN: This is somewhere between substance and grammar, more about grammar, but you take the second sentence, I think it will work better if you start with the second clause where it says "there is a means" so if you put it in provided there is a means of verifying informed consent was obtained, signed written consent forms need not, yada, yada.

DR. SHAPIRO: That is helpful. Very helpful and I think it does read a lot better.

Any other comments on 4.6? Okay. 4.7? 4.8? Okay. Let's go on to the recommendations in Chapter 5. 5.1? Okay. 5.2?

PROFESSOR CHARO: You kind of went by 5.1 faster than I did because I never got that far before.

DR. SHAPIRO: Sorry.

PROFESSOR CHARO: I know that we added something in here about focused on participant protection but somehow the sentence does not scan so can you just put an asterisk to double check it again? Should provide educational programs on research ethics focused on--I am not sure. I mean, I do not want to

rewrite it while I am at the mic but somehow--

DR. SHAPIRO: Okay. I understand.

PROFESSOR CHARO: It is just a tad awkward and it can probably just be edited.

DR. SHAPIRO: It was awkward before and it is a little awkward now and we will have to still work on it but that is not a substantive issue. We just have to get the right felicitous wording here.

Anything else on 5.1? 5.2? 5.3? Okay. 5.4? 5.5?

PROFESSOR CHARO: Sorry.

DR. SHAPIRO: Excuse me. 5.4?

PROFESSOR CHARO: Is it accrediting programs or accreditation programs?

DR. SHAPIRO: You are in now?

PROFESSOR CHARO: 5.4.

DR. SHAPIRO: 5.4.

PROFESSOR CHARO: Okay.

DR. SHAPIRO: I think so. It sounds--my usual rule is if it sounds right to me, I am wrong.

(Laughter.)

DR. SHAPIRO: 5.5? Why don't we--why don't we just take a few minutes to finish--let people read through all the recommendations. There is two pages worth. Let's take five or eight minutes and do that. In the mean time we will look back at some of the other

things.

(Whereupon, a break was taken.)

DR. SHAPIRO: Okay. I am sorry. Excuse me. Tom, 5.7?

DR. MURRAY: I can hear the shrieks of pain right now from the managers of academic medical centers. It says literally federal guidance should be issued defining and managing institutional IRB and investigator conflicts of interest. I know what we are trying to say but we have said something much stronger than we intended here. We are not going to--we are not asking that federal guidance should tell you how you have to manage all prospective conflicts of interest. So we need to--Alta has got an idea.

PROFESSOR CHARO: Let me try this out on you. "Federal guidance should be issued defining institutional IRB and investigator conflicts of interests and suggesting ways to insure the rights and welfare of research participants are protected". The last half is kind of mom and apple pie. Well, the defining is not so as to and suggesting--sorry, and suggesting ways to manage the conflicts. What is it that you would like the government to do if at all with regard to the management?

DR. SHAPIRO: I think it is--my own sense of this is that it is perfectly appropriate for the

government not to--I understand the concern about getting too detailed here and all kinds of conflicts cannot be anticipated but it is not unusual for them to define certain conflicts and to indicate what the resolution of those are, which is what management is. It might be disclosure. It might be something else. And we just want to stop short of sort of a--which I think Tom has in mind to suggest is a huge--a new book about this. So I do not know quite what the right words are but I think it is appropriate for them to indicate how these might be managed.

DR. MURRAY: With language--Alta, I think you were heading in the right direction. You had something about language proposing a federal policy framework. It might be guidelines. It might be, you know--we would be neutral on exactly how detailed that framework would be.

PROFESSOR CHARO: Federal policy should define conflicts of--sorry. Federal policy should define institutional IRB and investigator conflicts of interest and guidance should be issued suggesting ways to insure that the rights and welfare of research participants are protected. And guidelines should be issued for managing the conflicts.

DR. CASSELL: Conflicts of interest and guidelines to ensure--it is the ensure part that has

the verb in it that does what you want it to do.

DR. SHAPIRO: So perhaps it could be written as--when we begin we should say--if this is what people have in mind--federal policy should be issued to defining various conflicts of interest and guidelines--along with guidelines or something like it to insure the protection of et cetera. Something of that nature would be what we have in mind here.

DR. MURRAY: Am I making too much of a fuss about this or am I--

DR. SHAPIRO: No, I think this is a helpful change. It is a helpful change. No, I think it is a helpful change. Okay. We will change it accordingly.

Okay. 5.8? This is just, I think, perhaps something that got caught in the word processor here. The second sentence should--I think we had agreed that in particular investigator conflicts of interests should be disclosed. We did not say "all relevant." That is where we--that is what I remember.

PROFESSOR CHARO: I think I remember it the way Harold did that the compromise was to list all the various kinds of conflicts and then use the in particular to pull out the investigator conflict.

DR. SHAPIRO: If you recall this was a discussion about whether we should mention them all or just investigator and we came to this halfway place.

DR. MURRAY: Of course, I like the mistake better.

(Laughter.)

DR. SHAPIRO: Larry?

DR. MIIKE: Actually it is a different sense in the sense that in the original one when we said in particular, it was investigator conflicts but it was supposed to be disclosed to more than the participants. And then now we are talking about all relevant topics to the participant.

DR. SHAPIRO: That is a good point.

DR. MIIKE: So it is different. I actually like this one better.

DR. SHAPIRO: That is a good point. I had forgotten that. Let's do what we want here. Let's not worry about what we--what someone thought we said. Let's do what we want.

DR. MURRAY: I like the mistake.

DR. CASSELL: I like it too.

DR. SHAPIRO: Okay. How do you feel, Larry?

DR. MIIKE: I like this mistake better.

(Laughter.)

DR. SHAPIRO: Maybe we can make a few more mistakes like that. That is right. Our Freudian slips are better than our thoughtful--okay. We will go with it as it is then.

Okay. 5.9 we have to come back to.

DR. CASSELL: We could vote on those, the first or the second.

DR. SHAPIRO: We will come back to it provided we have time.

DR. MIIKE: Harold, could I just make a comment on these?

DR. SHAPIRO: Sure.

DR. MIIKE: I actually like the first one but I--just some wordsmithing. Should be at least 25 percent but a single member or the second one these persons may collectively represent only instead of at least. I think it changes the sense of--see what I am concerned about is that people will say, oh, default condition, 25 percent of all collectively, and that is not what we really mean.

DR. SHAPIRO: No.

DR. MIIKE: So I am making some suggestions about those specific words. It sort of turns the assumption the other way.

DR. SHAPIRO: Okay. We will come back to 5.9 in a moment if we have a moment. Let's go on to 5.10.

DR. MURRAY: Minor. One minor thing.

DR. SHAPIRO: Yes.

DR. MURRAY: Instead of the word "percent," I think if we said "distribution" or something similar,

"the distribution of IRB members with relevant expertise." Is that okay? Okay. But I like the recommendation.

DR. SHAPIRO: Okay. Is that all right with everyone? 5.11? Eric?

DR. CASSELL: Well, actually the way it is written now it does not make sense at the end but how about "federal guidance should be issued describing how institutions should monitor ongoing research," period?

PROFESSOR CHARO: Would you take a friendly amendment, "how institutions and sponsors should monitor"?

DR. CASSELL: Yes.

PROFESSOR CHARO: Thank you.

DR. SHAPIRO: Okay. Let me make sure I have that. Institutes and sponsors should monitor?

DR. MURRAY: Because the current language has institutions carrying out sponsors, which is--well, occasionally we like to see that happen but I do not think that is a recommendation we should make.

DR. SHAPIRO: Okay. That is fine. Okay. That is 5.11. Do you have that, Marjorie?

5.12?

DR. MURRAY: Minor. Just to tighten up the first sentence. The first sentence could read "federal policy should describe clearly the requirements for

continuing IRB review," et cetera. We have requirements. We have requirements describing requirements. So it is "Federal policy should describe clearly--"

DR. SHAPIRO: Requirements for continuing. Okay. Thank you. That is very helpful.

Other comments on 5.12? 5.13? 5.14? 5.15?

DR. CASSELL: Because of the rewriting we have alternative models. It is just as a matter we do not say what it is alternative to. We have to take that out and just take the words "alternative" out. Should permit models such as--otherwise you have to specify alternative to single institution review or whatever.

DR. SHAPIRO: What about if we--why don't we just say should permit central or lead IRB reviews? Is that okay? Does that satisfy?

DR. CASSELL: Yes.

DR. SHAPIRO: Okay.

DR. MURRAY: I think Trish made the proposal, which I liked, so that this would end--would end the participants' rights and welfare are rigorously protected. I mean, I thought that was--

DR. SHAPIRO: The participants.

DR. MURRAY: Right, the participants' rights and welfare are rigorously protected. Something to that effect. Maintain is a kind of weak thing here.

Larry rightly said that it does not matter what words we use, people are going to knock us for it but at least we should try to make our intentions clear that there should be no diminution in the protection of human subjects.

DR. SHAPIRO: That sounds fine. Other comments on 5.15? 5.16?

DR. MIIKE: Just one point.

DR. SHAPIRO: Yes.

DR. MIIKE: Are we wedded to a comprehensive compensation program or just leave it a more generic compensation program?

DR. SHAPIRO: I have no--I mean, I do not have any view on that. One view is as good as the other from my perspective. I mean just so long as there is a compensation program where we do not need another adjective.

DR. MIIKE: Yes, I think depending on the pilot--

DR. SHAPIRO: That is fine.

DR. MIIKE: --the pilot will tell you what you are going to need.

DR. SHAPIRO: What you are going to need. Okay. That is a good point. Okay.

Anything else on 5.16?

6.1?

Okay. Let's go back now since we have a little bit of time left, let's go back and try to see if we can deal with 3.4 and 3.5. I think Eric has a proposal for combining--am I correct, for combining 3.4 and 3.5?

DR. MESLIN: It is not printed out so I will read it slowly and mellifluously.

DR. SHAPIRO: Memorably would be better.

DR. MESLIN: "In general the oversight system should cover research involving human participants that includes any systematic collection or analysis of data with the intent to generate new knowledge or that involves exposing participants to manipulations, interventions, observations or other interactions." That was one sentence.

"It should also protect participants who are identifiable as a result of examination of biological materials, medical and other records or databases. Federal policy also should list those research activities that are not subject to federal oversight. It should also provide criteria for determining whether a particular study is a form of covered research and who determines whether a research activity is subject to federal oversight."

DR. SHAPIRO: That is a lot to assimilate at one time.

DR. MESLIN: Okay. I will be happy to do it again. Maybe just--I will break it down into the three sentences. Actually let's see if we can try and get another version even though I am reading it. Can you copy it?

"In general the oversight system should cover research involving human participants that includes any systematic collection or analysis of data with the intent to generate new knowledge or that involves exposing participants to manipulations, interventions, observations or other interactions. It should also protect participants who are identifiable as a result of examination of biological materials, medical and other records or databases. Federal policy also should list those research activities that are not subject to federal oversight. They should also provide criteria for determining whether a particular study is a form of covered research and who determines whether a research activity is subject to federal oversight."

We can get it printed out.

DR. SHAPIRO: Well, speaking for myself, at my advanced age, I cannot quite sign off on something that way because there are too many questions that occur to me that I can see easily on the page and I cannot see here. So I think we are going to have to--before we sign off on this one we are all going to have to see it

but there might be comments anyhow that might be helpful so those of you who have caught things--Larry, then Carol and Eric.

DR. MIIKE: I think the first sentence--I understand your intent but because you stuck an "or" in between those it turns out that manipulations, et cetera, et cetera, are not qualified by its being a research project.

DR. MURRAY: All of clinical medicine would be covered by that language as I understand it, which we probably do not want to do. Also in the last sentence we want--rather than who decides, we want a process by which is a better--I cannot remember the specific language but it is not a matter of who, it is a matter of the process.

DR. SHAPIRO: Carol?

DR. GREIDER: This is just a minor editorial. Rather than several "also, also, alsos" why not have a one, two, three like we have in the structure in one of the other recommendations, should, and have the one, two, three.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, it is the first sentence that I find clumsy so I would like to hear it just one more time while we wait to see it printed. The first sentence only.

DR. SHAPIRO: Eric, the first sentence only. The "only" underlined.

DR. MESLIN: "In general the oversight system should cover research involving human participants that includes any systematic collection or analysis of data with the intent to generate new knowledge or that involves exposing participants to manipulations, interventions, observations or other interactions."

DR. SHAPIRO: I am going to suggest--I am certainly not going to be satisfied with this until I see it and can look at it.

DR. CASSELL: Although I would like to say a sentence should not start "in general" like that.

DR. SHAPIRO: That is right.

DR. CASSELL: That should go to the second--generally and for the most part as Alistair MacIntyre would say, a sentence should not start out that way.

DR. SHAPIRO: Well, I do not think we are going to--we are going to have to communicate on this one until we get it right. I think we have a sense of what we want but we are going to have to really communicate to get it right. So let's see if there is--do we have anything on--now on recommendation--I will get to 5.9 in a minute.

We still--I am trying to just identify the ones on which we are going to have to have some further

communication in order to sign off on it. 3.4 and 5 is one, whether it turns out to be one or two recommendations. According to my list here, 4.2 and 4.3 are in that category because we did not quite get that language right. So it is 3.4/5, 4.2 and 4.3, and then the next one is, in fact, 5.9. I will come back to that in a second. And I think that completes it. So there are about five of these that need some further attention but let's see what you want to say about 5.9 or what anyone would like to say about 5.9, either the two categories that are in front of us, two alternatives that are in front of us or, in fact, you might have--Eric, do you have something else?

PROFESSOR CHARO: There is a third one in Marjorie computer that tries to take advantage of the things that worked in both of the existing versions and it goes as follows: "IRB membership should include members who represent the perspective of participants and members who are unaffiliated with the institution and members whose primary concerns are in nonscientific areas. All of these member categories should be represented at IRB meetings. For the purposes of both overall membership and quorum determinations, these persons may collectively represent..." No. What happened over here? "For the purpose of both overall membership and quorum determinations..." I guess these

persons -- "...these persons should represent at least 25 percent of the IRB." "Should collectively represent at least 25 percent of the IRB." Sorry.

DR. SHAPIRO: This is very close to the second one of these.

PROFESSOR CHARO: What it did is it got rid of the thing about the--see the--everybody went back and forth this morning and decided they wanted something in there about overlapping and then everybody went crazy and decided they wanted to take it out when they went around the second time. So what the rewrite does is try to say just explicitly that all of these member categories should be represented at IRB meetings. That takes care of Rhetaugh's concern that we lose any one of these perspectives.

And then it says that as a group the people who meet these criteria--and there is going to have to be at least one person representing each of these categories--collectively they have to represent at least 25 percent at the meetings and for the quorums.

DR. SHAPIRO: Tom?

DR. MURRAY: I think that gets us in a sort of reasonable compromise here. I would suggest as Diane suggested I think in an earlier that this is where it is probably useful to break out, you know, for the purposes of membership quorum; one, there should be at

least one representative of each of these categories; two, collectively they should constitute--and then your language of at least 25 percent. And I think just--because this is going to be misread, consistently misread and so we might as well be as crystal clear as possible but I think, Alta, I am agreeing with that compromise. I just want it to be presented as unmistakably as possible.

DR. SHAPIRO: Larry?

DR. MIIKE: Minor editorial thing is that this should be IRBs should include instead of IRB membership should include.

DR. SHAPIRO: Right.

DR. MIIKE: And I still would like you folks to consider my change at the end which is these persons "may" rather than "should" and "only" instead of "at least" because to me it then says you can have a minimal amount but that is not what we are conveying. You may not disagree with me that there is a content difference but I think to say "only" rather than "at least" and "may" rather than "should".

DR. MURRAY: Would you read the sentence, Larry?

DR. MIIKE: Well, the sentence would be "For the purposes of both overall membership and quorum determinations these persons may collectively represent

only 25 percent of the IRB."

DR. SHAPIRO: You want a limit there, is that--have I understood this correctly, Larry? You want a limit?

DR. MIIKE: No, it is the same thing but it is the same thing that is saying, you know, because we are saying they can represent all three categories, then of course there may be situations where there is all three--when you combine all three interests there is only going to be 25 percent of them but what--I am just trying to say I think there is a difference to say "at least" versus "only."

DR. MURRAY: When you were reading it I actually interpreted it the other way.

DR. MIIKE: Okay.

DR. MURRAY: I would say must represent not less than 25 percent of--does that make it clearer?

PROFESSOR CHARO: I think, Larry, what you really wanted to say was may represent only 25 percent but could be more.

DR. MIIKE: Yes.

PROFESSOR CHARO: And you were not really putting the phrase "but could be more."

DR. MIIKE: Yes, that is the only--

PROFESSOR CHARO: So there are two possibilities. One is we spell out the meaning of "at

least" with various phrases that are, you know, maybe signal it or we could also in the sentence that follows the recommendation, again as we have done in so many other places, we can say, "This is a floor and not a ceiling."

DR. SHAPIRO: Well, I think we are agreed substantively on what to do here so it is just a question of language. We all agree that it could easily be more. That would be quite satisfactory and even desirable many of us would feel. And so I think we are agreed on the structure here in what we want to do and we will try to make sure we get the language correct but I do not think there is any issue separating us on this one.

DR. MIIKE: One last thing, Harold, is that maybe we can combine that but replace the last sentence with the last sentence of the first choice with a "but" a single member. Think about that. The last sentence "for each category it should be at least 25 percent but the single member."

DR. SHAPIRO: Okay. We will pass out final resolution of this to make sure you are all comfortable with it. I am sorry, Diane.

DR. SCOTT-JONES: I am not sure we got what I thought Tom was saying just a minute ago that there must be at least one member from each of the three

categories. I do not think that is captured in either one of them.

PROFESSOR CHARO: The third version has it.

DR. SHAPIRO: It is in the version that was just--

PROFESSOR CHARO: The third version said that all three member categories must be represented at meetings, at each meeting.

DR. SCOTT-JONES: Okay.

PROFESSOR CHARO: I forget the--whatever it was. So it tried to spell that out more specifically.

DR. SCOTT-JONES: Okay.

DR. SHAPIRO: And I think we are all agreed on that issue. We want at least one person representing each of these. Okay.

From my tally of things, I think we may have taken this as far as we can go this afternoon. So we have essentially approved, I think, in substance really all the recommendations but we do have some language issues on 3.4/5 and on 4.2/4.3. And we will pass those out, I hope, as early as tomorrow morning so that we can then complete these.

And let me then review for you what our next steps are going to be. After getting the recommendations themselves done, we will go to looking at what is a very important part of this report now,

namely what we have called "Prologue/Executive Summary" together with recommendations out. My hope is that is a matter of weeks and then the report itself with all the various things that go with it, which are quite substantial, in fact, is going to be a question of months, not before it is on the web perhaps but before it is out.

So we have made some very good progress today and I want to thank those of you who were able to stick this out through the whole long day. We appreciate it very much and we will be in touch tomorrow morning so watch your e-mails, everybody because we are going to have a short turnaround time on this.

Okay. Thank you all very much. We are adjourned.

(Whereupon, at 5:03 p.m., the proceedings were adjourned.)

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