47th 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

HAROLD T. SHAPIRO, Ph.D.

DR. SHAPIRO: We have a number of things that I would like to discuss this morning. As I indicated yesterday, we have most of the morning for our meeting. We will adjourn no later than 11:30.

The two principle items I want to discuss is an issue that came up yesterday that I said we would bring it back today, actually Trish and others raised, and that is how are we going to define the population for which this report's recommendations are aimed.

One obvious possibility, there are many possibilities, one is are we talking here about competent adults or are we talking about a population we would define in a different way.

I am going to turn to Eric in a moment to get our discussion on that thing started because that will have a big impact on Chapter 3. We do not have to work out all of the impacts here today but knowing that will make a big difference to a number of our recommendations, and so that will be the first item on the agenda.

Secondly, I then want to turn to Chapter 4.

Chapter 4, if you recall, deals with the so-called local issues. That is the size -- not the size, the composition of the IRBs, accreditation, education, certification, et cetera, and some issues along those lines which we will need to discuss so that as we begin the redraft of the report we will know where the commission -- what the commission's views are on those particular subjects. So we will get back to that as a second item.

If there is time, of course, any other items that you would like to bring up can be discussed.

So let's go to the first of those items, namely define the population for which this report's recommendations are aimed and let me turn to Eric to begin that discussion.

REVIEW OF REMAINING ISSUES ON OVERSIGHT REPORT

DR. MESLIN: Well, just very briefly, we were chatting yesterday and a number of options came up that Harold had identified. I think it would be wise for you to consider stating clearly and early that the report's focus is on competent adults. The reason for making that suggestion, and it may be self-evident but just to follow up on the discussion from yesterday, is that the system of oversight was constructed principally with the adult in mind as the paradigm case

and exceptions and additional protections were built into the system for other populations or other issues.

Since this is a report that is intended to describe structural remedies and other broader strategies for improving the system as a whole, it does make some sense to focus on the best case scenario, the most prevalent scenario and that is involving the competent adult. Since you have already had a discussion about the decision to include or exclude embryos and fetuses as human subjects and to make language -- insert language about that and you have also -- effectively saying we are -- the report is not focusing on that and the reader should go elsewhere to get the commission's views.

You have also indicated that children which are -- is the subject of other considerable discussion, both in Congress and elsewhere, and probably warrants a report all on its own, that you are not going to be focusing on that exclusively.

So since you have set the precedent, it just seems to make a lot of sense to say it early in the report, i.e. at the beginning of the Chapter 1, this is what it is about, and where else -- wherever else you need to do that to make those cases. If you agree, it is not a long discussion but it -- I think it is

strategically important for you to say it now.

DR. SHAPIRO: Thank you.

Marjorie, did you want to add anything to that or what is your sense of this?

DR. SPEERS: No. Other than to say that I agree that I think it makes a lot of sense to focus on the competent adult and think about the system in terms of those who are able to give informed consent and then deal with the other situations after a proposed system has been put forward so I do not really have anything to add to what Eric said except that I recommend we make that change.

DR. SHAPIRO: Okay.

Larry?

DR. MIIKE: Then our discussion yesterday about 3.4, 3.10, 11, 12, really would be out with --

DR. SHAPIRO: It would change obviously.

DR. MIIKE: We just talk generically about vulnerable populations but not those specific ones.

DR. SHAPIRO: That is right.

Are there other views? I mean, does this seem -- Trish, I mean you are the one -- I promised you, I would bring this up.

PROFESSOR BACKLAR: I am happy but I also want to say what I just was discussing with Alta because

this then we can address here what we did not address in the Capacity Report, which the task force that -- the task group or whatever they were called that looked at our Capacity Report was concerned about, the scope but here we can look at people who have difficulties with decision making because of illness but not because that is their disorder.

DR. SHAPIRO: Alex?

PROFESSOR BACKLAR: And I think that --

DR. SHAPIRO: Excuse me. I am sorry.

PROFESSOR BACKLAR: Oh, that is all. I was just going to say I think that is very important to be able to do it that way.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: Yes. I want to underline the need to do that more than we do. It seems to me that what we talk about in terms of medical vulnerability is principally people who are drawn to research because they are sick and the research offers what they believe is the best alternative. And we get into the therapeutic misconception, are they getting treatment. That is one aspect. And I think that is one of those areas where what we try to say is isn't there a level of information you can provide and so forth.

But what Trish is talking about I think is something different. It is what Eric talked about when we were doing the Capacity Report. And in some ways challenge the whole notion that the mentally -- those whose mental impairments arose from mental illness were really that different than people who are seriously ill and it is not that in those cases the treatment alternative is the only one. That certainly is true for people for whom there is no good treatment now. But simply that very sick people have a hard time weighing choices. I mean, they are just -- illness impairs them physically and mentally, creates levels of uncertainty and anxiety, makes them different people than they were when they were not -- I mean all sorts of things.

But I do not know whether there is any fix for that. I mean, there is a fix for the other things. The kind of fix that usually frankly happens is informal surrogacy. That is to say other people become their proxies for ordinary treatment decisions. I mean, any of us who have had sick relatives know that during that process or any of us who have been sick know that during that process someone else, in effect, takes over a lot of the decisions and 99 percent of the time nobody is doing anything formal by way of advanced

directives or designation. It is just a process in which the authority shifts over from -- and as long as there is no objection and the doctors are comfortable with it and the person seems to be comfortable with it, and the family is willing to step into that role, it happens, and then it slides back to the person as they become more capable.

But when we are talking about research, supposedly that would not -- you know, that is not going to meet the IRB's requirements or things that we have said in the report so I think -- I mean, I think we really have something we have to confront here. So I appreciate Trish raising it but I think it is not -- the fix is not as easy and so 3.10 or 3.11 or whatever where there are discussions of the appointment of the proxies when you have more than minimal risk research and so forth may end up being unavoidable even though we are not talking about people who start off being in the category of those who are not competent adults.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Well, to extend this discussion then and, Harold and Eric and Marjorie, please stop me if I am going into something you want to discuss later.

As I agree with the idea that we want to take

out of this report people who have permanent or continuing incompetency and because I think just for the sake of argument for the moment it might make sense to accept institutionalized populations, whether it is civilly or -- in the civil side or medically side, nursing homes or prisons, whatever, as special populations in and of themselves because of the institutionalization creating either a legal or psychological impediment to exercising your free will. So they are competent but they may not be able to make decisions.

It opens up the possibility then of abandoning the notion of special populations for all the other vulnerabilities that we have identified and instead focusing on situations in which people who are not part of a vulnerable population are rendered vulnerable by virtue of the situation.

In the case of patients, I think that it will allow us to not say that sick patients are vulnerable because then we are going to get into sometimes they are, sometimes they are not, da, da, da. But what it can lead us to do is to say the following: In a situation in which research is being done on people who are currently experiencing an illness there is the possibility that the illness is going to interfere with

their ability at some point to make decisions and that, therefore, the protocol should include some -- something in there that explains how the PI is going to anticipate this problem, watch for the problem and make provision for the problem, and we might even be able to get away from having to go down that line of discussing the proxy consent here by doing a referral to -- and if it becomes a situation of formal incompetency. Right?

It also allows us to do things like say if you are dealing with patients that recruitment by their treatment -- treating physicians, regardless of the patient's physical status and mental status, poses a dilemma in terms of making sure that there is not any confusion about therapeutic misconception and no problem about differential behavior, and that the protocol -- we might kind of be somewhat controversial -- called for a practice in which the norm is the treating physicians no longer recruit their own patients but have somebody else do the recruitment.

Personally I think it would be a very good idea but I accept that it would be controversial. It also allows us to then detail other situations, whether it is people working impoverished populations in which if you are working with somebody who does not have a lot of money and you are planning to give money as an

enticement for this that protocol has to explain how this amount had been calculated and why it will not actually serve as some kind of extraordinary enticement, et cetera.

And in this way get away from the stigmatization problem because we are not focusing on the individuals, we are focusing on the situations. Correlate each one with a recommended course of action that forms almost like a modular approach. PIs that are going to encounter these situations in their protocols know that what they need to do then is take one of these remedies out of the tool box and plug it into the protocol. They will be able to anticipate the need to do this, this and this if they are planning to work in this kind of situation or that kind of situation.

And in that way it would not necessarily trigger the need for some kind of extended or in-depth review. It would trigger only the need at the initial screening to determine that they had identified the situations and identified the remedies that need to be in place.

PROFESSOR CAPRON: Can we operate with a presumption that the doctor should not be the researcher?

PROFESSOR CHARO: I could not hear you. I am sorry.

PROFESSOR CAPRON: Could we operate or suggest that IRBs operate with a presumption that the investigator should not be also the treating physician and you have to give a justification for it?

PROFESSOR CHARO: Yes. I mean, in fact --

PROFESSOR CAPRON: That goes to the therapeutic misconception in the end. It does not go to the temporary capacity argument and I do not think that the Capacity Report itself, the way we wrote it, is fully applicable to that situation because we really were dealing with mental conditions that have -- that are the things being treated and here it is not. I mean, you have heart disease. You are very sick in the hospital and your spouse is really making the decisions and now it is a research question.

PROFESSOR CHARO: May I --

DR. SHAPIRO: Yes. And then Larry.

PROFESSOR CHARO: I agree with you completely that these are distinct situations and it is with regard to that one something that said that anybody who is working with a patient population has to in their protocol state whether they anticipate these people are likely to be suffering from illnesses that will

interfere with their ability to make decisions. Some illnesses never will.

PROFESSOR CAPRON: Right.

PROFESSOR CHARO: Right. Others very well might and that where there is that possibility to explain how they expect to identify those moments and what they are planning to do as those things arise. We could make a list or we could ask that NOHRO make its list but it certainly would include things like, you know, offering repeated opportunities to consent and assent and dissent so that one is doing a kind of repeated check of continued desire to be present in this research study. Few of these illnesses cause the kind of enduring incompetency but if it does look like it is becoming an enduring kind of incompetency, how are they going to identify that moment because at that point they should be switching over to the different set of special rules.

So how are they going to identify the trigger moment to switch into different rules where you would need kind of formal interactions?

DR. SHAPIRO: Larry?

DR. MIIKE: I guess it depends on what we come up with. I can see us saying in the past the way it has been dealt with is that you sort of almost

arbitrarily because the situation brought it on that all of a sudden there would be rules for a special population as defined as children or prisoners, et cetera, and with the analytical approach that we are trying to take you do not get into that box. But then we should back up a bit and say that in a sense many of the research populations in a particular study are also vulnerable because of the therapy, et cetera.

So if we are going to talk about it in a generic way with a range of things then it does not get us into the box about talking about mental illness or something else again but then the question becomes in this report in the time that we have how much can we delve into remedies that we would be putting forth for it and so that to me is where our limitations are going to arise.

DR. SHAPIRO: I think the -- on that particular issue how deep can we get, I think what we can do in the report is -- if we go down this road -- is give some clear set of examples that we think are clear and appropriate but we cannot give an exhaustive list. We cannot think of them all and we will not think of them all but we can then give a sense of direction of how it ought to be handled and thought through, and IRBs, NOHRO and others over time will have

to work it out. I mean, I think that is as far as we can go in the time but I think choosing some good examples is really quite important just to give people a sense of how it works out.

David, and then Bill.

DR. COX: And that is really sort of this same issue in my mind with respect to physicians recruiting the right patients.

Alex, I would like to -- I mean, I wish we could actually make that -- have IRBs make that presumption but the -- I do not think that we can and the reason is because in many cases the -- as unfortunate as it is, having the physician be the researcher and recruiting the patients, that is the person that has the best expertise to do the study. So that what you want is an oversight on that but not sort of a presumption that that is not what is going to happen because, in fact, that is the majority of what happens today. So ultra sedatives would be controversial, it would be like super controversial, so on the other hand --

DR. SHAPIRO: You like it even better, right?

DR. COX: -- I think it is a real conflict. I mean, existing conflict that is big time but it is one of these grey areas where there is good and bad. So to

-- again have people recognize that this is a real dilemma but not work so much on what the remedy is.

DR. SHAPIRO: Okay. This is -- Bill, then Alex?

PROFESSOR OLDAKER: Yes. I would agree with David that if we just point out what the issue is that probably is sufficient to deal with this report. I view this report as an overall architecture to be dealt with in the future and hopefully enacted by Congress or an executive order and that is the important part of the report and trying to deal -- and I think putting off yesterday -- I might have argued differently on fetal tissue and stem cells but I think that it is more important that if we just point out there is an issue there will be others deciding these issues along the way. Whatever we write, no matter how much we would like, will not be the last word on this.

And so some of the issues if we just point out that they are going to be important issues to be dealt with by whoever is dealing with them and maybe giving a little direction, I think that that is sufficient for this report.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: Two points. Bill, I agree that on many of these things it will be important for

us to "point them out" but this is not an area in which there has been no pointing already. I mean, the -- it is -- there is some significance at any time when a presidential commission as a part of an official statement puts something out but our contribution here, I think, has to be at least some guidance. And I agree with Harold's characterization that it may end up being examples and ideas that are framed in ways that others would have to get to the regulatory language or whatever, and I think that we are backing away from some of the recommendations that look almost as though they were trying to be regulations themselves. But if we simply say there is a problem here, I think the answer would be new. I mean, just -- I mean, you know, yes, we knew that, now do you have some ideas what to do about it.

DR. COX: That is a good middle ground, Alex.

PROFESSOR CAPRON: But -- the second point I want to get to, David -- I mean, it seems to me that there are two prototype situations. One is where you have research going on principally in tertiary care centers, academic centers where patients get referred in and at the moment that they get referred in they have a physician who is referring them. And then they come to the other physician and typically, of course,

the idea is that, well that physician is the expert and is now their doctor taking care of them.

And what I wonder is in those circumstances is how often either the referring physician or some other physician at that facility can take on the role of being your physician and the researcher can be the person who is the researcher. To me that is the easier situation.

The harder situation is where all this stuff is being parceled out to the doctor's office and I go to see my physician and the physician says, "You know, there is a new intervention. There is a new treatment and I am involved in trying it out and I think you would be a great candidate for it." And this is my doctor. I mean, this has happened to me recently. This is my doctor. And, you know -- "And it is free by the way. It does not cost you anything."

DR. COX: My only point was it is complex. I wish -- it is more complex than it seems on the surface.

DR. SHAPIRO: Alta, and then Arturo.

PROFESSOR CHARO: Without trying to lay down a hard rule because I agree with the complexity and I share your instinct about the controversial nature of this, it seems that in this area as well as in some of

the others where we might identify situations that create vulnerabilities and some possible solutions that a tact we might take is as follows: That we identify the problems, that we identify some range of solutions that could be popped into protocols, an that we urge that we move towards the goal of eliminating these problem situations. These remedies are there to help people figure out how to do it.

And that over time it might be advisable to begin to think about having protocols that do not use any of these remedies to through full scale review so that people can check to see whether or not in this case it poses a genuinely unacceptable level of conflict of interest or the problem. Whereas, those that have adopted one of the remedies that we have identified or that are developed over the years would be eligible for a more rapid review because they have anticipated the situation and a solution.

Not that it would be put in place on day one but that in an evolving fashion what we would like to be aiming for is a series of problems, solutions. For those that do not choose a solution, a more rigorous review to see if they should have. For those that did choose a solution, a less rigorous review because they have taken advice and taken advantage of it. And in

this way create something that might be a little bit interactive over time and flexible but still gets us moving in the right direction and gets us a little further along than simply identifying the problem and dropping the ball there.

PROFESSOR CAPRON: You know, if I may, the problem with -- it seems to me with that solution is simply that research which does not have this problem, that is to say the researcher and physician are separated in their roles, could still be research that is really in need of IRB review.

PROFESSOR CHARO: This would not obviate the need for full review where there are other problems that arise. It is only that during the initial screening of looking for problems.

PROFESSOR CAPRON: What I think you could take that idea and modify it would be to say that as part of the review process there should be a capacity of subject/conflict of role review and that you can get out of if you have anticipated it and responded on the surface of your protocol in a way that says I know that is a problem, here is why it will not be a problem here: The patients I am dealing with typically do not have illnesses that upset them so much or if they do here is how I am going to deal with it. Here is the

conflict of role thing. I know that is a problem and I am dealing with it in the following way. You get through those steps without -- on an administrative review because you have done it. Otherwise the IRB has to --

PROFESSOR CHARO: That is exactly -- I think actually that is exactly what I had in mind.

PROFESSOR CAPRON: I am sorry. I knew that.

PROFESSOR CHARO: Okay.

(Laughter.)

DR. SHAPIRO: Arturo?

DR. BRITO: This helps ease a little bit, but I share with David the concern about being very careful to exclude physicians as researchers or being so strict with the guidelines or the recommendations for guidelines that would exclude physicians from researchers because then what is going to happen is you are going to go the other way and exclude an awful lot of people, an awful lot of communities, whose only option sometimes is to have their physician be the researcher also. And I can cite examples in the University of Miami, for example, the School of Medicine, the pediatric endocrinologists there are the only ones in Dade County that see uninsured children. For the most part they see almost all the Medicaid

children and they also are the ones that do a lot of the research there. So that is an example -- you would be excluding an awful lot of people of an opportunity to participate in research.

PROFESSOR CHARO: Arturo, just to be clear, the idea here is not to exclude physicians as investigators but as recruiters. And not even to exclude them as recruiters but I think what we are leaning towards here now is trying over time to get towards a system in which if they are going to be recruiters then the IRB might want to take a closer look at the protocol to make sure it is not one of those situations where it really should not be done. Whereas if they choose not to be a recruiter then that potential problem has been resolved and we can move on to see if there are any others that actually require full IRB review but if not, they are okay.

DR. BRITO: And I agree with the concept of doing that but I would just be very cautious of how we do it and what we recommend because if you make it overwhelmingly, you know, difficult then it is just going to create another bureaucratic problem I think.

DR. SHAPIRO: Other comments on these particular issues? I think it has been very helpful and I think we have identified here a framework --

grounds to put some words down here to see what they look like and how they coherently fit together before we make any final decision.

Rhetaugh?

DR. DUMAS: I like the direction that we are moving in and I would like to suggest that when we talk about -- in our recommendations that we focus on the goal or the condition that we think we should be aimed at and recognize that there might be several alternatives for getting there. And I think with the business of the conflict of relationships, one -- the goal is to have the client or patient free to make their own decisions without fear of the consequences because of a relationship or particular situation. That is the goal.

One alternative is -- well, the first thing is to have a review that takes this into consideration and an alternative is to -- while one alternative may be to suggest that physicians do not recruit their own patients, that is only one alternative and I think it should be -- we should present our recommendations within that format generally.

DR. SHAPIRO: I think that is an issue that came up in different forms yesterday and at different times yesterday cautioning us as we put the report

together not to think that this is the only possible way to achieve the objectives.

DR. DUMAS: Yes.

DR. SHAPIRO: There may be other ways, some other people might have better ideas and so on, which is clearly possible and, indeed, highly likely in at least some of the cases. And so we will throughout the report try to accomplish that objective, including here.

Okay. Anything else on this issue? This will, I think, you know, restructure Chapter 3 somewhat in important ways and we will have to get to that right away and we will do so and you will hear from us. We will come back to that issue in a while.

Okay. Let's step away from this particular set of issues right now and focus on -- I want to focus a little bit on Chapter 4, the material in Chapter 4.

Now there is a whole series of issues here. There is conflict of interest issues. There is IRB issues, compensation issues that are here and, of course, you have the accreditation, education, et cetera, issues.

Perhaps it would be useful -- and I want to get to each of those but perhaps just to be organized

about it, we can go through this chapter as we have some of the others and just ask what questions people have, what issues you are particularly interested in, and we spend a little time on that and then I would like to go through the recommendations one by one so that we at least make sure that we -- there are not issues that we failed to touch base on.

But let me see if there are some overall issues that people would like to address or some particular issue that you are particularly concerned about in Chapter 4.

Alta?

PROFESSOR CHARO: I am kind of a 4.4 gal but I am happy to wait if you want to do them in order.

DR. SHAPIRO: Which is 4.4?

PROFESSOR CHARO: It is the accreditation.

DR. SHAPIRO: Beg your pardon.

PROFESSOR CHARO: It is the accreditation recommendation.

DR. SHAPIRO: Accreditation. Well, we can take -- we will get back to doing them in order just to make sure we do not skip any but if you want to go there why don't we go there now because the accreditation issue is an important issue.

PROFESSOR CHARO: Well, let me start by asking

for some information, if I may, from Marjorie about the public reactions. I had advocated what was in a distinct minority that accreditation for -- well, actually maybe it is not 4.4. I was thinking about accreditation for investigators as opposed to IRBs.

DR. SPEERS: That is 4.3.

PROFESSOR CHARO: Oh, that is 4.3. Thank you. Certification. Certification, sorry.

I had been advocating that certification be needed only if you are planning to engage in research that is more than minimal risk in order to try and reduce the overall complexity of the system, the number of people who are covered to do occasional survey research, for example, which poses no more than minimal risk and would implicate legions of graduate students who are doing a single survey as part of their Ph.D. dissertation, et cetera.

I was in the distinct minority and was out voted but I would be interested in hearing what the public reaction had been to certification requirements and whether that might affect the discussion so I am not going to go to the mat on this one but I did want to re-raise it.

DR. SPEERS: On this particular recommendation we got a total of 38 responses, that 18 were positive

supporting the recommendation as it was and there were 20 that -- I will call them negative responses or not in favor of it. The major issues among the ones who did not respond favorably to it were -- one was the issue of cost and just the burden on the institutions to certify their investigators.

We got some set of comments that related to IRB and IRB certification actually because what we say is that IRB members and staff should be certified and that was interpreted that IRB members should be certified as IRB staff would be certified. Not that it could be different. And what has occurred among IRBs recently is there is now a national certification examination that IRB staff can take and so there was some misunderstanding that that meant IRB members should go through that same certification.

With respect to institutions and investigator certification, the comments that we got there were in one sense if you certify -- one lot -- I am sorry. One train of thinking was if you certify all investigators to reach some kind of common denominator it will reduce the certification to being meaningless.

Another was -- another line of thinking of the certification was to have it be appropriate for the type of research that they do, that certification would

not only be about research ethics but it also has to be related to the discipline. It has to be intertwined with the types of science or the methodology that investigators are using.

And the other thinking was it should be voluntary, you know, not mandatory.

I mean, those were the -- I think summarizes the kinds of thoughts that we were getting.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: I found that as a useful explanation as to why the language was changed. I wonder if what we mean then is to say all investigators and IRB members and staff should be certified in a manner appropriate to their role of conducting and reviewing research involving human participants, because just the phrase standing there at the beginning "as appropriate" could say, "Well, we think it is not appropriate at all to have --" when you are trying to say it is addressed to their role.

DR. SHAPIRO: I think that is absolutely right.

DR. SPEERS: Right.

DR. SHAPIRO: But in terms of the issue you raised, Alta, that is -- if I understood the issues, do we really mean everybody, my view is that we really

mean everybody and I think it is -- and even though that means students in some cases, graduate students and others who are conducting surveys, as I -- my own -- as I thought carefully about what it would take to be certified, it does not seem like an overwhelming issue. I think it is going to take time to investigate just what works, what does not work, what kind of materials are going to be required, how do you tailor make them for people doing surveys in anthropology versus those doing -- I do not -- biomedical research. It is going to take some time.

But it is not overwhelming compared to what -- just take the students issue. Students have to prepare themselves in hundreds of other ways to conduct research, which they are doing all the time. And so I really -- my own view was it meant everybody because as I think about the system, people out there doing the work in contact with actual participants or subjects, they have got to know what is at stake here. That is the way I think of it.

So just as one person, I meant everybody when I read this but there are other views.

Larry and David.

DR. MIIKE: I think we should make that a little bit more explicit in the text. I think in the

text it says that, you know, it is a flexible system, institutions can set up their own, et cetera. But there is this issue about every student and every graduate student is going to come up. So I think it is worth putting a sentence or two about what we mean in that particular situation.

DR. SHAPIRO: Okay. David?

DR. COX: I share your views about this, about having everybody do it. I also share the views of the negative comments that if you have an accreditation that basically has -- the accreditation process will sort of bring down the means and -- you know, if you have everybody do it, not everybody -- you know, the people that do it the best are not going to be the standard.

My point on this, though, is that the accreditation process is not how you get people to think ethically. The accreditation process is how, you know, they show that they think ethically. And it is the institutionalization of having all the students and everybody realize that this is important.

My own view is that this is starting to happen. It is starting to happen perhaps for the wrong reasons but I do not care what the reasons are if people are starting to take these points seriously and

that -- so having the accreditation is not going to, you know, make people ethical, but what it will do is help ensure, just as some of the comments over the past few years have, is the educational process starts to work. So I am -- I think it is a -- again another one of these complicated problems, but I see the comment about that -- you know, you are not going to fix this with accreditation, I agree, but accreditation is one of the processes that helps fix it.

DR. SHAPIRO: I think the -- this is another area where we are obviously going to have to learn exactly what works over time. It is not going to be solved right away and will make -- even if we are to implement this in some way, mistakes will be made and so it is another area where we have to understand this is what our goal is and here is a way to implement it, and there might be some better ideas out there over time.

DR. COX: One footnote though, Harold, is that I do not see it as onerous. You made that point and I agree. I do not see that this has to be a big deal in order to get people accredited.

DR. SHAPIRO: Other comments or questions on this particular issue?

Okay. Other issues in Chapter 4?

Alex?

PROFESSOR CAPRON: Well, are we now on 4.4, which is what Alta --

DR. SHAPIRO: Yes, that is correct.

PROFESSOR CAPRON: The issue to me in our wording here is being clear about two points as to what we envision. We are saying NOHRO, or whatever, should encourage organizations to develop accreditation programs designed to ensure that institutions conducting or reviewing human participant research have in place appropriate mechanisms to carry out ethically sound research.

Now when we say encourage organizations to develop these programs, the encouragement can be of several types, and I thought in the text there was some suggestion that what we were really aiming for is that NOHRO should recognize the validity of certain accreditation programs as a means of achieving what would be, in effect, a federally imposed requirement, so that if you are accredited by a body that NOHRO says has developed an appropriate accreditation program you would be appropriately accredited. If you joined, you know, some group that is putting together a sham accreditation program, NOHRO will not recognize it.

So it is more than just encourage

organizations to develop. It is really recognize the validity of it, it seems to me.

The second point then is that we state that these accreditation bodies should use uniform sets of standards and develop procedures for monitoring. And what is not clear to me here is whether we envision that there would be one uniform set of standards and the difference would be different accreditation bodies would then implement them, or if what we mean is simply an accreditation body would use uniform standards in all of its own accreditation activities but another accreditation body might have other standards. Is there some sort of minimal set of standards that we would expect that an accreditation body would use in order to be recognized?

So the phrase "uniform" here is unclear to me. Uniform within the organization? Uniform between organizations that are running accreditation entities? Those two --

DR. SHAPIRO: I have the -- my own view is -- on the second one I had the same view. I have been stumbling over this “uniform” and what it meant so I do not have a good answer but I think it has to be clarified. Maybe Marjorie or Eric has some idea on that.

On the first one my interpretation would be -- I think the words are not quite right -- is that it is not just that we encourage you, you do it or you do not do it, that is your business, but that NOHRO's job is to recognize accrediting institutions as genuine, and if you get accredited by one of those then you are all set.

PROFESSOR CAPRON: Right.

DR. SHAPIRO: Otherwise there seems to be no reason to do it.

PROFESSOR CAPRON: Right.

DR. SHAPIRO: But I do agree that the wording is not correct. And on the “uniform,” I have been stumbling over that, as Marjorie knows, for a little while as to what it means but, Marjorie, do you want to say -- and then Larry after that.

DR. SPEERS: Okay. We mean the former, which is consistency across the accrediting bodies. They would be using -- maybe a better word is a common set of standards.

PROFESSOR CAPRON: You do mean that?

DR. SPEERS: That is what we --

PROFESSOR CAPRON: So --

DR. SPEERS: -- that is what we meant.

PROFESSOR CAPRON: -- if -- we know groups

like NCQA is being hired by the VA, I guess, is that right?

DR. SPEERS: Yes.

PROFESSOR CAPRON: And PRIM&R, or however you pronounce that, has developed, or is in the process of developing and has submitted to the IOM standards. Now those are not the same standards. They are not using the same, and that is very similar to what happens in the hospital field where the Osteopathic Hospital Association has a program. It is a small program that is the Joint Commission in the hospital area. In the nursing home area there are several groups. In laboratories, they all -- because in that area there are federal conditions of participation that are established -- they are all found, if they are going to be -- if they are going to get deemed status, they are all found to fulfill federal conditions of participation, but they do not have the same standards.

Now occasionally, particularly with the Joint Commission, its standards can be out there and another organization can accredit against those standards and use their own personnel to do it. I mean that is -- because the -- you know, the manuals are all published and so you can do that. The decision rules are not published, but the manuals, the standards are

published.

So there is not uniformity in the sense of commonality, but they all meet some minimum standard, and the accreditation process is where you would expect to come in as opposed to developing somewhat different standards for trying to achieve the same goal in terms of quality and consistency.

DR. SHAPIRO: Okay. Quite a few people want to speak. Larry, then Rhetaugh and Steve.

DR. MIIKE: I agree with Alex in the sense that -- even if we meant what Marjorie had intended, then NOHRO has to get involved in setting those standards and it is -- and the way it is written now it actually says -- the first part on uniformity is really what Alex is saying. And the second part, NOHRO overseeing the accreditation process, then they get a little bit more involved. So I would have to go with Alex on that because that -- we do not really -- I should not use the words "we do not really care" but essentially what we are saying is that as long as the results are okay, the internal process is good enough.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I think that we need to spend time to get clear on the results that we are seeking, because I see the accrediting body, or the process, as

a mechanism for getting there, and I am not really very clear on where we want to go. So I think up front at the very beginning, our recommendation needs to be tweaked so that it will focus on the results that we are trying to achieve or the outcome of the goal of the accreditation. That is -- it is not just a set of standards. It has to be specific -- more specific than just a set of standards. It has to be the kind of outcome that we are wanting to bring about and I do not have it clear in my head but I think we need to work on that.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: This question is for Alex.

DR. SHAPIRO: A question for who?

MR. HOLTZMAN: For Alex.

DR. SHAPIRO: Okay.

MR. HOLTZMAN: Because again the word "uniform" has lots of different meanings in this context and that makes it difficult. Clearly we do not want the accreditation standard for an institution which conducts anthropological research to be the same necessarily as one that conducts drug research. But within any given subtype, are we looking for uniformity?

PROFESSOR CAPRON: Well, I -- should an

accrediting body be uniform in its approach to organizations that do the same thing? I would say yes. I mean, otherwise you have arbitrary decisions.

MR. HOLTZMAN: All right. So I think there is a sense of uniformity or commonality in which we do want to have --

PROFESSOR CAPRON: Right.

MR. HOLTZMAN: Right.

PROFESSOR CAPRON: I mean, consistent -- I mean, I would describe that more in terms of consistent application of standards and -- always come back to what Rhetaugh just said --

MR. HOLTZMAN: Right.

PROFESSOR CAPRON: -- which is it is towards the goal of a certain level of quality of their review process and monitoring, internal monitoring and so forth.

I do not know how many -- I mean, clearly there are institutions that do not do any biomedical research and only do, say, sociological and anthropological, and there are some on the other side. A lot of -- I suspect a lot of the IRBs we are talking about are at places where they review a fair variety of things and it is likely -- it seems to me unlikely that the American Anthropological Association is going to

come up with IRB accreditation standards. It is possible but I suspect that they will not see that is a --

MR. HOLTZMAN: High priority.

PROFESSOR CAPRON: -- high priority, right.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: There is no possible way that we can duplicate here the work that is going on by the bodies that are attempting to put together an accreditation program. It is very complex. Witness the discussion just now about whether you would accredit for one field or another or for all fields at once because, indeed, most of these fields are disappearing in the interdisciplinarity of the modern university so it may not be possible to have these subtypes in any case.

I agree, however, that there needs to be a core set of competencies that are being measured to the specific goal to answer Rhetaugh's question of the following: Is the IRB aware of the range of its discretion as opposed to the areas of which it has no discretion? That is, does it understand what it is absolutely not allowed to permit and does it understand where there are differing opinions? In my ideal world where there are differing opinions, they would be

tested on having some minimal awareness of the arguments on one side or the other so they know why they are choosing one thing or another even though we do not tell them what they are choosing. All right. That is a tougher thing to test but that would be in my ideal world one of the core competencies that they would have.

And then there is going to be some degree of review of their procedural competency, that is their ability to know how to go about funnelling paper and assuring appropriate reviews, and that will be a challenge because that is exactly where OPRR ran into problems when it was going out into the field. The concern had been that their emphasis was too much on the process and too little on the outcome of the discussions.

But I would argue in favor of this very limited role for two reasons. One is that we have got a tremendous amount of overlap between 4.3 and 4.4 in our recommendations. That is we are certifying people and then we are accrediting the bodies that consist of nothing but certified people. So we are getting them from both ends.

And so we do not have to be -- we do not have to be -- can I use "nutzoid" to go along with "wazoo"

from yesterday? We do not have to be nutzoid on the accreditation if we are only dealing with people who are already certified and getting a whole variety of other kinds of educational modules and testing.

DR. SHAPIRO: Yes, but the same is --

PROFESSOR CAPRON: It is true of hospitals.

DR. SHAPIRO: -- it is true in almost all accrediting processes.

PROFESSOR CAPRON: Right.

PROFESSOR CHARO: But, you know, we do not --

DR. SHAPIRO: People in the system have to work also.

PROFESSOR CHARO: We do not certify every person who works in a hospital, but we are talking about certifying every staff person. But putting that -- the second thing is I actually can foresee an interesting process in which different accrediting bodies actually have very different philosophies about human subjects research.

By the way, I think I am going to have to beg for us to go back to subjects on the whole because I hate this word "participants." I cannot use it.

You know, we saw announcements from the Christian Dental and Medical Association about things having to do with stem cells and such, and I can easily

imagine that we might find some body wanting to accredit for a very particular philosophy of human subjects research the way we have hospitals that have -- you have Christian hospitals, you have Christian Science, you know, healing facilities, and you can imagine that this day will come and it will actually in some ways be helpful to investigators because the accreditation, kind of, announces to the world some parameters in the way they are going to approach potential protocols.

We need to leave room for that and a core competency area without absolute uniformity across all would permit that kind of development.

DR. SHAPIRO: Okay. Other comments on this particular issue? I think we share a common sense that we really want to get -- NOHRO wants to recognize bodies that have some mechanism of assuring the consistent application of some standards that achieve certain goals, and we need to get the language that does that.

DR. DUMAS: Do we want NOHRO to define those standards?

PROFESSOR CAPRON: Indirectly they are because if they are going to recognize an accreditation program what they end up saying is the standards its applying,

we have reason to believe will achieve the goal as you talked about it, and that another one comes along with its standards and they say that does it, too, or it does not. So, in effect, indirectly they are defining what are acceptable standards.

DR. DUMAS: For measuring, like, core competencies. I like that idea of having a statement that -- I do not know whether NOHRO would define and evaluation core competencies or expect the institutions to define and evaluate core competencies for review and whatever.

PROFESSOR CAPRON: To me the hardest thing in this field now is that the cutting edge of other accreditation programs is really performance measurement rather than standards. Standards looks at your capacity to do something. Performance says how you are doing it.

DR. DUMAS: How you are doing it, yes.

PROFESSOR CAPRON: And I think the view now is you need to do both. When you are doing hospitals, it is possible to say -- we expect to be able to say what is your rate of re-operation on people, what is your rate of infections, and if you are having trouble there, it indicates that although you supposedly have the mechanism, it is not working and you have to figure

out why it is not working.

The big ideology in this field of human subjects research review is you can have local variations in the way things are done and that is part of the reason that we have local review, and I think we disguise that much too much on the basis that the IRB will reflect the culture of the institution and the locality, so that in Boston they have a certain set of values and in Los Angeles they have something else, and there are two IRBs looking at the same protocol and come to different decisions. That is okay because they reflect their locality.

DR. DUMAS: But in each --

PROFESSOR CAPRON: I suspect that what it is going to be is just like what Jack Wenberg, et al., have found about variations in doctors practices. They are not explained on a rationale basis. They are explained because of -- sort of, indefensible in the sense of principled differences between people and institutions. Therefore, when you are measuring the outcome, it cannot simply be that this protocol -- I mean, you cannot sort of run model protocols through. You can send a lab a battery of samples and you expect the two labs to come up with some high degree of similarity in their results. You cannot do that with

IRBs.

DR. DUMAS: But you might have --

PROFESSOR CAPRON: Under our present ideology at least you cannot do it.

DR. SHAPIRO: Rhetaugh and then Steve.

DR. DUMAS: You might have local differences in how they are achieved, but each one, I believe, must rationalize a relationship between what they are doing and the outcome that they are expected to achieve, and it seems to me that that is where the accrediting body comes in, that the accrediting process shows that whatever the customer, the procedure, what it is, as locally defined is in conformance with a set of broader expectations and standards.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Yes. I am just going to endorse what Rhetaugh just said, Alex. In any field that involves human judgment does not -- is going to have a range of what can be considered right. It does not mean that you cannot have a review process which can articulate a set of standards to be able to judge whether or not that conclusion and that process was done in a way that meets that standard.

PROFESSOR CAPRON: May I just respond? I do not disagree with that. I am just saying that you end

up having to use much more of a standards based approach than an outcome. That is all I am saying. Because the outcomes themselves we -- we go into the process saying we expect no uniformity of outcomes when IRBs are doing their job in a conscientious fashion, and we rationalize that by saying that they are reflecting values and cultural traditions that relate to their local community or to their own institution, and I think the latter is going -- is an assumption rather than anything that we know, as opposed to just variation among people.

But you can perhaps say are they doing a conscientious job? Do they know the rules and are they applying them in a way that is, as you say, within a range of judgment? It is just that we cannot use the kinds of devices that are now being used by other accreditation organizations as a check on whether the standards are working well. That is all I am saying.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I think there is actually an area in which performance standards would work very well. It is probably the most crucial area of all and I will mention it, but I am hoping not to introduce a general discussion of how to accredit all these things. And that has to do with what I was calling before the

core competencies. To test whether or not an IRB correctly identified that they cannot review this research -- they cannot approve this research because it involves somebody who cannot give consent and they did not get second consent from the correct person.

To say that this cannot be approved because it involved -- I am trying to list -- I mean, there are a list of do's and don't's. With prisoners under the current regs you absolutely have to have it reviewed by somebody who is familiar with prison conditions.

With children there are limits on parental discretion. There are things, as I was saying before, that are beyond their discretion and one thing that performance standards can test is whether they correctly identify where they have no discretion and then make the right decision in light of what they are supposed to be doing.

And then beyond -- and that is going to affect mostly the IRBs that are handling research that -- it is going to affect IRBs that do not do a lot of this stuff and where you want to catch the ones who are not all that familiar with the rules.

And then after that where you are into discretionary areas, I do not think -- I agree, you cannot test it because it is by definition an area of

discretion, but I do not think we should eliminate the idea completely.

DR. SHAPIRO: Okay. Any other comments on this?

Yes, David?

DR. COX: Alta, I think somebody already has taken the ten commandments. I do not know what we should call these but as a concept, I mean, it is crystal clear. And my only little rejoinder to this, Harold, is that for me this is how I rationalize, you know, accrediting individuals but then accrediting the organization institution, too. It is the double whammy to basically be able to make sure that the ten commandments are there but at the same time with the individuals make sure you have read the ten commandments. So it is -- I think some people may see this as over -- you know, overly bureaucratic.

But the -- since you cannot force people to do everything in lock step as we have all agreed, but you have to have some way that there are certain boundaries that people do not pass.

DR. SHAPIRO: We have -- you know, I really hope we will not go along with this idea that somehow certification -- education certification, accreditation is some kind of big huge burden in relation to the

privilege these people are getting. It is really almost trivial.

DR. COX: Indeed.

DR. SHAPIRO: And it is hard to realize that we have not done it before. Now we have to get them right. No use making it too burdensome and all those things which we all have said.

DR. COX: But I guess the point of my comments, Harold, is that I think it may not be clear in terms of how the report is written now about why we do accreditation for the institution as well as the people and that this discussion we have been having has been, I think, very helpful amongst ourselves.

DR. SHAPIRO: We certainly ought to make that clear.

DR. COX: Probably it will be helpful to the readers.

DR. SHAPIRO: Alex, and then Steve.

PROFESSOR CAPRON: Just two other points. I very much agree with what you have been saying and I hope that we give attention to two things. One is the educative role of the accreditation process, including the people who come on site to do the accreditation.

I think there is a tension between being both an evaluator and a teacher, but all of us who are

teachers do that all the time ourselves and we do not think we are disqualified, and there can be a conveying of information in that process and an encouragement towards better practices at the margin where you are not even at a risk of accreditation but just -- the second thing is it is like informed consent in the sense that even if you do not think that you get perfect informed consent in all cases.

One of the goals of the informed consent process is to encourage self-scrutiny in advance by the investigator. I am going to have to sit down and explain this project to somebody and what questions are they going to have for me. Have I thought it through? Can I explain it? Can I tell them how I have anticipated if a problem arises? We have thought of that and here is how we will respond and so forth.

And accreditation can have the same effect. In fact, it may be a bigger effect thinking through your process and getting ready to be judged than it is -- and having a set of standards against which you know you are going to be measured than the actual on site evaluation. And we should talk about that role of simply encouraging people and making them aware that they really are going to be judged in a way that the assurance system just does not do now.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: I would like to endorse your thought, Harold, that I think we have an opportunity in this 15 pager we are going to put up front to get away from the measured kind of rhetoric we have in the report and when we are dealing with this kind of issue just right up front, right. We -- you know, doctors are certified or licensed. Hospitals are accredited. Universities, cab drivers are licensed. Before you take a human subject in your hands as a researcher and want that privilege, it is outrageous that you are not.

And I think we can use that kind of --

PROFESSOR CHARO: You can go and buy a gun to shoot them but you cannot do research on them.

MR. HOLTZMAN: Right.

(Laughter.)

MR. HOLTZMAN: And I think again --

DR. SHAPIRO: Do you want that in there, too?

PROFESSOR CHARO: It is in the transcript now.

MR. HOLTZMAN: I do not think -- I guess what I am saying is I do not think we should shy away in the 15 pager from that more over the top kind of rhetoric, which is in fact what is driving us at the principled level.

DR. SHAPIRO: That is a good point. Okay.

I would like to turn to another aspect of four. Maybe someone can tell me. Which is the recommendation that deals with IRB membership? I have forgotten the number.

PROFESSOR CHARO: 4.9.

DR. SPEERS: It is 9 and 10. The new 9 and the new 10.

DR. SHAPIRO: The new 9 and the new 10.

PROFESSOR CAPRON: Page 35.

DR. SHAPIRO: Because this is an area where we got a --

MR. HOLTZMAN: You got a perfect good --

(Laughter.)

DR. SHAPIRO: Right. The -- and one of the issues regarding -- 4.9 was the one I had in mind right now. I just want to get -- this has been a change since the last draft that was out. That is if you recall it was -- we had -- 50 percent was the key number before, right, rather than 25 percent, which is in the current draft. And that -- well, I will let Marjorie characterize the comments, but as I understand it, people thought it would be difficult to meet the 50 percent requirement. And, therefore, it might be, as this recommendation suggests, that a way at least to

begin right now is to start with a 25 percent requirement.

But this is something we need to discuss because we never discussed that explicitly and it is -- right now it is a placeholder and really up for discussion as to whether we as a commission think 50 or 25 is right or some other number which we might try to defend. Obviously any single number taken too seriously has got some arbitrariness to it, but in terms -- I think everybody knows what we are trying to accomplish here and I would be interested in how commission members feel about that.

PROFESSOR CAPRON: Is there someone on the line?

DR. MESLIN: Hello.

PROFESSOR CAPRON: The White House.

DR. SHAPIRO: That is right.

(Laughter.)

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I second the motion.

DR. SHAPIRO: To which?

PROFESSOR CHARO: The new recommendation.

DR. SHAPIRO: The new recommendation. Okay. Are there other comments here?

PROFESSOR CAPRON: Well, would we face more

acceptance if we, in the recommendation itself, said a substantial proportion and then in the text talked about 25 percent or something? The -- when you have a number in there it looks more regulatory. I think we have two points.

One, the present rule which has a number, but does not specify how large the committee can be, means that some committees are very large, 20-25 people, and you have got one person who is both a nonscientist and a public member. And we know enough about the dynamics of small groups to know in those circumstances, you know, Solomon Ashe, et al., have shown us that one person has a hard time holding to their own views and expressing them. And so there is a great value in having a substantial percentage.

Now if it were 20 percent in one institution and 30 in another, would I expect them to behave very differently? Frankly, no. If it is five percent or two percent or one out of 20, yes, I do expect a difference.

And what we are trying to achieve is getting away from the mistake the present rule has of talking about a number rather than a percentage and saying it cannot be a low percentage. It should be a substantial proportion.

I just think it would make our recommendations seem more in line with our general thrust of not writing the regulations to talk about that and the reasons behind it.

DR. SHAPIRO: I came to think as I looked at -- I thought about this that 50 percent was -- whatever else you might think about it -- unrealistic. That is we would not be able to man these IRBs and it just could not maybe be done in many situations. Not all, but in many situations. And I am very amenable to the suggestion that you have made and I -- I quite agree that that is really what we have in mind. But how do others feel about it?

Steve?

MR. HOLTZMAN: I am fine with it. I just do think in the text then we have to make clear that meaningful representation is not one. Just -- and so, therefore, using the 25 kind of example --

DR. SHAPIRO: We have got to anchor it somewhere. It may not be directly in the recommendation but we have to anchor it somewhere in the report.

PROFESSOR BACKLAR: Actually meaningful representation is not just a few. Two or three is not -- two or three people may not be adequate.

DR. SHAPIRO: It may or may not be depending on the size of the IRB. If it is a six person IRB that would be very substantial or meaningful. If it is, you know, 40 -- well, there are no 40s I presume.

Rhetaugh and then David?

DR. DUMAS: You know, there is a part of me that does not like the idea of dictating the level of percentage. But there is also another part of me that knows that in some cases if this is not done people will consider two people out of 25 or 30 adequate or meaningful. And if we are really serious about the need to have the composition of this committee determined according to certain objectives then I think I would be more inclined to make the statement and suggest the proportion.

DR. SHAPIRO: Inside the recommendation?

DR. DUMAS: Yes.

DR. SHAPIRO: Okay. Other views? David?

DR. COX: Yes. So I prefer the opposite, not to put the number in the recommendation but to have a discussion like we are having in the text and then -- but I share your same concern, Rhetaugh. But then the accreditation system deals with those people, because when you are coming through and you look at what that IRB is, then those people get told, "No, I am sorry,

you know, that does not cut it."

So then what you are doing is that you are telling people how to do the right thing. You are not dictating what the number should be, but when they come before you with a group, okay, that does not pass the red face test in terms of that kind of measure, they do not get accredited.

DR. DUMAS: Yes, but the standards do not say that I had to have 25 percent. The standard said a meaningful number and I can argue that one is a meaningful number.

DR. COX: Yes, but your accreditation group, okay -- at least the way I am thinking about it since we are letting people -- we have the ten commandments and you can argue that.

DR. MIIKE: You know, Rhetaugh, the current recommendation says NOHRO will set the number. It does not say that it is up to the institutions. We are just talking about not putting 25 percent in, but NOHRO would set the number.

DR. DUMAS: Okay.

DR. MIIKE: So that would be uniform.

DR. COX: So that is where -- that is your protection. It is that body.

MR. HOLTZMAN: There will be a number set.

DR. DUMAS: Okay.

DR. SHAPIRO: Eventually that is right.

DR. DUMAS: Okay.

DR. SHAPIRO: Okay. So I mean the principle issue here is that -- I do not hear any enthusiasm for the original number or area as -- because I think that really is not do-able at the current time. And what we are aiming for, and appropriately articulated, is something in the 20 to 30 percent area will have to be worked out. That is what we mean by significant and so on.

Okay. That is very helpful. Thank you very much. I wanted to make sure that I checked that with you.

Is there any concern regarding -- again sticking with 4.9 -- the way these members are defined? We are talking about people who are not otherwise affiliated with the institution and talking about nonscientists. I am -- as Marjorie is probably tired of hearing me say this -- I always find it hard to understand who nonscientists are but I will work on that.

DR. MIIKE: I am a nonscientist.

(Laughter.)

DR. SHAPIRO: That is right. The question is

who else? Who else is in that category?

Steve?

MR. HOLTZMAN: It is actually a great point because I think what immediately comes to mind again is the biomedical model and so we will put in a bunch of anthropologists and now you have got anthropology research so are they -- did the biomed just become the nonrelevant scientist. So, I mean --

DR. SHAPIRO: That is exactly the point that I have been stumbling over.

MR. HOLTZMAN: Right. So maybe it is -- were you about to say something, Marjorie?

DR. SPEERS: Well, we did add -- what we did add to the text this time was OHRP's interpretation of actually what a scientist is and so the flip side of that is what a nonscientist is. OHRP defines a scientist -- I have not actually quoted directly in the text but it is basically anyone who has training in a science or in the scientific method and they interpret that to be --

MR. HOLTZMAN: Everyone.

DR. SPEERS: Well, they interpret that to be physicians and nurses and anybody trained in science at the bachelor's, master's or doctoral level.

DR. SHAPIRO: And science is what in that?

MR. HOLTZMAN: That which uses the scientific method.

(Laughter.)

DR. SPEERS: So the question would be whether we want to offer a different definition or interpretation of what a nonscientist is or a scientist.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: First of all, that only reinforces the whole problem of biomedical model. Your recitation just made it worse.

(Laughter.)

PROFESSOR CHARO: Second, the idea that somebody with a bachelor's is a scientist is laughable. I speak as somebody with only a bachelor's in biology, but I think what we are trying to get at here is lay people. Is there some reason why that is insulting? Can we not use that phrase?

MR. HOLTZMAN: The lay relative to what again?

PROFESSOR CAPRON: Yes, it is relative to what.

PROFESSOR CHARO: Nonspecialist. Non-Ph.D. Non whatever.

MR. HOLTZMAN: Well --

PROFESSOR CHARO: I would like -- I think we

all know what we want and the only thing we are struggling for is a word here. We want people who are not expert in the areas of research that are the subject of discussion.

PROFESSOR CAPRON: That is --

(Simultaneous discussion.)

PROFESSOR CAPRON: You can have a cell biologist on a biomedical IRB and they can be defined nonscientist as to that science.

PROFESSOR CHARO: Well, before you all jump up and down and say that is right, I think there is a second aspect to it. We want people who are representative of the potential subject population because the role of this person on the IRB is not only to be somehow unemotionally --

PROFESSOR CAPRON: Committed.

PROFESSOR CHARO: Right. Disinterested in the research and in the progress of that field but also to be able to represent for the rest of the people there something about how a potential recruit would react to the documents, to the recruiting methodology, how they would imagine the risks and benefits would affect them, to give feedback. So it is not just that, you know, the physician is reacting to the sociologist survey. You know, it is more than that.

MR. HOLTZMAN: Yes. Let's put it in a three valued logic here, because you may be making another point, right, which is there is a difference between someone whose primary identity does not lie with the investigator and someone whose primary identity lies with the subject. All right.

PROFESSOR CHARO: Yes.

MR. HOLTZMAN: Or we can --

PROFESSOR CHARO: Yes.

DR. MURRAY: Mr. Chairman?

DR. SHAPIRO: Yes.

DR. MURRAY: This is Tom.

DR. SHAPIRO: Tom, how are you? Welcome.

DR. MURRAY: (Via telephone). I have been listening for about an hour but this is the first I have spoken up. I did not want to interrupt and I did not want to interrupt the flow and I had nothing particularly to say but I do want to say something about this. We could simply say rather than using the term nonscientist, nonresearch investigator or something comparable. I also think the 50 percent. I still think that is the right number, 50 percent, and I may choose to write a minority report on that but I am -- we may have to give in on this one. No one -- it works in other locations but I can understand why

administrators would be loathe to complicate their lives in this way.

DR. SHAPIRO: Okay. Thank you, Tom.

Tom, are you able to hear us clearly?

DR. MURRAY: Not very clearly, no, but I do not know that there is anything you can do to resolve that.

DR. SHAPIRO: I am not sure either. We will try our best.

Okay. Steve, did you have -- you were trying to work through an example.

MR. HOLTZMAN: No, I was just asking Alta that it is one thing to say it is not the primary identity with the research investigator. It would be a further to specify, which as I look at it, you know, have we done that about representation either on an ad hoc or whatever basis of the group under investigation.

PROFESSOR CHARO: My impression at the time we discussed this in Salt Lake was that we were attempting to capture both of those phenomenon and that when we talked about people who were unaffiliated with the institution we were talking there about people who were disinterested in the progress of the research, and in some sense that overlaps with your category, Steve, of somebody whose primary identity is not that of a

researcher. Right? The idea there was somebody who really does not have a stake in whether this gets approved or not. And that when we talked about what has been deemed here the nonscientist, my impression had been that that was, in fact, a category that was supposed to represent people who were identifying themselves as likely potential recruits.

And that was why we were trying to capture both and that is why this thing turned into a 50 percent number, although for large IRBs it is rather unwieldy because it means if you need 30 scientists and such to do all of your work you would need an IRB of 60 people and it did pose a logistical challenge, which resulted in that resistance.

I am very comfortable with having the two categories overlap in terms of unaffiliated and somewhat unspecialized, whatever, but I would not want to have lost in this shuffle the idea that one of the primary jobs here is to bring not the attention of people who are reviewing the protocols week after week, and have become familiar with it, even if it is not in their own field they have become familiar with protocol language, with consent form language, have become a little bit numbed to the whole business, but to bring to it a, "Wait a second, if I got this I would be

completely confused, or I would think that I was getting cured, or I would think that somebody is going to come back and, you know, tell me I won the lottery."

DR. SHAPIRO: Okay. I think on this issue, the so to speak nonscientist issue, I still think we need a better set of words here. Let's not try to work them out here but if any of you have any ideas in this respect that would be helpful because I found it very, very difficult to understand what that was. I stumbled over it every time I read it.

PROFESSOR CAPRON: I think it is much easier to say in place of nonscientists persons not involved in the fields of research which come before that IRB. And that achieves one meaning of nonscientist.

I do not think that short of insisting that the community representatives themselves not be scientists or physicians, and many IRBs use people from the community who are themselves professionals, I mean the reason you can get someone to give their time is that they have an interest in the field. They do not do research necessarily but they are a physician and they identify with the research process. They qualify as a community -- a non -- they do not have any attachment to the institution other than service and so supposedly they avoid that conflict.

Getting people who really will have the attitude of -- and the approach to research that a subject would have would mean you also -- you do not get that by having Ph.D.s in history and English who are in -- as your nonscientists.

PROFESSOR CHARO: That was just my point.

PROFESSOR CAPRON: Yes, I mean, I agree with you but I mean -- I am agreeing with Steve that if we want this we are really talking about three, not two categories. We are talking about people who are unaffiliated institutionally, people who are not involved in that field of science, and a separate category of people who have some resemblance to the people who are in the catchment area, as it were, of the researchers for whatever kind of research they are doing.

And we were very specific about that when we talked about people with mental impairments you should -- if you are doing a certain kind of research you should have some people, or person at least, there to whom identifies with the subject because they are a patient, or they are a family member of a patient, or a member of an advocacy organization. And, you know, a Ph.D. in English may say, "Well, I do not know what an aliquot of something -- why did you use that word? Use

some other term." But in terms of looking at something and saying, "I do not understand how to read this because it is written at a college level," that may never occur to them because they are used to reading things that are complex.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Well, I mean, apparently you are agreeing with that point because, I mean, that is exactly what I am saying.

PROFESSOR CAPRON: I am not disagreeing with you.

PROFESSOR CHARO: But I would like to put on the table the following viewpoint that of all the possible roles that these folks can play, the most essential and the one that we should not allow to be lost under any circumstances is that of representing the point of view of potential recruits. More important than unaffiliated, more important than unspecialized is the attitude of potential recruits.

We have got other places we are dealing with the conflict of interest issues that tackle, to some extent, the same concerns that the requirement for unaffiliated persons tackles. But the crucial thing from my experience -- it is only with one IRB, a little bit with two, but it is limited but nonetheless the

crucial thing is getting past the pattern of acceptance that comes from familiarity with the research setting and with research protocols and with recruitment techniques, and getting to people for whom this is novel because that is going to be the typical situation for a recruit. That is the way to avoid the problems that are so frequent.

The people who testified before us that they felt betrayed when they were recruited into research trials, and you look more closely and you find that everything was done according to Hoyle but nonetheless they felt betrayed. Why is that? Because somehow even doing it technically according to the rules conveyed a submessage and conveyed some other message that they were receiving that was inaccurate and the only way to pick that up is to have somebody who has that kind of naivete when they approach the research protocol for the review process.

PROFESSOR CAPRON: You want these people to rotate frequently. Seriously, I mean, they serve -- if they serve a year they become inured.

PROFESSOR CHARO: I am not going to try to lay down every part of the rule here. I think that would actually be a fabulous idea but mostly what I want to get across is that as we rewrite this thing and we

begin to struggle with language that the one thing that does not get dropped out is the possibility of getting those kinds of people on there. I do not want language that will allow unaffiliated doctors to become the community members as they are now, because Alex is quite correct that is quite frequent, and lose the whole purpose of this recommendation in my mind.

DR. SHAPIRO: Trish?

PROFESSOR BACKLAR: One of the ways that you can write this in to get the rotation is something we did in the capacity report, which was that depending on the protocol being addressed that you bring in people for those particular protocols so an IRB that looks at various different things should bring in people that are either patients or advocates and family members that would be connected to the kind of work that is going on.

PROFESSOR CHARO: May I --

DR. SHAPIRO: Yes.

PROFESSOR CHARO: That is exactly what often will happen in the area of research with prisoners now. You will often have extra people brought in specifically for those protocols and it works for very specialized settings where there is just no knowledge in the general public of the logistics and dynamics

within the setting. But I would like to keep that still as a supplementary technique. The dynamics of small groups also include the notion that people who are new in the group are a little more reticent and their opinions are not necessarily given the deference they ought to. The people I am talking about frequently are already at a disadvantage by lack of degree, inadequate vocabulary to express themselves, unfamiliarity with the range of things that have been discussed before and ultimately dismissed as not a serious problem.

So in every respect they have got an uphill battle and I would like at least to have some kind of continuity for them for some period of time so that they can become imbedded in the group and their opinions taken seriously.

DR. SHAPIRO: Okay. I think we have a general sense of where we have to go here. It is very helpful. Let's turn our attention now to another recommendation which perhaps is not as central to this chapter but I just want to get people's judgments on it. In fact, this is the very last recommendation here. There are other issues we have to deal with. I do not mean this is the end but it just happens to be on my list here.

And this is recommendation 4.17 if I have got

the right number here. It has to do with a compensation system and whether or not we want to make any recommendation. Putting aside the issue of whether -- how this should be addressed, who this recommendation ought to be addressed to, whether it is addressed to the Congress or someone else.

The question is whether we feel strong enough about this so that a compensation system ought to be established for research injuries. People have this. People have the number?

DR. MESLIN: Page 63.

DR. SHAPIRO: Page 63. Has everybody got this? Okay.

My own sense of this is, again putting aside who is addressed in the way the thing is phrased, is that it is something important to consider. My own view is, however, that we -- if we are going to put something like this in, we ought to say something about how this type of system might be financed. I have some ideas about it but I do not want to get to that right now. So let me just see what ideas people have on this kind of a recommendation regardless of where the financing is.

Larry and then Alta.

DR. MIIKE: Well, like I said early on I was

against it but since it is stated in such an innocuous manner I will not write a dissent on it but if you get -- the nuts and bolts of it all is how you are going to compensate this and how are you going to define an injury within the causation aspects and the parsing of it.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I was comfortable -- not with the phrasing again because of the whole thing about Congress --

DR. SHAPIRO: No.

PROFESSOR CHARO: -- but I was comfortable with it except for the fact that it specifies an administrative system, and I do not think we have begun to discuss administrative systems versus all 50 states deciding that they were going to take care of this through the tort system, which is another option. It is unlikely to happen but I feel uncomfortable making a recommendation about a particular form of the legal remedy without having had a real discussion about it, nor do I feel like this group is really well positioned to have that discussion.

So I would suggest something like "Human research participants should have prompt, easy access to compensation for medical rehabilitation costs caused

by research participation" and leave the form of the system unspecified.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: Well, this is a more modest recommendation than the one -- the one I favor would be more modest than what we have here and I guess I would say that the recommendation the President's Commission came up with on this, which is that the office ought to conduct an experimental trial. In other words, identify some institutions to participate, try out different forms of compensation. How easy is it to determine the causation issue, which is always the stumbling block? What happens to the level of claims?

The fear, of course, is that you develop a system in which people see this as an easy way to get compensation and start claiming things which they never would have regarded as compensable events for which compensation was even appropriate. That may or may not turn out to be the case.

I do not know how anyone could adopt a system without some actuarial expectations. I mean, how would you fund them and that is what the experiment would be designed to show. That recommendation was made in 1982 or something. It has never been acted on. Twenty

years ago we provided -- I mean, I would not know reading the description leading up to this that that is what we recommended. You quote the President's Commission as saying that there should be a system of compensation. We thought there ought to be,but the details of the system remained to be worked out and even whether there was a great enough need.

I think we probably ought to make sure that we have gotten any statistics, if there are any, from those institutions that have continued to have programs in the interim. The impression they give is they do not have major problems. They have a very low level of -- but there should be a national test of this.

DR. SHAPIRO: David?

DR. COX: Yes. That is actually my problem with this. It is certainly -- you know, when this happens you want to do the right thing by people but how often does it happen. So I am having a real difficulty here if we make a big deal about this and it becomes a real contentious point. If it is a big fight over things that do not happen very often and it detracts from ultimately what -- you know, what the prize is then this is not a thoughtful approach.

I will tell you I do not -- I am not -- I do not know what the data are on that. You know, how

often this is a problem. But my -- but my impression is that it is not a problem very often.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I have difficulty with the recommendation and it seems to me that there is nothing that I know of that would prohibit a person from going through the usual courts of law to get compensation for damages or whatever. So if I had a recommendation at all related to this I would want it posed such that it would not prohibit a person from seeking compensation for medical and rehabilitation costs incurred as a result of the research.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: First, I would like to endorse Alex's suggestion that we return to the President's Commission recommendation about calling for some kind of experiment. That is a very nice idea. I actually was not aware of it and I read it so long ago I just forgot it. I think that is a nice thing to do and it actually is something concrete.

With regard to Rhetaugh's comment, nothing here would preclude going to state court and even though I was advocating before that we not specify a particular system because that option exists, I also recognize that it is a really terrible option. It is

very difficult to use it. I would be happy to explain some other time the list of things that pose obstacles but it is certainly not the best way of handling anything in the realm of injuries, let alone this.

DR. SHAPIRO: I guess the key piece of data that is missing or that no one has is what -- how many injuries do occur, what is the nature of those injuries, and the difficulty of deciding when the event has happened. I mean, it is not like deposit insurance in the sense you know when a bank has failed. You know, that means deposit insurance comes in. Identifying the event is not so easy here.

PROFESSOR CHARO: Well, the adverse event reporting system does begin to get at that because for the covered research areas there is a reporting requirement that lists events and also speculates about causal connections.

DR. SHAPIRO: Larry?

DR. MIIKE: You know, the closest analogy is the vaccine compensation system and the way that was developed was --

DR. SHAPIRO: Which one? I am sorry. Vaccine.

DR. MIIKE: Childhood vaccine compensation system. And really the experience with that has been

way below what they thought it was going to be.

DR. SHAPIRO: Yes.

DR. MIIKE: But the only way they could deal with compensation is they knew certain kinds of reactions would happen and so they just put a time limit. You got the inoculation at X time, within that time frame if these kinds of things happened. Because there is no way to prove individually that something happens.

DR. SHAPIRO: I had not thought of that aspect. That is a really important point.

PROFESSOR CAPRON: And that is complicated here and the reason for an experiment is --

PROFESSOR CHARO: You do not know.

PROFESSOR CAPRON: Excuse me.

DR. MIIKE: The ones that are going to occur are the ones that are already essentially ill and they are going to have a --

PROFESSOR CAPRON: Sick.

DR. MIIKE: -- complication.

PROFESSOR CAPRON: And the variation in what the reaction should be. It is not like a signature.

DR. MIIKE: Right.

PROFESSOR CAPRON: You get a paralysis after a vaccine, okay, that is a signature result.

DR. MIIKE: I can support Alex's --

DR. SHAPIRO: Okay. So let's try to -- if that is satisfactory to people, we will try to write something in that fashion.

Okay. Why don't we take a break for 15 minutes and we will come back and go through the rest of this chapter?

(Whereupon, at 9:45 a.m., a break was taken.)

DR. SHAPIRO: Colleagues, let's continue our discussions. Trish, Arturo, let's sit down.

Before we go on to -- obviously before we go on to Chapter 5 let's stick with Chapter 4 and see what other issues, questions, comments anyone may have on any aspect of it.

David?

DR. COX: So after our discussion, what I did at the break is went back and sort of looked at the recommendations in the order that they are right now. And one of the things that I think came out of our discussion, at least for me it clarified things a lot, was this -- the logic of why having an individual certification as well as an institutional accreditation, the way things read right now is that it puts that individual certification before the institutional accreditation. And the -- I am just

wondering if the -- you know, if it does not flow better the other direction, which is that you talk about having the centralized place that has the ten commandments, then what it does is it accredits the institutions because they have a responsibility of being able to make sure that people follow the ten commandments but as part of that, okay, you accredit the individuals. So it is more a flow from the top down. As the recommendations read now that flow is jumbled up.

DR. SHAPIRO: Okay.

Steve?

MR. HOLTZMAN: Just to give you a different way to think about it, David, it is not clear to me this flow really matters.

DR. COX: Okay.

MR. HOLTZMAN: So take docs. You accredit hospitals and you certify or license docs. It is not really a flow, right. Remember there could be a researcher who is not associated with an institution who is going to conduct research, right, so all that is in play is the fact that he was certified.

So I am not sure that the model you have as a way of thinking about it is really driving this. I think it is two different --

Dr. COX: It is indeed not driving the reason why we have it that way, Steve, but I am just thinking of it as a pedagogical thing for people to be able to understand for the majority of structures because most of this is being applied in a structural context so certainly from an ethical framework it does not flow that way but just in terms of the context of which it will be applied to most people. So it is just I do not feel strongly about it but it was just a --

PROFESSOR CAPRON: Steve, in terms of the presentation here, we talk about education and the education aims at preparing you to be a certified researcher or IRB member. So in terms of the flow here I think the recommendation 4.3 before 4.4 makes sense. It makes it easier to read it here.

DR. COX: It is just implementing it.

DR. SHAPIRO: We will review it as we go through the chapter. Other issues that people want to -- yes, Alta?

PROFESSOR CHARO: 4.8, conflicts of interest.

DR. SHAPIRO: Yes. I am glad we got to that.

PROFESSOR CHARO: My experience and what I heard at a conference last November specifically on conflicts of interest continues to suggest to me that

financial conflicts of interest are often not the most significant ones and yet we tend to focus on them in part because they are the most quantifiable conflicts of interest. This means for me that this recommendation,which says things like "but especially financial conflicts, which has a special sentence on financial conflicts just following it and then talks about other kinds of relations,has a tone that does not match my experience about what really is a more serious obstacle and is a more challenging dilemma, which is the capturing of the psychological phenomenon.

The review of work by your department chair. The review of work by a colleague in your department who is as yet untenured. Review of work that has -- as will happen in study sections -- some implication for your own areas of research.

And I would prefer if it were possible,but I am not sure exactly how to do it, I confess, to somehow change the emphasis toward trying more creatively to capture those things and manage them, which may involve managing them through disclosure and ease of recusal, self-initiated recusals, with somewhat less emphasis on the purely financial conflicts of interest.

And just as an aside on the financial ones, those are getting more and more subtle to capture as

well because of the variety of financial interests, whether it is specific money for recruitment on a per capita basis,or it is receipt of grants,or it is stock options,or it is options or financial interest in companies that are competitors potentially to the companies that are involved in this research.

So it is an area that not only does not,in my opinion, frequently be the most -- it is not only not the most serious but it is also not as easily captured as we might imagine from some of this language.

DR. SHAPIRO: Thank you.

On the issue of conflicts of interest in general, the general topic, I had some conversations with Eric and Marjorie this morning. There are, of course, a lot of initiatives out there right now, a lot of organizations taking initiatives, and while we have not had an extensive discussion of this and do not have any detailed program to offer, I am really quite anxious that we not inadvertently undermine very positive things that are happening out there.

And so I have asked Marjorie and the staff to really put together a compendium of these things so we can review what all the various recommendations are out there to give us some better guidance and to make sure in particular that we do not undermine some

organizations who have gone out there and taken some real initiative in this area.

Now I do not have all the details at hand so I do not know exactly where we are going to come out but I do want to look at that to assure that we are not in the position of coming around and saying -- someone will look at what we say and they will look at what they say and they will say, "Gosh, you guys are sort of a generation behind in your thinking here."

So while I do not propose that we do anything in detail because we have not studied it in detail, I do want to make it at least consistent with and in support of other thoughtful initiatives that are out there today.

And I do not have any language for that now but there will be as we get to the next version. There will be some language and text around that.

The points you make are good ones. I mean, this is a tough area and it is becoming more subtle all the time in some sense.

David?

DR. COX: And the way the recommendation is written now is that -- and again I do not have any solutions to this. It is almost as a placeholder for me because everybody knows that there is conflicts of

interest in this.

DR. SHAPIRO: Right.

DR. COX: But that what we really need to do is to have laid out what are the ones we need to really worry about and -- because as Alta says, they are very complicated right now and people stumble into them without even knowing it. So -- but that is a whole sort of report of its own.

DR. SHAPIRO: Right. Other comments on this general area?

PROFESSOR CAPRON: Are we going to differentiate between the conflicts of interest that might arise for people on the IRB versus investigators, because on the IRB it just seems to me there should be no question that you insulate the process from anyone with a direct conflict. For investigators, it is much more complex for the reason that Alta suggests that we have not in the past paid a lot of attention to the conflicts that are inherent in the desire for advancement in one's field and the like that can mean you have a loyalty to something other than the research subject obviously.

I think the reason there has been so much emphasis on financial conflicts of interest is not only that they are more familiar from other fields, that is

to say a board member of an organization is supposed to absent herself from a discussion when the organization is dealing with another organization in which she is also a director and has a financial stake. But it is because they are new, relatively new to a lot of the biomedical settings that they did not exist in the same way before. So they seem more shocking than the familiar ones. And it may be that it is just a reminder that other ones are equally bad or it may be that there are -- have been mechanisms that have modulated the effect of the other ones.

PROFESSOR CHARO: I agree completely with what Alex said towards the end of his comments. I want to react a little bit to his comment about the IRB members. The notion of a direct conflict is itself a little problematic. What constitutes a direct conflict becomes a matter of interpretation obviously. And the shared affiliation creates dilemmas because so many institutions have very tangled lines of both authority and financing so that there is a tremendous amount of interdependency among people.

One of the interesting things that I am realizing now is not emphasized in this report but is implicated by this observation, is the role of the independent IRBs. Because, of course, one of the

advantages that they offer is that they do simplify many of these problems because of the disassociation between the investigator and the investigator's institution on the one hand and the IRB on the other.

I realize now we have not emphasized them as a phenomenon. It may be that this is an appropriate point to mention them, to mention that they offer a host of advantages and disadvantages that are somewhat distinct from institutionally based IRBs, and that it is worth seriously considering whether we want to be encouraging the development of that trend.

DR. SHAPIRO: I think I recall but, Marjorie, help me out here. I think I recall we, in fact, do that somewhere. We may not tie it directly to this issue. That is what I do not remember.

PROFESSOR CHARO: Can you remind me where that is?

DR. SPEERS: Yes, there are two places.

MR. HOLTZMAN: Page 32.

DR. SPEERS: Thank you. It is in Chapter 4 and then we have also added a section of the independent IRBs being a new phenomenon in Chapter 1.

PROFESSOR CHARO: Okay.

DR. SPEERS: But where we really address what you are talking about here is somewhere in Chapter 4.

PROFESSOR CHARO: You said page?

PROFESSOR CAPRON: 32, bottom of the page.

PROFESSOR CHARO: Oops, I am on the wrong chapter.

MR. HOLTZMAN: Just before the recommendation.

DR. SPEERS: Yes.

MR. HOLTZMAN: On the one hand and on the other hand, they are independent.

DR. SHAPIRO: That is right. That is some kind of independence, right.

(Laughter.)

DR. SHAPIRO: Is this independence or what.

PROFESSOR CHARO: My chapter is out of order is the problem.

DR. SPEERS: Here.

PROFESSOR CHARO: Oh, here I am. I have got it.

DR. SPEERS: It may not be enough and you may want to look at it.

DR. SHAPIRO: Yes. I do not think -- I think it is not -- certainly not phrased the way you did it, Alta, at all. It did not mean to say that, but the notion is there and whether we should focus it a little more --

PROFESSOR CAPRON: I like your phrasing,

Steve.

(Laughter.)

DR. SHAPIRO: Okay. Other comments on this or other recommendations in this chapter?

Marjorie or Eric, do you have any of these -- any of our recommendations in this chapter which you would like specifically for the commission to respond?

Marjorie?

DR. SPEERS: Yes. I am confused on the numbering. It is the -- it is the new one that we added. It is proposed recommendation 4.10. And I just want to make sure the commissioners are comfortable with that --

DR. SHAPIRO: Which is that one, just to make sure I am looking at the right one?

DR. SPEERS: It is the one on the IRB having appropriate expertise to review the type of research that is submitted to that IRB.

PROFESSOR CHARO: Where you mention specifically historians and --

DR. SPEERS: Right.

PROFESSOR CHARO: Right.

DR. SPEERS: There is no need for a discussion if there does not need to be any but I just -- since we

had added that in I wanted it to be --

MR. HOLTZMAN: You just -- you picked up -- you left out the word "social."

DR. SPEERS: Yes, we do have that. Otherwise I do not have any questions for this chapter.

DR. SHAPIRO: Any other issues, questions from members of the commission?

Okay. Let's take a look at Chapter 5 and issues or questions that might come up that might be on your minds there.

Marjorie, do you just want to summarize what Chapter 5 is about or is supposed to be about?

DR. SPEERS: Well, in Chapter 5 there is one -- there is a section on resources and one recommendation related to resources that I think we would like to discuss. In addition, in this chapter what we try to do is to provide a brief summary of the report by highlighting how this report -- what this report does in terms of improving the system, what it means to institutions, investigators and to participants, and then to try to fit it very briefly in the context of some of the previous work of NBAC and interests that -- general interests or themes that have emerged over these various reports that you have done.

The only comments that we have received on

this chapter related to the recommendation regarding resources and, in general, those comments were positive and supportive of that recommendation, which is not surprising actually.

DR. SHAPIRO: Well, I, in fact -- I am sorry, Steve.

MR. HOLTZMAN: My only question is -- and again this is a matter of how detailed we want recs. If you took the preamble of the rec and if you just inserted the words, you know, "institutions should dedicate --" let's see. "Federal agency and institutions should dedicate resources to local and central or whatever oversight activities." You could end it there and all the rest of the detail could go into the body of the text instead of in the rec. So that is just one of those we need to decide.

DR. SHAPIRO: Let me ask something which is a question I wanted to pose on this recommendation that is in variant with respect to that particular issue and that is really what is item two in this recommendation 5.1(2) where it currently says, "Federal agencies and other sponsors should make funds available to institutions for oversight activities." Now I had a -- what might be a modest, maybe not modest suggestion here, namely that we say, "Federal agencies, other

sponsors and institutions should make funds available for oversight activities."

The only difference here is that institutions are asked to play a role in devoting some resources to this as well. That is how I would have gone about it and I just want to know how people feel about that so that people who are carrying out the research, those institutions, whether academic institutions, other institutions, would also play a role.

And I feel it is important because I think institutions, while always pressed for resources, as everyone is, really have not paid enough attention and have not devoted enough resources to it, and I do not think it is enough to say that no one has given us any for it, which is also true and we want to change that.

So -- well, it is obvious. There’s no use in me explaining. It is so obvious what is meant here.

David?

DR. COX: So I think that is a third check. When people have to spend money on something, it is yet one more place that makes them pay attention to it, so I like your suggestion.

DR. DUMAS: I do, too.

DR. SHAPIRO: Any objection to that?

MR. HOLTZMAN: They will just move it into the

overhead.

(Laughter.)

DR. SHAPIRO: Well, that is another argument because the overhead is capped and it depends on where it comes. We touch that elsewhere but that is an administrative issue and it depends -- at least for federal government overhead it is capped. It is not capped elsewhere but that is right.

Okay. Are there other issues? That was the really -- the other issue I had, which -- do you mind if I mention it, Marjorie, on the -- I think that as I have already told Marjorie that the interpretation of the data in Table 5.1 is not adequate in my view because there are really two points to be made from the data that has been collected here. One is that the sponsors to these activities could well afford, for example, to support OPRR or its successor better than they have. I mean, that is one point.

But this is an inadequate measure of the resources because many of the -- take NIH as an example. They require institutions to put a lot of resources behind this, to take this as a measure of the protections, or resources put into protections, for NIH sponsored programs is -- if I understand the data correctly -- not the complete story.

So we are going to still -- I mean, the points that are made here will still be made but I want to be a little broader in understanding just how you get to the resources that are actually devoted to protection.

PROFESSOR CHARO: I am sorry. I did not quite understand exactly what you are saying.

DR. SHAPIRO: Well, take a look at NIH. It has got $480,000 for something and $2,700,000 for something else. Okay. And they have got this huge research budget. $8 billion, or something of that nature, of human subjects research. Well, that is not a measure of the resources being put into protection of those subjects who are in that research because the Wisconsin IRB --

PROFESSOR CHARO: Got it.

DR. SHAPIRO: -- et cetera is devoting much more than all this put together. I mean, all of Wisconsin --

PROFESSOR CHARO: Right.

DR. SHAPIRO: And so I did not want to leave the impression that that was all these subjects had going for them.

PROFESSOR CHARO: Right.

DR. SHAPIRO: It is true that NIH could well support -- do better for OPRR or its successor and we

want to make that point but this is a small issue. I do not want to --

PROFESSOR CAPRON: Well, are you objecting simply to the title on the table because the column headings --

DR. SHAPIRO: No.

PROFESSOR CAPRON: -- dedicated administrative unit and budget for dedicated administration unit is accurate.

DR. SHAPIRO: Accurate. All I want to do is be fuller in our interpretation of this. I want to make the points that are made here. I do not want to object to any of those points, but I do not think they are adequate by themselves because I think they may convey an impression that the federal agencies sponsor this research and this is a level of resources devoted to protection, which is not accurate in my view. It is a level they devote towards it --

PROFESSOR CAPRON: Well, that is what it says. Federal agency support.

PROFESSOR CHARO: No, Alex --

PROFESSOR CAPRON: I am not following.

PROFESSOR CHARO: It is -- actually one way that -- I do not know if we have the information to do it. One way to help get that would be to distinguish

between intramural and extramural research because for intramural research if there is a dedicated administrative unit that is there for the intramural research then you actually have the right correspondence.

PROFESSOR CAPRON: Right.

PROFESSOR CHARO: When it is extramural then you can say here is the administrative unit; here is the extramural budget; asterisks: much of the review goes on with the extramural investigator's own institution, therefore this number does not correlate with the total expenditure on protections for those subjects.

PROFESSOR CAPRON: But that is not what this -- - the title --

PROFESSOR CHARO: I understand that the title is correct. Understanding what actually -- I appreciate now what Harold is saying about the misleading conclusions one could draw from it.

PROFESSOR CAPRON: If the conclusion is to what extent -- if the question is to what extent do federal agencies themselves devote their resources to activities connected to the oversight of human subjects research, this table tells you that.

PROFESSOR CHARO: Right, but that is not an

important question.

DR. SHAPIRO: It may tell you that, then I say it is not the right question. It is not a full enough question.

PROFESSOR CHARO: Yes.

DR. SHAPIRO: That is all I am saying.

PROFESSOR CAPRON: It seems to me the other thing is --

DR. BRITO: I agree with Alex in the sense that -- isn't the point that we are making here is that we want a lot more money going to -- from the feds to the institutions for supporting the human subject protections. If that is so, then these tables -- they make that point. I mean we are asking for indirect costs --

DR. SHAPIRO: We will wait until the text is done and you can take them -- like it or not like it. My view is that it is -- I will not repeat myself. I said it before. I am not going to repeat it again. But let's wait until we see the text and see if you like it.

PROFESSOR CAPRON: But do we have any ability to provide another column that says --

DR. SHAPIRO: Probably not.

PROFESSOR CAPRON: -- and it breaks it out.

The Wisconsin IRB doubtless has research that goes to the Department of Defense, the Department of Energy, the Department of Health and Human Services, the Veterans Administration, there is probably a long list of how would you -- even if you knew what the FTEs there are --

PROFESSOR CHARO: I was not suggesting that we would be able to construct that table. That is exactly why I turned and said I do not even know if we have that data. Right. But I appreciate the point about how this question could mislead people because it is asking a question that is not -- it is only one of a number of questions. And one of the most important questions that is not being asked and answered in the table is what is the amount of -- what are the resources being spent on the protection of human subjects and to what extent does the federal government play a role in that.

We do not know the answer to the first question.

PROFESSOR CAPRON: Right.

PROFESSOR CHARO: And if we answer only the second, one could be misled to think that it is also answering the first.

DR. SHAPIRO: Other questions about Chapter 5?

Okay. All right. Are there any other issues, suggestions, injunctions that you want to give us as we head to create the next draft?

COMMISSION-NEXT STEPS

HAROLD T. SHAPIRO, Ph.D.

ERIC M. MESLIN, Ph.D.

DR. SHAPIRO: It seems -- I want to turn to Eric to talk about logistics for our next meeting, which we have to set a date for. We do not have to do it right here but we have to do it in the next couple of days.

PROFESSOR CAPRON: I thought we had a date.

DR. SHAPIRO: Well, Eric, why don't you indicate where things stand in that respect?

DR. MESLIN: I think it makes sense to not do the April meeting. It is too close to this. There is work that needs to be done. More writing that needs to be done and rather than rush the staff and rush the commissioners to review, we looked at a bunch of May dates. As a minor matter, we only had one date secured for April, we could not do a two day meeting even if we wanted one. It would have only been the 17th or 18th. So the dates that are clear at the moment are 15, 16, 17 and 18.

PROFESSOR CHARO: Of May?

DR. MESLIN: Of May. And in obviously consecutive pairs. It may not be necessary to --

PROFESSOR CAPRON: What happened to the ones that were reserved.

DR. MESLIN: Just a second. I will get there in a second.

PROFESSOR CAPRON: Okay.

DR. MESLIN: Those first four dates can be either in singles or in couples, 15-16, 16-17, 17-18. A long time ago you had protected the 22nd and the 23rd in your calendars. So I am going to send around this -- these dates again because no doubt your calendars have been filled in some way, shape or form and we will poll you again for those dates.

I would like you to try and see if you can protect two of them.

MR. HOLTZMAN: Two pairs?

DR. MESLIN: No, to be able to say I can come on two days. I am going to give you choices of twos. Even though it is possible that we may only need a one day meeting, but I would like to have you lock in the pair that we have all agreed to and as soon as we get closer to that time we will confirm whether it is one or two.

PROFESSOR CHARO: And it will be a Washington

based meeting?

DR. MESLIN: And it will be a Washington based meeting, not regrettably, although lobbying was made last night for a Hawaii based meeting.

The time table for this is roughly as follows: Within the next week to ten days -- I am sorry, ten days to two weeks, you would see a version of this Part 1 or 15-pager, however it is going to be described. You would also then be seeing chapters as they become completed. You would -- we would hope to have all of the chapters to you -- having seen them, a week at a time or separated by a week, no later than the end of April.

So you would have seen this 15-pager plus all of the chapters "revised" with new text with enough spacing so that you can comment by the end of April. And that would give a full -- if it were the mid-May meetings -- a full couple of weeks to e-mail back and forth about what your final conclusions were and then come to the meeting. Whether it is that week or the week after, the 22nd and 23rd, will be determined by the poll.

DR. SHAPIRO: Eric, if I understand what you are asking us about is that your preference would be if it is feasible for the commission to meet rather than

the 22nd and 23rd, to meet the previous week.

DR. MESLIN: Yes.

DR. SHAPIRO: If that turns out to be feasible, we will have to all check our calendars. That is our first preference. The second preference, if we cannot -- if that turns out to be infeasible for any number of reasons then we will go to the 22nd and 23rd.

DR. MESLIN: Yes.

PROFESSOR CAPRON: Could you explain why you want to change the May date for those of us who sort of have built our lives around the calendar that you gave us last fall?

DR. MESLIN: More options and trying to give a little more time -- not trying to push it too far to the end of May.

PROFESSOR CAPRON: That is less time.

DR. MESLIN: Well, we want to make sure that we are able to get this done in a reasonable amount of time before the summer time and GPO printing and other logistical issues. It is not -- there is no secret reason why. We wanted to get some earlier dates. April did not seem to work out so we went to the next available clear dates for as many people as we knew about starting with the chairman.

DR. SHAPIRO: Yes?

PROFESSOR CHARO: Eric, I am assuming the way you described it that as each chapter arrives that will be the moment at which the recommendations for that chapter arrive. Did you consider and reject or, if not, would it be possible perhaps to send out recommendations as they are finalized even if the text in those chapters have not been finalized so that if there is tinkering on the language of the specific recommendations we can be doing round robins on e-mails on those even prior to the chapters.

DR. MESLIN: Yes.

PROFESSOR CHARO: It helps to make -- if the text comes with recommendations where there is still some substantive disagreement about the recommendation then the text cannot properly be finalized until we have made the policy choice.

DR. SHAPIRO: Arturo?

DR. BRITO: I am sorry. I missed the beginning of your conversation or your comments, Alta. I was a little distracted. But it does not make sense to make comments based on the conversations we have had over the last few days before the chapters are revised over the next week or two.

DR. SHAPIRO: Let me make a comment about that. Any commissioners as a result of our discussion

over these two days has some issues that you would like to articulate or to be included or issues that are on your mind, the sooner we get that, the better. So even this weekend is a good time to send us e-mail on that because that is very important.

I mean, I have a lot of notes from the meeting and I am going to try to mobilize them this weekend and get them in so that the people who are going to do the revising will have the benefit of that. So that should be done immediately without waiting for anything, and that is really quite important.

As I mentioned at the beginning of our meeting, some of you, I know, have already handed in some marked up text to Marjorie and Eric of suggestions you had, some are in text, some are in recommendations, and that is also extremely useful. So if you either have them or want to fax them in or just hand them in right now if you have it available, that can be very, very helpful, and that should happen right away as soon as it is feasible for all of you.

Okay. Other comments, questions, business? Okay. We are adjourned. Thank you very much.

(Whereupon, at 10:39 a.m., the proceedings were adjourned.)

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