32ND MEETING

OF THE

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

DR. SHAPIRO: I would like to call today's meeting to order. Let me just spend a few minutes reviewing our agenda for the next day or two that we will be here in Washington.

First of all, let me begin by thanking all members of the commission who were able to make it today. We have a pretty intensive schedule of meetings, including another one which is only about 15 days from now in Cambridge, and I want to thank you for making time for this joint effort.

Turning to our agenda, we will be spending maybe all of today discussing various aspects of our stem cell report, just use a quick way of describing what it is, so we really will have all of today, both this morning and this afternoon, to discuss issues that are still outstanding with respect to that report.

My objective is to mail this report off to the President after our meeting in Cambridge in July. I have forgotten the exact date. The 13th and 14th. That means we have to resolve an awful lot of the issues today with leaving some issues left over for what we can communicate between each other between now and the Cambridge meeting and finally at the Cambridge meeting.

We really cannot allow ourselves to go beyond that meeting.

That is a commitment, we have to -- that I have made to the President and we have to live up to that. So we will have to come to closure on these issues and I think that is quite achievable.

In fact, I hope we will come to closure on an awful lot of the issues but perhaps not all of them today and we have some time tomorrow afternoon also to look at some issues after we have had a chance to think things over, overnight. Tomorrow morning we will go to the other agenda items.

As you look at your agenda, tomorrow morning we will be looking at the federal oversight activities. And also the report to the Advisory Committee to the Director of the NIH, we will have a report on that tomorrow morning. And an update on our report on the oversight issues. And then we will return to what issues are still in front of us regarding stem cells at that time.

So we have -- we should -- we have a lot of time allocated for our discussions around this report and an awful lot of issues to discuss.

Now the way I would propose that we proceed today is I am not going to ask the commission to go

through this report, chapter by chapter, at this meeting. I think there are substantive issues which we have to address and we ought to turn our attention to that.

I know that some of you have received the latest version of this report just on Saturday or depending on if you were traveling you may not have yet have even received it but there are substantial changes between the edition -- the version we sent out approximately ten days ago and the one we sent out three or four days ago. And for those of you that need a copy if somehow your travels did not enable you to get the second copy I am sure we could find a way to get you a copy today.

We are very anxious to get from the commission members any suggestions they have regarding the particular chapters themselves, editorial suggestions of any kind, plus any substantive issues. I, myself, have noticed even in the latest versions there are a couple of places where, in fact, the report is wrong, it is just a misstated. Our position is simply misstated and so I ask you all to go through that extremely carefully as we will do and as I will do, and I spent most of yesterday going through the second version, and still find some issues which need to be addressed.

But I do not want to get bogged down today

into various kind of editorial suggestions, important as they may be. I would much rather focus on the substantive issues.

So I have made a list myself of six issues which I want to discuss explicitly with the commission and then, of course, we will go to the chapter six where we can look at particular recommendations and through that discuss other issues that will come up at that time.

I think that is the most effective way of getting resolutions on any issues that might separate us and then we can focus on just how we want to structure the report, whether the current chapters ought to appear in that order or some other order, or whether current chapters four and five ought to be collapsed into one chapter, and whether chapter -- I guess it is chapter three now, which is the ethics chapter, ought to be chapter five and so on and so forth. Those are all significant issues but not issues which I want to put as a first priority to discuss today.

So let me indicate which issues I want to specifically revisit before we even go to the recommendations just to make sure that we understand where we are and so the report writing can proceed.

I will just list them in no particular order of importance just to give you a sense of the issues that

I would like to revisit with you and then I will turn to Eric to see if he has any other issues to pass on to the commission and then we will go directly back to those issues.

The six issues that I want to discuss even before we get to the recommendations themselves are, one, what it is we are going to say in this report as opposed to what we said in the letter that we sent to the President last -- about six months ago regarding the human-animal hybrid issue. Again just to talk in shorthand about these matters.

The current version of the report simply reiterates in a rather terse and offhand -- I would not say offhand, but rather terse fashion. It says, "Here is what we said." Now that may not be as sufficiently responsive and we want to decide where we really stand on this issue and, in particular, how we want to put that in this report.

I want to secondly revisit the issue of the way we have divided the sources of embryos in this report, that is we have those embryos, for example, created solely for research purposes, and we suggest treating those in one way and those -- and other embryos from other sources in other ways. I want to revisit that to make sure that is central to our discussions. It has

been central to our discussions all along. I just do not want to leave it -- you know, make sure that we have explicitly addressed that and remain comfortable. After all it is discussion with that distinction.

The third has to do with the oversight, national oversight and review. It has an acronym in the report, I guess, of NSCORP but anyhow whatever name one gives it. There are two critical issues to discuss there in my -- there may be more but there are at least two.

One is that as the recommendations are currently written in the current version of this, the national oversight and review really is two parallel review mechanisms in the following sense:

That the protocols using materials derived from fetal tissue really -- if you look at those recommendations carefully -- flow into the current oversight mechanism, modified and amplified somewhat as we have suggested, whereas only those that deal with material derived from so-called excess embryos go to the new national oversight.

That may be an artifact of just the way these were structured and it would not be a big job to change that so that all, let's say, went through NSCORP and I want to explicitly review that with you to see what the commission would like in that respect.

The second issue has to do with the national oversight, is what criteria this oversight is expected to consider. I, myself, do not find satisfactory the language that is currently used in the draft of chapter six which talks about rather broadly speaking social issues which makes me really rather uncomfortable and whether it is -- I have forgotten the language used -- worthy of, or something like that, federal support. Anyway it seemed to me to be looking much more at a priority issue than an ethical issue and I, myself, think this needs to be clarified and we have had some discussions of that and I want to return to that today.

The fourth issue is not an issue discussed before but it has been very much on my mind and I want to -- I have some ideas on it and I want to see where the commission feels, and that is the question of the international movement of these movements. And for us, I think, the issue really focuses on what, if anything, we want to say about materials of this nature that might be imported, that is sourced abroad, and what criteria those need to -- we want to lay down in that area.

I have sort of a rough idea of what I call international equivalents, that is it ought not to matter where it comes from. Our criteria are what they are and they have to be set aside no matter where they come from

but I mean that needs some explicit discussion.

The fifth and probably perhaps the easiest one of these to deal with is payment issues. You may recall that in chapter six of the current version the -- it suggests that there be three different levels in which activity may be involved and asks for restrictions on level one, if you recall, and no restrictions on level two and three.

I, myself, find that really rather problematic since there is no guarantee of any kind that these units would be separate from each other and, therefore, it is an arbitrary issue of transfer pricing and it does not seem to get at the issue. I think it also be a level two detail for this report but in any case we need to discuss it to make sure we understand what message we want to send in this respect and then we can worry about articulating it.

Finally, there is an issue which I know has received a lot of discussion, and that is the issue of distinguishing between use and derivation. My own view is that the language that at least we have used in some of our versions is in some sense unfortunate in the sense that it has been interpreted not unreasonably given some of the language we have used as saying that there is no ethical distinction between use and derivation.

I can only now speak for myself on this issue, not certainly for the commission, and that is certainly what -- was not what I was thinking as we were talking about this. I think that is not the relevant issue, whether there is an ethical distinction between use and derivation. The issue is whether both these activities should be eligible for federal funding, whether or not there is an ethical distinction between them but we need to revisit that together so that we can understand how we feel.

Now I have mentioned these six points because as I think about drafting -- helping to draft the final report, I really need to understand where we stand on all of these before I can really in my view feel satisfied with it. There may be other issues which other commissioners will want to bring up.

So if there is no objection we will just deal with these issues and begin our discussion with these issues and then see if there are others of substantive issues of this nature which the commission wants to discuss but then go to the recommendations and just go through them one by one and see how we want to alter them and which ones we find acceptable and which ones we do not, so on and so forth.

Yes, Larry?

DR. MIIKE: Will we have an opportunity to make some general comments about the report before we get into that because I have some concerns about the current draft of the report so I do not want to go directly to the recommendations. I would like to be able to say something about those before we go into the recommendations.

DR. SHAPIRO: Fine. That is okay. I just do not want -- I have no problem with that at all.

DR. MIIKE: Not editorial.

DR. SHAPIRO: I do not want to get bogged down with that. We need that -- we need the help there. It is not that we do not need help from the commissioners on that. We need help. I just do not want to use our valuable meeting time for that. I would like all the commissioners to do what I have done, only do it even better, and that is that I really extensively marked up my current draft, and will give that to the staff before I leave so that we can -- they can take whatever benefit there is of that. I hope as many other commissioners as possible will do that as well.

Certainly we can seek to deal with general issues. So let's do that just before we get to the recommendations themselves.

Ruth?

DR. BACKLAR: The remark that I would like to make -- do I have to press something?

DR. SHAPIRO: No, you are on.

DR. BACKLAR: Even though this is not -- the remark I am going to make will only -- the issues that you have discussed would need to be discussed first but I am concerned about one thing, and I mentioned this to Eric, and that is that we early on in the report refer to Pat King's remarks about overlapping opinions and consensus and we never in the report actually look at that. We never say, well, this is where these opinions overlap and that was another issue.

We are not talking about overlapping consensus. We are talking about overlapping opinions and then you get consensus. It seems to me that if you are going to write a report like this you are going to have to show that somewhere where you do have that. That is all.

DR. SHAPIRO: Let's -- we can deal -- you know, we ought to take advantage of all such observations and that would be extremely helpful.

Eric, do you have anything you want to add at this time?

EXECUTIVE DIRECTOR'S REPORT

DR. MESLIN: The only thing is to inform the

commissioners that we do have another staff member joining us. Behind you is Dan Powell, who is an undergraduate student joining us from Princeton, who will be with the commission's staff for the rest of the summer and we are delighted to have Dan with us. There will be some other staff announcements at upcoming meetings.

DR. CAPRON: A question?

DR. SHAPIRO: Yes, Alex.

DR. CAPRON: Understanding that we are not going to go through the report piece by piece, there are a number of topics in the recommendations which are not included in your list of six issues. Do you plan to go through the conclusions and recommendations in addition to those issues or do you want --

DR. SHAPIRO: Right, absolutely. Yes. And I do not mean these to be a discussion to be restricted to these. I just want to get to these six now. There may be others we want to add to it and then we will go through all of the recommendations. These are just six that came to my mind as I read through the report. That is all.

DISCUSSION OF DRAFT REPORT

DR. SHAPIRO: Okay. Let's begin and we will just begin with the list that I generated and see where people stand.

The first one, I am going use shorthand in a lot of my discussion today so I will just call this the "human-animal hybrid" issue. It is my own view that this is too tersely dealt with in the current version and that we have a responsibility to say something more than we have said so far but I would be interested in how other commissioners feel about this.

Larry?

DR. MIIKE: I read those as separate issues. I thought that the very short letter that was sent early on about that issue was the end of it. And then the second question was they had spent a whole lot more time on the stem cell issue. So I do not really see the need for us to get into any greater detail on hybrids because the issue does not seem so much -- we are clearly separating the issue about chimera human beings from the issue about stem cell research.

I do not want us to start wandering through those areas because that is a whole other topic. Anything along the line of the animal-human hybrid at whatever level of cells seems to be able to be covered by our discussion about the embryonic tissues as well as the stem cells so it would just be a subset just like somatic cell nuclear transfer is just a subset of creating embryos for research purposes.

DR. SHAPIRO: Other comments?

Carol?

DR. GREIDER: I guess I agree with you that it comes very quickly and then is not really dealt with again. Although I agree with Larry that we sort of dealt with this early on, it does come up as a source of stem cells and it might be better to point that out throughout the report rather than, you know -- or be more explicit of that, that people are talking about using that source as a source of stem cells.

DR. SHAPIRO: David?

DR. COX: So I agree with both comments that were made. I think that my primary comment is that I think that this issue of the human-animal hybrid tends to confuse the issue in terms of the stem cells. And although it is stated that human-animal hybrids are a source of stem cells, I, for one, am extremely unhappy with quoting New York Times newspaper articles as the basis of scientific fact. I feel so strongly about it that I really would object to that being included in the report as a basis of scientific fact.

On the other hand, to point that -- to make that point that although it has been stated that this procedure is a source of stem cells, the evidence for that does not exist in my view, scientific evidence, and

to also point out that to do this would involve the creation of embryos for research purposes, which as we come to point number two, I think -- to lay out that that is the context that it would be in.

But to summarize, I think that Larry is right. It confounds separate issues. It makes -- the issue of stem cells is complicated enough without dealing with human-animal hybrids. And to clarify the point of why they should be separated because right now there is no evidence that this approach -- evidence by my view that this approach has been successful at making stem cells and that it would require making embryos for research purposes, and leave it at that.

DR. SHAPIRO: Bernie?

DR. LO: If I can make a sort of more general comment, which I think this specific topic illustrates, one of the problems, one of the challenges we face at a certain point, I think, is the -- we need to focus on the big issues and not spend disproportionate time on minor or side issues.

So in that spirit I would support what I think Larry and David were saying, not to get into something which right now is not that important and really I do not think is the major source of concern.

My second point is that I think that we need

to be very clear that we are talking about policy issues that have to do with federal funding, not the sort of -- the underlying ethical problems of would it ever be ethically acceptable to have this kind of research.

I think the more we can sort of focus on the policy level of what is appropriate for federal funding and not get into ethical issues which we are not asked to deal with -- I mean, there is nothing, I do not think, that is going to stop a private corporation from trying to do that and we may have ethical concerns about that but I do not think that is necessarily the topic of the report and that I think is what drives a lot of the interest here.

You know, boy, if you could do this or if you could do that, you could -- would that ever be acceptable and I think that is a different report than what we should be trying to write.

DR. SHAPIRO: Let me tell you what my own thinking on this is. The language we used in that letter -- that letter, of course, was written as thoughtfully as we could in a very big hurry. We had to get -- to respond within a day or something. And I am very satisfied with the letter. On the other hand, the letter uses very strong language. It uses, "In this connection should not be permitted." It does not say should not be

eligible for federal funding. It says, "Should not be permitted."

I am trying to decide in my own mind whether I feel it is appropriate to leave what we have to say to that. That is about as strong a statement as you can make. And in trying to think this through I need some help from some of you who are certainly much more qualified to talk about this than I am.

As I try to think it through I imagine a situation in the future some time when let's say we know a lot more than we know today about just how human development takes place in its various -- in its early stages when we know a lot more about how the mitochondria and other -- and egg and the sperm interact, and how that message system relates and supports each other. And when at that time we know a lot more about that and would I still be happy with the "should not be permitted," which is a stronger statement than "federal funds should not be used."

And again just speaking for myself, I do not know what I would feel. It would depend on the nature of the scientific evidence at that time. I agree with David that we do not really know what has happened here yet. And certainly the New York Times would tell us. No one has told us. Not only the New York Times.

So we cannot -- but as I think about it in relation -- and I do not think we should spend a lot of time in our report on it either but as I think about it in relationship to the report, as Carol has said, this is another source -- potential source. We do not know if it is a source because we have not characterized whatever it is that is produced here in a way that -- at least as I understand it. You can correct me, Carol and David.

But it is a potential source.

But in any case it would be what we have called research embryo even if it was a source. We do not think this should be eligible. If we stick with that distinction this would just fall into the category of things that are just not eligible for federal funding and that is where we stand if that is how one feels about it. That is how I was trying to argue it through in my own head.

Alex, Bette and then Eric.

DR. CAPRON: I think Bette was --

DR. KRAMER: That is all right.

DR. SHAPIRO: I do not know who was first.

DR. CAPRON: I will wait. I will yield to the lady from Virginia.

DR. KRAMER: I can understand that what you are not comfortable with is the absolutely phrase "should

not be permitted." So as I looked at it, it seemed to me that it was something that ought to be discussed as one of the possibilities of scientific investigation in the science chapter. It could then be referred to when it was appropriate in the following recommendations, as we discuss possible future developments and how future -- how the possibility of future advances ought to be handled in the scope of the general recommendations that we are setting out in this report.

DR. SHAPIRO: Alex?

DR. CAPRON: I have a sense I missed something because I was not at the Miami meeting when the letter was drafted but I thought the letter was much less controversial than you are presenting it right now. What was not to be permitted was the creation of a child through this methodology. That is fully consistent with everything we say even if it were a human egg and not a cow egg. So that does not seem to me is the topic of this report. That was the cloning report.

And it seems to me that at other points in the letter you say these fusion technologies have many uses, some of which are valuable. I think we are then on the ground that Carol and David have sketched out, which is it is not yet established that this a source of stem cells.

If it were a source of stem cells there would be scientific questions as to whether the stem cells would be as useful for the many other scientific or other uses as ones derived without hybridization but we do not know that yet and there is nothing in principle that would say that that is -- raises problems different than the ones we deal with in this report, which, as David said, immediately become the creation of an embryonic line for the purpose of harvesting the stem cells.

So I am satisfied with what we do with it although it is very brief at the beginning of chapter one and then the appendix A with the letter.

But have I misread your "should not be permitted?" I thought it was restricted to the creation of a child.

DR. SHAPIRO: I would have to go back and check to be honest with you.

DR. KRAMER: That is what it says.

DR. CHILDRESS: I think it does say that, in fact. We do have it in the packet. As I look at section three it looks as though if this line of research does not give rise to human embryos we do not believe that ethical issues arise and so forth. Indeed, we see certain possible advantages of going in this direction without the need to create human embryos at some future

point.

DR. SHAPIRO: Okay. So as I understand where we want to come out on this, it is -- my own view of what I am listening to here is would cause us to add a few sentences to this report, various possible -- not to change anything, which is -- would be fine with me.

DR. CAPRON: And not, in effect, to amend the letter.

DR. SHAPIRO: No, I do not want to amend the letter.

DR. CAPRON: Well, I thought you were saying that that language was perhaps too absolute.

DR. SHAPIRO: No, I was trying to just point out -- excuse me if I was misunderstood. I was just trying to point out that trying to figure out whether we wanted to say something really strong or not. That is what was on my mind. And my view is that I am perfectly comfortable with what Carol and David had to say. I am not comfortable with -- however, with just -- I think we need to say a little more in the report but it is in terms of sentences. It is not in terms of chapters. We have to say more to -- and maybe some of the kinds of things that Bette said might be helpful as well.

Okay. Let's go on to the next one. We have been making the distinction all along in our own

recommendations, it is perfectly well reflected in the report, between embryos or material -- between research embryos, we might just use that, and other ways of deriving these kinds of materials. And I just want to make sure everyone is comfortable with that. That has been a part of what we have -- we have been on that path for a long time. But nevertheless this is a time when we are going to decide once and for all, you know, whether that path is right.

We will have to think about just how the recommendations read but does anyone have any concern about that distinction?

Carol?

DR. GREIDER: So you are talking about the there different distinctions. One being derived from fetal tissue. Two being spare embryos. And three being creation for research purposes. Because I do have some concerns just about the language and the ways things are stated in the third category of the creation of embryo for research purposes, and that has to do with sort of the language and how things are structured in that sentence, in that section.

And, specifically, it gets to the issue of a statement that is made in chapter six on page 19 that the issue of somatic cell nuclear transfer and that creation

of an embryo by -- the product of somatic cell nuclear transfer is clearly a human embryo. I think that that is a statement that is perhaps too strong and I know that this is -- we have gone around about where we are going to put somatic cell nuclear transfer.

But I would feel much more comfortable stating that it is highly likely to be or is very likely or is thought -- you know, evidence would suggest that because I think we do not know scientifically -- we do not want to have people who do the experiment to know whether that is a human embryo or not. The only way to do that is to create a human.

And so given that I think that the structure of having the issue of somatic cell nuclear transfer come before in vitro fertilization to generate a human embryo is backwards. Clearly generating a human embryo by fertilizing with a sperm and an egg is creation of a human embryo. So I think we should deal with that issue first and then put the somatic cell nuclear transfer second and not state in such strong language that we believe that this really is a human embryo becasue there has been some debate. I would not want to get into those issues about whether it is or is not but I do not think that we can state it as clearly as we do that it is.

Then the third thing would be very careful in

the language in dealing with that that we are talking specifically about taking a diploid nucleus and putting it into an enucleated oocyte because somatic cell nuclear transfer can refer to a lot of other kinds of activities. It does not have to be transferred into an oocyte. It could be transferred, for instance, into a stem cell. You could create a stem cell first, take out the nucleus, and then put in another nucleus. That would still be somatic cell nuclear transfer.

I do not think that we are very careful in the language here to distinguish between those possibilities.

DR. SHAPIRO: Thank you. I do not have any trouble with that. That is very helpful. We want to write this as accurately as possible. From what I understood, Carol, I quite agree with everything that you have just said and that is also consistent if I have understood what you have said with the distinction I think we are attempting to make here and so I am perfectly comfortable with it and we will certainly work hard to get that.

DR. CAPRON: Could I ask, Carol, do we know whether the last possibility from animal work is feasible?

DR. GREIDER: I certainly do not know the

answer to that question. However, I think it is probably going to be the first thing that is going to leap to a lot of scientists' minds especially if one says that it is not appropriate for federal funding to take an enucleated oocyte. Certainly it would be the first thing that I would -- that would leap to my mind. I do not know of any published experiment that has done that. Not that I know of. That does not mean it has not been done but I am certainly not aware of it.

DR. SHAPIRO: Other comments or questions?

Bernie?

DR. LO: Going back to the bigger issue of the sort of tripartite organization, I think that is something we have talked about. I certainly support it. I think the consensus we reached -- I think Carol's comments are really helpful.

I wanted, again, to sort of voice my concern that we have not really met the challenge of addressing the issues on the level of federal funding for some levels but not for others. Most of the -- I think we have not really integrated chapters three and six and I am concerned that some of the conclusions in chapter six not only are not built up -- are not led up to by chapter three but chapter three actually reads in a different direction.

I am really concerned that the arguments in chapter three again are philosophical arguments. Are there ethical moral distinctions between A, B and C? And that question is, is there an ethical warrant for funding of some of A, B and C but not all of A, B and C? And there are prudential pragmatic issues about addressing -- going slowly, preceding with caution to use the Canadian language, which I like very much, which I think we really need to develop because the arguments in chapter three are not, I think, going to be a persuasive compelling argument for the conclusions we reach and we need to get a better foundation for that. It is a challenge, I think, we really need to try to address.

DR. SHAPIRO: Eric?

DR. CASSELL: I would not like to see us be too narrow about simply federal funding. Although we may revert to that and say specifically federal funding, we should not preclude ethical arguments on a wider basis. For one thing, if we do that on this narrow basis we are talking about today only and the document does not offer guidance for people in the future. Also, I think we have more to offer than that around this table and I think we should use our expertise more broadly.

DR. CHILDRESS: I do not know whether this is the appropriate time but I would like to pick up for a

moment, if I could, the comment that has already been made about the relation of three and six, and I do think that a lot of work is needed there in order to bring the two together in a way that is coherent but that also can present to the public and to policy makers some sense of our wrestling with these issues. I think in one of Bernie's e-mail comments he noted that there was really no sense here of the kind of dilemma that many people experienced in this and I think a sense of that kind of wrestling somehow gets washed out in chapter three and then chapter six becomes much too detailed in its discussion so that I find myself losing the thrust.

So if we can keep our big questions in mind, and there may be some debate, I tend to go along with Bernie on the view that federal funding is the thing we have to keep foremost and some of these other issues are secondary to that, and may have to be addressed as part of our effort to deal rigorously and helpfully with the question of federal funding. But if we keep in mind what our fundamental task is and let some of these other things fall into place accordingly then perhaps we will have a report that will really do what we want it to do and accomplish its ends.

DR. SHAPIRO: Anything further on this sharp distinction that we have drawn between research embryos

and other material?

DR. CAPRON: I perhaps lost between the comments of Bernie and those of Eric the train of thought because it seemed to me that the thrust of what Bernie was saying was that we were not restricted to talking about the funding issue and he thought that some of what was in three had much broader implications and then Eric it seemed to me took that the next step and said, indeed, if we want to be helpful to people in the future we should be grappling with those issues.

Jim's comment was closer as he began to what I thought the report was about, which is about the federal funding issue. In other words, I do not actually see any concern being raised that as with the cloning issue our commission would be in a position to say there should be statute passed at the federal and state level prohibiting any of this. In the absence of that prohibition then we are talking about activities that we can expect and we already gather between the work by American Cell Therapies and Geron and so forth is going forward.

So the real issue is does it go forward with federal support and with federal scientists involved?

Now that being the case I agree with Bernie's e-mail, which Jim also endorsed, that we have to make

clear why federal funding has any moral imperative to it that a prohibition on federal funding would defeat or would undermine that imperative to be able to have this work go forward in the way that other important work does but I still see the federal funding as the major issue.

Now is that what we are all saying because for a while I thought Eric and Bernie were pushing us in a broader direction and I do not really think we should get into too much of a broader discussion nor do I think the oversight mechanism that we are talking about having set up -- while we need to give it some guidance and criteria, and you come to that later as one of your other topics, I see that still in the context of at the future would steps arise with -- would occasions arise where the federal funding would be extended to other categories of the creation of stem cells? Not a general question of should there be prohibitions or should there be something else on this?

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I tend to see it just the opposite. It seems to me that our major focus is on the ethical issues and the implications of the use of stem cells. And that the issue of federal funding then follows from whatever we would recommend or determine with respect to the ethical issues.

So I would not put the federal funding as the first priority for this group but rather the ethical issues as the priority and then the federal funding would follow from that and it raises a question of whether or not we would believe that although certain -- we would recommend that certain research would not be federally funded that it would be okay to do, and I do not think that is what we are saying.

Does that make sense?

DR. CAPRON: You said we would not get to that issue?

DR. DUMAS: Huh?

DR. CAPRON: We would not get to a statement as to whether or not this work, although not federally funded, would be okay to do?

DR. DUMAS: Well, see, my concern is if we are going to look at the ethical implications and we do not believe that certain kinds of -- that we are at a stage to support a certain kind of research as ethical to do then the -- then we are not recommending that it be done. We do not have any control over what happens in the private sector. We may not have control over what happens in the public but what would be follow would be that based on the implications -- the ethical implications that the government would decide that they

are not going to fund that kind of research.

DR. SHAPIRO: Bernie, and then Carol?

DR. LO: Well, let me try and clarify what I tried to say earlier because I think I may not have been clear. We were asked some very specific questions to comment on and I think it is our duty to give recommendations on those questions, which really had to do with federal funding. Having said that, I think clearly we were asked to give the ethical rationale for those recommendations. To that extent I definitely agree with Rhetaugh that we should look at the ethical arguments and construct the strongest possible argument for the conclusions and recommendations we choose to make.

My concern is that when I read chapter three and then read chapter six, I do not see that connection. In fact, I think it goes the other way. In chapter three, if I were to ask my students to coiffure out the last part and based on what you just read tell me what the recommendations ought to be, we would sort of like -- in chapter three there are not a whole lot of distinctions between different categories, which in chapter six we turn around and say we are going to fund this one but not that one.

I think it is that sense of disconnection

that bothered me a bit. I think we need to come up with an ethical rationale for the conclusions we reach. Now we sort of went about it in a way that let's see what we can agree on but then there has got to be an ethical rationale for that agreement. I do not think we have really articulated it yet in chapter three. I think it is really imperative we try to do that.

DR. SHAPIRO: Carol?

DR. GREIDER: In response to Rhetaugh, I read this whole report as being very limited to the issue of federal funding for these issues and I apologize I have not been here for the last two meetings but when I read it, it looked like it was very narrowly focused and I was not exactly sure where that came in.

Now if we were to address the issue of the -- all of the ethical issues irrespective of funding, I would have a very different feeling for the recommendations. I would not come out in the same place that I do.

So that would shift a lot of the issues so I think it is important to know what we are really talking about recommendations for and also I think that because of that we should be very careful in the report to state what the implications are for saying that we are going to support or not support federal funding.

For instance, if we do not support federal funding for a particular area we have to recognize that it is going to go on in the private sector and what are the implications of the fact that these things will go on in the private sector and that you are not allowing in federal oversight because it is not supported by federal funding. And I think that we ignore that issue entirely in this report. Just what are the implications of that?

DR. SHAPIRO: Jim?

DR. CHILDRESS: In response to Rhetaugh's suggestion, it seems to me that there are ethical issues surrounding the question of federal funding and that our primary task is to try to explore those and to see which way the ethical arguments point us in relation to the question of federal funding but we could talk about a lot of other ethical issues.

And I guess one question would be whether, indeed, we go too far astray at some point in talking about other ethical issues and do not focus specifically enough on those that would actually relate to the question that we have to address.

So there would be a wide range of ethical issues that we could cover here that I am not sure we should and it seems to me that much of the question is the focus but if I might add to that. It seems to me

that closely connected to it is the question of style and rhetoric and that where this report falls down at this point to a great extent is that there is no cohesive style throughout and that is not simply a matter of -- I think it is something irrelevant to substance but rather is closely connected with it because it is really through how the report is written that we can -- this is what I called earlier this sense of wrestling.

And if we cannot -- well, I just urge you to speak very sensitive to that in trying to work this out because I think that whatever impact the report has will depend to a great extent on what we are able to do on that level.

DR. SHAPIRO: Larry?

DR. MIIKE: I think we have been discussing the ethical issues around it and it has been related to the source of the stem cells, and going back to the Princeton meeting if I did not articulate it in an ethically literate matter, I did say or laid out what I thought my opinion was in terms of cells from aborted fetuses, cells from excess embryos, cells created from embryos for research. And I think the current drafts are -- the draft is making an attempt to raise the ethical issues that are particular to each of those areas.

And then when one looks at that there is a

spectrum of ethical issues that gets more complex -- less chance for a consensus as we move along to the embryos created for research purposes only. And there is a direct relationship to that with federal funding.

And what we are saying or at least I am saying is that there seems to be enough promise now in this -- for the fruits of this research to allow federal funding for some aspects of it all and there does not seem to be such a shortage that we need to create embryos for research and that the research does not seem to have gone to a point that we need to create embryos for research.

So what we are coming up with is saying that it is okay in cases one and two and then we move on to the review mechanism that is going to take a look and see whether, in fact, the research is coming up with a promise that we think it has now and then a reassessment of that at some later time.

So I think that we are discussing the ethical issues around this and it is in relationship to the federal funding but it is not one or the other and I do not think that we wander off into a long discussion about the ethical issues around these and get away from the federal funding side.

The thing that bothered me about chapter

three, and I do not have the most recent version, was that it raises this ethical issue. It shoots them all down and it leaves you with nothing. So I do not know where we go with chapter three.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I just wanted to clarify the source of this discussion, whether we are to be focusing on federal funding and the associated policy issues or broader ethical issues. And is it that President Clinton's letter to us asked us to focus on federal funding? Is that where that idea is coming from?

DR. SHAPIRO: I do not think that is where the idea comes from, no. I think -- I mean, I think it is an interesting conversation if I may say so. I mean, every time we decide to go one way, and the committee at the next meeting says we ought to go the other way, and every time we decide we ought to start with a general and go to the specific, at the next meeting we hear we ought to go from the specific to the general.

So I would really ask us to really think a little bit about how we got here. It really is quite simple and it is not to argue that the rhetoric is appropriate or that we could not substantial improve what we have. I think we certainly can and should. But I think it really is really a rather simple matter.

We -- if you recall back when we knew we had a limited -- well, let me start it a different way. One cannot deal with -- in my view with the ethics of federal funding without reminding ourselves what the general ethical issues involved here are all together. It is just specious to think we could do otherwise.

And so it is not say we have done it properly or it could not be improved or so on but I think we have to for the purpose of the -- we have an education job here as well as just a policy recommendation job here. And so I think it is really irresponsible for us not to try as best we can to lay out the issues but I accept the point that we have to lay them out in a way that is most helpful in also pointing to where we are headed but not only to where we are headed because other people will head in different directions.

We have laid out arguments which is quite correct in chapter three which other people might take in some other direction. I do not see there is anything wrong with that. This is not a restricted set of arguments focused just on why we are recommending what we are recommending.

Now I think that we got to this point because we did focus -- we decided early on to focus on whether or not we thought that these were -- what this

implication was for federal funded. We decided very early on that is where we are focused on and that is where our recommendations took us.

We decided very early on that we were not going to address the issue sense of what would be morally acceptable for people in the private sector without federal funds to do. We could -- the chapter three contains observations which others might -- they can use to decide what would be appropriate to do in the private sector. We decided not to take that on and to focus on what was appropriate and what kinds of activities would be appropriate for federal funding, and that is where we are headed. What kind of oversight we would need.

Now I do not want to get us into an argument here -- that is exactly what I was trying to avoid -- as to just how chapter three ought to be structured. We need a lot of advice on this and I am very appreciative of all of it because it could certainly be and needs to be substantially improved.

So where we are heading here in our recommendations is deciding what we think is appropriate for federal funding and why.

Now it simply is not true in my judgment that ethical issues or ethical reasoning would lead you to say whatever is appropriate for federal funding would also be

appropriate for private funding and vice versa. That is simply not a sustainable position in my view. I think you can very well make an argument and I think that the requirements for federal funding in a morally contested area -- and after all we are here because this is a morally contested area.

This is not an area where someone has an ethics which says, look, this is the result and there is no other possible result. We are in an area which is genuinely morally contested. That is different approaches to this will yield somewhat different views and in a morally contested area one has different requirements for federal funding than what would be true for the sector over all, and that is what is driving us here.

If you look at the material, I now do not remember exactly which chapter it is in at the moment but there is a description there of why it is -- what one would sacrifice from an ethical point of view if federal funding were not allowed in this area all together.

Now one does not have to be convinced by that argument but there is an argument laid out there as to why federal -- or ethical issues as to why the federal funding is allowed or not allowed.

Now we have to face the fact that in this

area, an area as complex as morally contested as this, that what we are trying to do here is recognize that there is moral disagreement out there and trying to design a federal policy that acknowledges the moral worth of other points of view besides our own and reach some kind of a compromise that really reflects both different kinds of ways of approaching this and morally relevant ways of thinking about this issue.

There is no right -- absolute right and wrong in my judgment. This is now speaking for myself here. But I do think it is important for federal funding to do as -- for federal actions in general and federal funding in this particular case to do as good a job as one can to reflect the moral worth's of different points of view here and that is the division we tried to make.

And we made that division early on by saying that one way to do this, certainly not the only way, and that is what I was really trying to focus on here, is to say that some of these sources would be acceptable for federal funding and some would not, and that is the way it is structured.

It still seems to me a very good structure. That is not say we have argued it correctly or it is not to say that we -- I mean, there has been some very excellent suggestions made here today by Bernie and Jim

and others here which we ought to try and incorporate but it is very important to understand what it is we are crafting here. And I think -- in fact, it has been remarkable that really -- you know, we decided when we wanted to go about this that we should begin by thinking of what it is we wanted to really recommend.

We did not decide to begin the other way around. We sat there and said we ought to begin by deciding what it is that we feel good about recommending and then try to build the best possible case for it and that is the way we have gone. We have learned as we have gone along. We have learned from other people. We have learned from our hearings, which have altered some of our thinking, and especially some of the rhetoric that we use, and we have learned from lots of different people as we have gone along in this effort.

And so I think in this area when we are trying to decide about the research, embryos versus others, as legitimate sources or legitimate areas for federal funding, it still seems to me viable. From what I hear around the table everyone seems to agree with that although people disagree with just about how we articulate it which is an important issue. I mean, I want to acknowledge that is important.

But I want to now come back to what I -- a

point I raised and only that point right now. Namely whether that -- call it a compromise if you want or that configuration of the ethical issue still feels comfortable to people or whether people take some serious exception not to how it is argued, which is another important issue, but to the basic idea itself.

DR. DUMAS: That is very helpful to me and perhaps because I missed some sessions. I had missed that point and I appreciate that. So I feel much more comfortable with the focus that you just described. And I am sorry about moving off the point -- off the focus.

DR. SHAPIRO: We are all struggling along.

DR. DUMAS: Yes.

DR. SHAPIRO: We are struggling. As Jim says, wrestling. I think that is right.

Alex, Bette and Carol.

DR. CAPRON: I had three quick points. The first is I do not think that we in this area should confuse federal funding with federal oversight.

DR. SHAPIRO: Right.

DR. CAPRON: It is certainly possible in our whole human subjects discussion to talk about things that are not federally funded but where we think oversight is appropriate.

DR. SHAPIRO: Right.

DR. CAPRON: The second thing is that I think the framework that you have articulated as a reiteration of how we came to this point and so forth, it might well be that if we reverse chapter four/five with chapter three it would be clear because then we would, in effect, say the present resolution of the ethical balance has been as follows as to the fetal tissue and so forth. Then ethical reflection on the current wrestling or balancing in light of what is known so far and with an eye to questions that will arise as the science proceeds, and then the answer "on federal funding."

The third point -- but maybe you want just to limit -- because my third point goes to sort of the weight of the process on the federal funding issue. I do not know if you did not want to talk about that but just the three. If so, I would like to have has a seventh issue this question of how one links the federal funding issue to the broader issue.

DR. SHAPIRO: Let's leave that until we get to the oversight area.

DR. CAPRON: Okay.

DR. SHAPIRO: Bette?

DR. CAPRON: I will be back.

DR. KRAMER: Harold, thank you very much. I think that is a very helpful review of where we have been

and where we have come to. I think the problem that I have been struggling with is I am very content and I think it is a good way to consider it the way that we have broken the issue down. I think that as I have read the material and I have read the reports in the press and thought about it over the past month or so that we made the assumption or we made the decision that if the use was okay the derivation was okay.

And I think that that is where -- that is an issue that I have revisited in my own mind and I would like us to revisit because again going back to remarks that were made earlier in terms of reaching a compromise position in a morally charged area, it may be that there is room for a compromise if we consider each of those possibilities separately.

DR. SHAPIRO: Thank you very much, Bette. We will revisit that issue explicitly. I think it was the sixth on my list. No priority order but I think that is an important issue.

DR. KRAMER: Right. But I think that it is hard to get to some of the more technical aspects before you consider -- to me that is very basic.

DR. SHAPIRO: Yes. I am certainly happy to get to that sooner rather than later. It is no problem for me.

Bernie?

DR. LO: Carol.

DR. SHAPIRO: Excuse me. Carol and then Bernie. I apologize. I am losing track of my list here.

DR. GREIDER: I would just like to respond to something that Larry said a few minutes ago. If I could paraphrase you, this was sort of -- again the three issues. The derivation of stem cells from fetal tissue, the derivation from excess embryos and the creation of embryos for research purposes. And you said that you thought that there was -- the consensus was that there was no need currently to create embryos for research purposes because it was not necessary at this point but I would like to point out that since we are including somatic cell nuclear transfer under that category it is not just whether things are available or not.

What we are saying is that there is a whole area of research that is toward deriving autologous transplant type material which we are saying is not appropriate at this time. It is not just the number of available research products but it is a whole area of research which we are setting aside.

I just want to be very clear that that is what we are doing here and when I responded to Rhetaugh earlier saying that whether we are talking about federal

funding or in general that I would come out different on the recommendations, that is the area where I feel I would come out differently. It gets back to the issues that we raised in the cloning report about cloning just to derive stem cell type materials versus cloning to create a human being.

I felt that we left open the area of creating material for transplants and we precluded the area of creating human beings and I felt very comfortable with that. So I just wanted to point that out that your three categories I did not feel actually reflected what we are doing here in the federal funding area.

DR. MIIKE: Can I respond?

DR. SHAPIRO: Larry. If you do not mind, Bernie, I think Larry has a response. Do you mind waiting?

DR. MIIKE: Exactly right and I do not have any problems with not funding stem cell research -- I mean somatic cell nuclear transfer research for stem cell purposes at this point in time and I do not think that is contradictory to our cloning report because the cloning report was talking about the universe of uses and we -- and, you know, we also had said about five year moratorium, et cetera, and revisiting. So I do not have a problem with that.

I think the research agenda is large enough in those first two areas that I feel comfortable about shutting out, to put it bluntly, this other area at this current time.

DR. CAPRON: For federal funding.

DR. MIIKE: Yes, for federal funding. Right.

DR. SHAPIRO: Bernie?

DR. LO: Well, I wanted first to second what I think a number of people said about how helpful your comments were, Harold, and I hope that language can be captured in chapter one, chapter three, chapter six because I think it really does set the stage of trying to form public policy in, as you put it, a morally contested controversial area.

To add to that I think that the way we went about doing things is very defensible where we start out saying what is it that we can agree on rather than what theories can we agree on. Every time I come to one of these meetings my kids ask me very tough questions about what we are doing and why we have to go back and do it.

(Laughter.)

Yesterday it was coupled with a question of what is an urban legend, which I actually got the wrong answer to, but I think I know what a philosophical legend is. There is this famous story about the old -- your

commission, Alex, the original President's Commission where Tolman and Johnson were sitting around and they sort of remarked that, "You know, we disagree on our fundamental philosophies but we seem to agree on recommendations."

And they actually constructed some fairly nice arguments as to why it makes sense to try and find where the points of agreement are rather than trying to go about it the other way and saying can we argue each other into each other's -- agreeing with each other's moral philosophy.

I think people cling to these agreements for different reasons and some of the reasons we arrived at would not necessarily stand up to the kind of logical analysis that is the brunt of chapter three.

I think if we can somehow get that in -- because otherwise I think we run the risk of being labeled as expedient. We reached our conclusions and constructed the arguments to support them. And that I think would be a very unfair analysis of that approach.

DR. CAPRON: It is like professional philosophers.

DR. LO: What?

DR. CAPRON: Actually the discussion you are referring to occurred on the National Commission but we

had our versions of it.

DR. LO: Okay. Whatever.

Let me just sort of add to Alex's point when we get, Harold, to your issue number three, the national oversight review.

DR. SHAPIRO: Yes.

DR. LO: To add as a subpoint the possibility of having oversight even if we do not fund it. I mean, there is this argument that is always raised, we must fund it because that is the only way to assure adequate ethical oversight and I just do not think that is the only approach to having oversight.

DR. SHAPIRO: That is very helpful and we will get to that point.

David?

DR. COX: So by listening, and it certainly -- my own view, I have not heard anything but praise for the logic in the argument that you laid out, Harold, beginning with the fact that not all things necessarily deserve federal funding.

And I think that to put that logic -- I am just sort of summarizing what everyone has said. To put that logic as a fundamental thing in the report is extremely important because I think that it is a confused issue. It was certainly confused by me. Well, how can

you have something that is ethical and fund it privately but not publicly.

Well, in fact, that is the compromise and that is how our society works. To state that up front is extremely important because I think that is the part that people confuse very much. Then we go forward from that. But then -- and then how is that being changed now?

So every one has said it but I would just like to also put my two cents in on that because I think that it lays a framework by which this starts to make sense to people.

DR. SHAPIRO: Okay. Arturo, excuse me, I am sorry.

DR. BRITO: Back to what Dave just said. I have written here a couple of points about this. I think, in part, at least at the root of disparity between chapters three and six is the fact that I believe we were basing a lot of our ethical arguments on the current laws and like -- I think it was Eric who said earlier that there are certain ethical issues that we are never going to resolve, either us nor any other commission for that matter, like the moral status of the embryo, et cetera.

So I think it is -- we put it right up front like David just said. It would make it a lot more cohesive and then chapter three and six would go a lot

better together and just say that we are -- you know, based on current laws these are what we recommend and these are the ethical issues within those laws instead of the other way around and I think it would flow a lot better.

DR. SHAPIRO: Thank you. Let's go on to another aspect of our discussion. Really on my list now, and I know there are other items coming up, there are two issues which I think are really critically important and one is the question of oversight.

DR. CAPRON: Would you object to following up with what you were calling six because six --

DR. SHAPIRO: No. That is what I was just about to say.

DR. CAPRON: Okay.

DR. SHAPIRO: I was just about to say that.

DR. CAPRON: All right.

DR. SHAPIRO: The two were the oversight issue and the use/derivation issue, again talking in shorthand here this morning. And I am quite happy to go to the use/derivation issue first since that is what Bette suggested. It is a critically important issue and so let's go to that issue now.

Again let me just begin by, I think, repeating what I said before. My recollection of our

discussion on this, and please correct me if I do not recollect this properly, is that we thought that if we were to say that the use of these stem cell lines would be eligible for federal funding that it seemed to us not entirely straight forward to say that derivation would not be eligible. It was not that there was no ethical distinction between the two. I think we used unfortunate language there a couple of times and I think people have noticed that.

But we did come nevertheless to some kind of tentative conclusion that if we were going to say at least from certain sources that the use of these cell lines was perfectly appropriate for federal funding that its derivation in our judgment should also be eligible for federal funding. That is different from saying these are ethically equivalent. That may or may not be the case and we can argue that separately. We do not need that argument to say this.

And as I thought about it at the time, my own thinking was that if we are going to create -- make their use available it is going to create a very significant demand for these cell lines and it was less than straightforward in my mind to say, oh, well, we can separate ourselves from the derivation itself. That was at least my own thinking on that issue but this is a

critically important issue. Let's just see where we all stand on it. Obviously there are people with different perspectives on this issue.

Who would like to speak to this issue?

Bette, and then Tom.

DR. KRAMER: Okay. As I sat down and read the report again, you know, from the beginning, I had two overwhelming reactions to the science chapter. I thought it laid out in a -- really in a very effective fashion all of the possibilities that the current advances could possibly lead to and I thought it made a very exciting and compelling case for continued scientific investigation.

At the same time -- at the same time when I thought about it at the end of the chapter, it seemed to me that there was a lot of basic science that yet had to be developed. Now, please, the scientists sitting at the table, correct me if I read that wrong, and I know these things can happen quickly or over a longer period of time and that the timing cannot be forecast. But those are the two impressions that I came away from the reading of the science chapter.

So at the same time over the past several weeks as I have noticed the reactions in the press both to our draft report and to those people who have a

problem with the use of embryos and I could see what was happening, and that was that people were alarmed by what was reported as our conclusions and I could see the forces rallying to shoot it down before we even had a chance to complete our deliberations.

I became concerned about it and I started thinking about where is there room -- where is there room for moral compromise and I am not sure if this is correct but it seemed to me that if we could separate approval for use possibly from approval for derivation at least for an interim period of time that possibly there was room -- now I am talking with regard to the use of the spare embryos.

I did not have a problem with the use of the fetal transplant because, as I read it, it seemed as though all of the regulations or most of the regulations were in place and that those issues had been worked through and had been more or less accepted.

It was with case two that I found that there -- that is where I thought it began to get very, very sticky and I went back and I reread Alta Charo's piece on the "Hunting of the Snark" and there were some other pieces that were presented in that briefing book. I have already forgotten which month it was. Maybe it was January.

And, you know, I was concerned because I did not want the same thing to happen to this report that happened to the Human Embryo Research Panel Report and I wondered where there was room for us to possibly address people whose position might be, whose moral considerations might be offended by that but nonetheless could be urged to make some sort of a compromise because of the potential for scientific development.

DR. SHAPIRO: Tom?

DR. MURRAY: Thank you, Harold.

I think this is going to be an important -- this distinction between derivation and use is going to be an important one in -- it is important just intrinsically and it will be important to the public perception of the report in my belief.

I think we have tended to conflate three different kinds of questions. Let me try to state what the three questions are as I understand them.

First of all, whether the derivation of these stem cells and the use of the stem cells are morally distinctive. That is whether they are different from one another morally. Secondly, whether either or both are morally justifiable under the current circumstances. And, thirdly, whether either or both ought to be publicly funded. Those are three separate questions. I think we

have gotten number two and three clear now that they are different. I think we have not gotten number one clearly different from number two.

Two former colleagues of mine from the Human Embryo Research Panel, Carol Tower and Ron Green, have written a letter to the commission, which I regret apparently has not yet been circulated but which will be circulated I am assured, where they reiterate their clear view that derivation and use are morally distinct but also their conclusion is that both can be morally justifiable and both -- in fact, I think they would support both for public funding.

But it is very clear that we could differ from them at either point two or point three but I think they are unequivocal about point one, namely derivation and use are different moral questions, at least different enough to warrant separate justifications both for permissibility, et al. and for public funding. I am glad to see that we are engaged in the issue and I will have more to say about that -- my own views on it in a moment.

DR. SHAPIRO: Alex?

DR. CAPRON: I agree with the position that you have stated and that Tom has reiterated that there are arguments that can be made to distinguish use and derivation but to answer Bette's concern I do not think

that the people who are most critical of the notion of work in this field who have already spoken up through the letter from the congressmen and the senators to Secretary Shalala would be satisfied or will be satisfied with the sense that the National Institutes of Health has tried to put forward that they are in some sense hermetineuically (sic) distinct categories. I mean, hermetically, excuse me. Not hermetineuically. Excuse me. Hermetically speaking. They may be hermetineuically distinct, too.

(Laughter.)

DR. CAPRON: But hermetically distinct categories that funds poured into one do not flow into the other. It seems to me that particularly when we are asking the question of federal funding, we are in a position of facing statutory prohibitions on federal funding as well as prohibitions put forward by executive order and the question put to us by the President and I think by the American people is do the present circumstances argue that for this category of research, not for all research with embryos, but for this category of research there are now good and sufficient reasons that those prohibitions should be lifted.

I do not think that we will make a case that is convincing if we say, well, yes, lifted as to use but not as to derivation. I think people will see that as an

attempt to avoid the hard thought and the ultimate justification that is necessary here because it is -- to use the analogy that I used in that article a little while ago, it is like the shoemaker and the elves. I mean, instead of saying, oh, well, the shoes are just here, I do not know where they -- I am not responsible for how they got here, I have nothing to do with it. The elves just make them at night. That is not the case. The elves are being paid with the federal dollars in this case.

And we ought to bite that bullet and as to those things which we think can now be justified or where we provide an argument as to what would need to be discovered and shown to be of research and therapeutic value for other things to be justified by the oversight mechanism in the future, we ought not to try to hide behind, well, this is just use.

I think that is what the use/derivation distinction does. It invites people to do -- I think it is what NIH has tried to do and I do not think it will convince the people who need to be convinced.

DR. SHAPIRO: Tom and then Larry.

DR. MURRAY: Well, Alex has stated well a plausible view. I just do not agree with it. We could describe what is going to make the distinction between

derivation and use as hiding behind the distinction. I do not feel that is what I am doing.

I think the argument that funds will maybe at least indirectly flow towards derivation is -- I understand that but as a matter of public policy I thought we did that all the time. I thought, for example, we would provide funds for say special education even in religious schools for the students who needed special education even though we recognize that that meant, in fact, it freed up funds within those same schools for religious education purposes but we make a kind of line.

Sometimes we give funds for certain restricted purposes fully recognizing that it may, in fact, had indirect impacts that will permit other funds to be spent for purposes that we do not think we should give directly to. I believe that is true in many cases of public -- many arenas within public policy.

I have a slightly different take on who our audience is that was implied in Alex's comment. I think there are people out there who will simply -- there is nothing we could say that will have the slightest impact on their views, which may be held for sincere religious or ethical principles or for pragmatic political principles, political advantage. I mean, that is just

the way the world is.

I think we speak to the great number of Americans who have complex views about this and who are undecided. I think that many of those will find the distinction between derivation and use actually important in terms of federal funding. At least I want to put that out as a hypothesis and let us talk about it.

DR. SHAPIRO: Larry?

DR. MIIKE: My view is more with Alex but I think we need more in this area. For one thing if we do not -- if there is no federal funding -- and these are propositions that need to be tested. If we do not fund derivation then all federal research will be hostage to sources that come from private sector with the kinds of arrangements and restrictions that go on.

On the other hand, it may be a moot point if after -- I cannot remember which meeting but the IVF clinic doctors who came to testify in front of us said to me after the meeting, "It is going to be a moot point after 100 or so of these. You will have perpetual cell lines and you will not need any new ones." I said, "I did not think that was the case because I did not think that has been perfected." But there is an opinion out there that it may be a time limited issue.

So I think that we need to -- if -- we need -

- if we are going to move along the line that we support the derivation as well as use we need to look more into why we would support derivation and would that, in fact, in the research projects that come up -- is the derivation part of the funding a critical component of any research project or is that just something that they can do on the side and not seek federal funds while still having this a part of their project. So I think we just need more information on that.

DR. SHAPIRO: David?

DR. COX: I really think that this discussion about derivation and use is critical and I think if we are going to have the discussion we should be precise. So we are making statements as though that if we -- that there is no source of human stem cells if we do not use human embryos and that is not correct. Using germ cells from fetuses is a very separate issue and it is a source of providing human stem cells.

Now if we are -- so when we talk about, okay, use versus derivation, I would be for one -- I think it is a disservice to basically talk about derivation solely in the context of human embryos. That was one of the distinctions early in this discussion that having stem cells derived from germ cells as opposed to early preimplantation human embryos was a very critical

distinction and I do not want to lose that distinction. That does not mean that this discussion about derivation versus use is not important but to imply that if we do not use embryos we are not going to source I think is not factually correct.

DR. SHAPIRO: As I understood, David, what Bette recommended was, in fact, sort of a combination of what has been discussed here, namely -- please correct me, Bette. I am just trying to summarize what you said. Bette was comfortable with derivation from fetal tissue but not from -- or at least suggesting that we not be for it in the case of embryos, not that you could not have it from fetal tissue.

Is that right, Bette?

DR. KRAMER: Right.

DR. COX: Yes. No, I understood. Bette was quite precise. Then the discussion got less precise and so I just wanted to state that for the record and then point out that from a personal point of view I hear what you are saying, Bette, loud and clear. And I am presently on the fence for exactly the reasons that you bring up.

On the other hand, I think to lay out what the loss -- so in the context that if we do not go ahead and say it is okay to use embryos then it does not make

sense because we are going to be doing the uses and there is no way to actually get the stem cells without using embryos. I think that argument just does not hold water.

On the other hand to derive stem cells using the human fetal tissue is a shlug (sic). It is like trying to swim the channel with bricks on your feet because it is extremely difficult to obtain that tissue at the right time, at the right place, at the right age. It is possible.

So the question is how many such stem cell lines does one need. So I think that this will be possible to do. And just talking purely from a scientific point of view, I mean as a scientist I could live with that. But on the other hand, we give up quite a bit by not being able to derive stem cells from embryos, a lot of flexibility in terms of really being able to do enough experiments to see what is the best way to get stem cells, what are the characteristics of stem cells. So there is a lot given up for that.

What we are talking about is a trade off here, though. So I think that is what the discussion is but I do not want to have the discussion be in the context that if we do not use embryos that we cannot create stem cells because that is not true.

I did not mean to imply that Bette said that

but that -- the discussion, I do not think, was clear. Thank you.

DR. SHAPIRO: Other comments on this issue? Well, I think it may very well be that we are divided on this issue. My own view is really unchanged from where we were although I do not think we stated it in a very effective or even very accurate way. I accept Tom's distinction between distinctiveness, whether or not it is justifiable and whether or not public funding ought to be authorized was -- I think those are important distinctions. I really -- I certainly accept that and I think it is far easier to show that they are distinct than that they are not so that -- and I think -- so I accept that they are distinct and not the same.

The language we use in some of our drafts was very confusing on that and we are justifiably criticized for that language. But nevertheless my own view comes out on the same spot, that -- and of course we have to make the arguments that it should be appropriate for public funding for the derivation as well as the use for all kinds of reasons which we can certainly articulate but I think we may very well be divided on this issue and if we are we will just see what the division is and those who want to feel separately about this they are certainly welcome to -- whichever side it works out. I mean, I do

not know how this will even -- I do not even know how this will work out if we take a vote on it.

DR. MURRAY: Thanks, Harold. And we may divided and that may be the way it is and that would be unfortunate but if that is the reality, so be it.

I think we do not need to be divided on certain parts of the text, particularly beginning on chapter three, page three, and then picked up again on chapter three, page nine. I will not examine in detail the language where it essentially sort of gives away the -- gives everything away on complicity since I am sure people are complicit. I do not think it is that simple and straight forward that it is an argument that was clearly rejected in the fetal tissue transplantation debate and yet we sort of just buy it here without even argument and I think that was a -- that is a big mistake. In fact, a substantively big mistake.

So at the minimum can we agree that that language needs to be rather thoroughly revised?

DR. SCOTT-JONES: Could you say again what you are talking about?

DR. MURRAY: Yes. Chapter three, there is on page three, a discussion begins on complicity. It continues into page seven and then on page nine, about the middle of the page, there is a sentence, for example,

as long as embryos are --

DR. SHAPIRO: Line, please.

DR. MURRAY: Yes. Line 17 and continuing. "As long as embryos are destroyed as part of the research enterprise researchers using embryonic stem cells and those who fund them will generally be directly or indirectly complicit in the demise of embryos," et cetera, and then some of the language that takes away from that.

I just think that is careless language. We need solid argument there. I sense that that language sort of flowed from the commission's decision that we ought to fund both and so we kind of read back into it that there was no distinction. That is a mistake. We should not commit that mistake.

DR. SHAPIRO: Carol?

DR. GREIDER: I just wanted to second what Tom said. That was one of the major points that I wanted to raise in this report was the language on page nine in chapter three. I did not understand at all how that flowed from the early discussion of complicity. The first part of the discussion on complicity was whether or not researchers that used stem cells derived from fetal tissue were complicit and the answer was clearly not. And then suddenly we jump over to whether researchers

that use stem cells that are derived from spare embryos are complicit and suddenly the answer is yes.

I did not understand that logic at all and felt that I disagreed strongly with it. And so I second that, that language really, I do not think, reflects what was stated earlier in the chapter.

DR. SHAPIRO: Okay. Thank you.

Bernie?

DR. LO: I think that is what we have been saying. This is an important issue and it is one where I think there are divisions. It would be helpful for me to hear the best argument that those who believe that it is a worthwhile distinction making for the purposes of funding and, therefore, there were some moral distinctions to be made to actually see that spelled out better.

So part of it may be that the arguments now in chapter three are not the best arguments and I would really invite Tom and Bette to sort of maybe at a break to try and at least in summary format make those arguments stronger and perhaps some of us might be persuaded.

Even if not, I think that distinction is certainly out there enough that we should clarify the nature of the argument and even if we end up not agreeing

to say here are the arguments on both side as well stated as possible.

DR. SHAPIRO: Alex?

DR. CAPRON: Yes. I would just assume demote this argument very substantially. If we did something along the lines of what I suggested before that we put the legal chapter before the ethics chapter then part of the conclusion of the legal chapter would be -- in terms of what issues are before a body like this -- would be -- it has been suggested, in part, citing the Harriet Rabb memorandum, that the way to avoid this as an issue is to say that federal funding can be provided for the use, though not for the derivation of the stem cells. Or that is to say -- excuse me. Yes, period.

We believe that it is not so easy to separate those two and not only -- not getting into statutory interpretation which I -- I mean, I think that she has got a -- something decent on the language but probably not on the intent of the people who wrote that statute for what that is worth.

Then state there why we believe that any argument about this issue should be capable of meeting the issues of derivation as well as use and that is a statement of what we are going to try to discuss rather than saying that we believe those two in your type one

issue are morally equivalent.

It is just that we believe that the public discussion ought to rise to a level where the issue of derivation is as fully addressed as the issue of use and that is what we turn to then in the transplanted chapter three in terms of evaluating the moral arguments that are the wrestling or the weighing that the President's letter asks us to do.

It sort of says are these changed circumstances? Are the circumstances new enough so that that balance has to be restruck? And then our conclusions that come out of that I think would be more straight forward and we do not get into this complicity language at all, which is a whole new can of worms as far as I am concerned for some of the reasons that Tom mentioned by his analogy.

DR. SHAPIRO: Jim, do you want to --

DR. CHILDRESS: I think Alex has pointed a direction really for restructuring this in a way that can help us clarify and perhaps also resolve some of the issues but I would also go back and underline what David was emphasizing, that we tend in our discussion to just throw around derivation and use abstractly but as a matter of fact they work only in a specific context and thus directing our attention to the different sources.

If we keep that in mind then we will really have to make it very contextual. That is we will have to see, much better than chapter three currently does, how that distinction works out and could work out with a fuller understanding.

So if it would be possible to -- for members of the commission or even for us to get some others involved on quick short contract papers on this particular distinction and how it might work out. Perhaps we could gain something that would be very useful for our report.

And the fact that the distinction -- perhaps in the NIH statement of views -- it does not mean that there was not something important here to look at. It is just a matter of, you know, trying to figure out what that is in relation to the different sources. I do not think we can avoid the complicity discussion if we are going to be true, in part, to the way the discussion takes place in the society because that is an important issue that connects very closely with the use/derivation and it is one that as we heard in the discussion with religious leaders is an important one.

DR. SHAPIRO: David?

DR. COX: So I like what Jim just said. This issue of are there possible alternative sources is a

major one. A major place where people are trying to come together in a compromise. One of those source -- alternative sources is adult stem cells. I will just say from a scientific point of view they do not cut it but stem cells derived from germ cells do cut it from a scientific point of view because they do have the same kinds of characteristics.

So I think having as clear a distinction of alternative sources and saying where they stand scientifically is important and that needs to be better clarified in the science chapter.

The issue of complicity. To me this was a critical issue but let me just make a personal statement about where I come on it. I ask myself am I complicit with everything everybody does in the world because I am tied one way or another to what every human being does and I say, "Well, that does not make any sense because I cannot be responsible or complicit with what everyone does." So that is one extreme.

On the other hand, do I have any responsibility for what anyone does and the answer to that is sure because there are some things that I feel very strongly about.

So it is not that there is a line when you are complicit or not complicit. It is the extent. How

far does that reach go? And that is where I am on the issue of complicity. It is not a line. It is a moving boundary and so that if we try and define what the line is we are not going to be any more successful than we are going to be at defining what life is. When life begins.

On the other hand, to state that that is the issue and say because it is a moving boundary there is no line to it and people are going to differ about it, about what is complicit and not complicit. That allows us to move forward. So the -- but I think that if we are trying to adjudicate when you are complicit or not complicit in this issue we are asking for big trouble.

DR. SHAPIRO: Alex?

DR. CAPRON: Well, I mean, there is a strong sense of complicity that is causation, in effect. This would not have happened had I not done something. I indicate my need for human embryonic stem cells. They are not going to fall out of the sky. Someone has got to create them through a process and I know that.

That is -- that is why I am bothered by this notion of our separating these out as to the kinds of activities which are before us, which is federal funding. I mean, it is a little bit like this Washington phrase of plausible deniability (sic) or something. I mean, we do not want to get into that moral quagmire. Endorse, it

seems to me, a route which says that that is the way to go on all this.

DR. COX: But because of exactly that point, Alex, that is why if you go back to what the present regulations are in terms of using fetal tissue, it separates, okay, the people that want to use those stem cells with an iron gate from where the other things are so that there are ways of dealing with this issue so that the --

DR. CAPRON: That is right. The woman's choice to have the abortion is not something which is brought about by the researcher's desire to have this source of cells. That is going on. There are millions of abortions going on. The question is if a person has gone through that process and had the abortion and said the tissue may now be used, Congress of the United States has said that is all right for federal funding.

DR. COX: So this is what our report should lay out and say. So that it is not that we do not talk about the complicity issue but we have just gone through it.

DR. CAPRON: Yes.

DR. COX: We just did a scenario. Let the report say it.

DR. CAPRON: Yes, I agree.

DR. SHAPIRO: Tom?

DR. MURRAY: Yes. If there is to be a distinction with respect to funding between derivation and use, I do not think it will be based on a claim that somehow -- the clean hands argument. The clean hands argument that somehow if I had -- you know, as long as I do not derive them I am somehow completely -- you know, completely clean of any taint, moral taint that would attend to that, that is not the place I would put it.

I would -- the argument that I think is more persuasive has to do really with the public policy. It has to do with if there are a number of American citizens out there, not a majority but a, you know, notable number, who are deeply offended by the destruction of embryos, and if it is possible to come up with a public policy that would permit embryo research to go on without significant impairment.

I mean, stem cell research to go on without significant impairment, by funding its use but not its derivation, and if that would, in fact, to some extent take the sting out, the moral sting out for the people who are offended by the destruction of embryos then I would want to listen to that argument and at least consider it.

I am not sure where I come down on it today

and I am not sure I stated it very clearly from the puzzled glances around the table and I am really thinking in terms of, you know, you should always do -- if you have two options that get you the same result, both of which are morally justified but one is much less -- does not offend people as much as the other then I think you should simply respect those people's moral sentiments.

DR. SHAPIRO: Bette?

DR. KRAMER: Tom, thank you for stating it so well and, you know, I mean I quite agree with what you are saying and -- I mean, this does not represent my personal point of view but it represents to me what I think is appropriate when you are doing public bioethics.

I think as -- I think I said earlier that one of the things that was clear to me from reading the science chapter was how much there was yet to learn, what are the differences between stem cells derived from the different sources, whether it is fetal transplant, whether it is spare embryos, whether it is somatic cell nuclear transplant, whether it is possibly adult cells. I mean, there is a lot of questions out there. How long is it going to take them to understand how to turn cells on and off so that genetic therapy becomes a reality?

There is a lot of basic science that still needs to be done. So -- and we do not know. We do not

know are the existing cell lines or the cell lines that will continue to be produced by the two known means, is that going to be sufficient for all the research that needs to be done to go forward or will there be a need for further sources. We do not know how compelling it is going to be for the use of these spare embryos to be available.

So there are all these questions out there and, therefore, why push so hard? Why push so hard on people for whom this is a moral problem if there is a way of structuring our report and our recommendations to accommodate them in the interim while science goes forward?

It seems to me that there is another possibility -- one possibility would be, yes, to support all use, all downstream research from currently -- from currently produced cell lines, from those produced -- I mean, when I say support, I mean federally fund the derivation from fetal transplants and in principle -- in principle, endorse federal funding of derivation from spare embryos but hold off until such time as there has been made a compelling case for it to be instituted either because of scientific advancement or because the promise is becoming more of a reality.

And, therefore, there is a shift that people

understand that in their own -- in their own assessment of the benefits to be gained that there is -- they are willing to make their shift.

I do not see the need to go out there and confront people -- confront people for whom this is a real moral problem when it is not absolutely necessary at this time. I have not stated it well but this is how I just -- this is how I feel about it.

DR. SHAPIRO: Carol, and then we are going to break.

DR. GREIDER: I just wanted to address one of the things that I heard you say, which is as it says in the science chapter there is a lot of questions that are still to be answered out there about the differences between the cell types and what characteristics they have derived from different sources.

So your final conclusion that perhaps we do not want to yet go forward with the stem cells derived from embryos to me goes against the fact that we do not know enough about it unless you go forward to some degree, which I see our limited degree is using spare embryos, you will never get the information to know whether there are differences or not.

Currently there is this one cell line that is out there but from a scientific point of view having one

cell line derived once is not going to tell you a lot about the reproducibility.

DR. KRAMER: Can I just answer that? I am assuming that in the private sector they are going to continue to derive additional cell lines from spare embryos as this one was done. Personally I regret tremendously that the whole area had not been federally funded and that that work was not done within the public sector but that is -- you know, that is over, that is done.

DR. SHAPIRO: Well, I think I understand -- Trish, if it is quick.

DR. BACKLAR: I just wanted to ask one question. I would like somebody to make it very clear what it is that we would lose by not federally funding work on spare embryos?

DR. SHAPIRO: The question was, and some of you can feel free to answer it --

DR. MURRAY: Derivation or use, or both?

DR. BACKLAR: On the derivation.

DR. GREIDER: I think that the number of people that are going to go out and try various experimental protocols is dramatically different whether or not there is federal funding. The people that have access to, you know, alternative sources of funding --

that is one issue and the other issue is the oversight issue.

Now I appreciate the comments that have been made earlier that we can maybe separate oversight from funding but currently I have not heard in the framework about how one would do that. So I think in terms of the federal oversight that that is another big issue and then there is the issue of -- that we have not even gotten to -- of sort of monetary gain for these.

Do we want to push it into the private sector where everything is going to be limited by a certain number of institutions which stand to gain monetarily from this? That is what I think we give up by forcing it into the private sector.

DR. BACKLAR: And that is, I think, going to be extremely important, however we come out in this report, to make sure that we examine and lay out the losses that may incur.

DR. SHAPIRO: Diane Scott-Jones?

DR. SCOTT-JONES: I think there is another loss associated with Carol's last point and that is just that science should be open and that it should be communicated easily and freely among everyone, and I think that that may happen less when it is in the private sector entirely than when it is in the public sector.

DR. KRAMER: Right.

DR. SHAPIRO: I think -- I just want to put the -- we are going to break now but we are going to come back at some time during the day, at least take a straw vote and see where people's opinions lie. We do not necessarily have to make a final commitment.

I must say for myself I am unpersuaded by the arguments that we should separate for purposes of federal funding here the derivation and use.

DR. CASSELL: You were unpersuaded?

DR. SHAPIRO: Unpersuaded.

DR. DUMAS: That it should be separating?

DR. SHAPIRO: I do not believe it should be eligible in the sources we talked about but there is a lot of -- I understand -- very good arguments on the other side but I would caution us to be careful about arguments based on presumptions we cannot really establish. Like we can do everything we want by restricting ourselves. That is not always the case.

Anyhow, let's take a break and let's try to reassemble at quarter to 11:00.

(Whereupon, a brief break was taken.)

DR. SHAPIRO: Colleagues, if we could begin our meeting again, please.

We have roughly a half an hour to spend

before public comment. Public comment is at 11:30 and I want to get to that as close to the scheduled moment as possible out of respect for those who signed up for public comment. So we will spend the next half hour, it may not be enough, of course, but we will at least begin our discussion of the oversight mechanism if I could use that as a characterization of one particular model that you have in front of you.

Now there are a number of very important issues to discuss here, which we really have not had an opportunity to discuss before now and that is -- at least some of the key issues are oversight over what. Is this oversight over publicly funded research in this area? Is it oversight over all research done in this area? Is it oversight over the research that deals with embryonic material? That is the use of excess embryos for derivation and/or use. Or is it oversight over that plus similar effort -- analogous efforts, excuse me, dealing with material derived from fetuses -- fetal tissue and so on?

So there is a very important issue of just what it is oversight for. Now maybe we could begin our discussion by focusing on that. I really do not want to focus too much on whether it is, you know -- there is this many members or that many members. That is really a

kind of small issue. In the end someone has to think carefully about that. That is probably not where we can spend most effectively our time.

But perhaps we could begin by seeing how people feel regarding oversight over what. What should be the scope of its responsibilities and what are the criteria regardless of what it is providing oversight for. What are the criteria for which this oversight is being executed?

David, and then Larry?

DR. COX: So the -- as I stated earlier, I believe that we already have a foundation on which to begin this, which is the guidelines on which fetal material can be used to derive stem cells from fetal germ cells. And those criteria are laid out quite clearly and are already sort of accepted in society.

I think that to have that as a starting point, and this is primarily oversight in the generation of cells, and what the source of the material is and what those conditions are, whether the source meets those conditions, and so I think that having oversight on that of any stem cell line that is created, whether it be from fetal tissue or from embryos, would be my choice because it is a common set of criteria.

The embryos may have additional things to

them but that what we really want to pay attention to is this -- the very reason the fetal guidelines were set up is that you separate the use from the generation and it is not the same people. So I think that that is, to me, a primary thing that the oversight should pay attention to.

A secondary thing, though, which comes in terms of the use, and I would really like to make this distinction between the oversight for the generation versus the oversight for the use, I think it would be a mistake to have oversight of what the uses are of every time one has an experimental protocol for use. We had this discussion at the last meeting.

And a recommendation that came up that I was -- at the last meeting that I was very in favor of is have like an Institute of Medicine report of what are the uses that you would like not to see happen versus those you would like to see happen so you have guidelines for IRB's and other things and not have it be protocol by protocol in terms of use.

DR. SHAPIRO: Larry?

DR. MIIKE: I echo Dave and actually the way that the current draft recommendation reads is confusing because it talks about review of scientific merit and ethical issues and then later on in a paragraph it talks

about policy and ethical issues.

I think that what -- NIH is going to set up some kind of a mechanism. I do not think we need to recommend an oversight body like a RAC. The individual research projects are not of the potential dangers that the recombinant DNA type activities were worried about. Here we are talking about areas which I do not think are as controversial as that.

So I would settle for the following mechanism: Some sort of creation of pedigree along the line of what David was talking about, and we may not need a very formal mechanism for that. That might be done internally.

I think Eric had brought up the issue about a registry of projects so that people could see the range of kinds of things. I think the peer review process would be adequate for judging the scientific merit of the specific research projects proposed.

And then somebody like the Institute of Medicine that would review -- it may not have to be yearly. It could be after some time has passed to see whether all the excitement is being realized and what is actually going on. A body like that could combine policy, ethics and scientific expertise together to review that.

So I am not looking for a national body that does project review and I agree with David on that but more or less to say that if we are going to recommend limiting the types of sources of stem cells -- the sources then we need a mechanism to assure that and then we need a registry for the research projects.

Now the registry could be opened up to the private sector but my guess would be that they would be very loathe to tell you what they are doing. So I do not know what we would do on the private side unless we move towards some fairly rigorous regulatory matter.

DR. SHAPIRO: Bernie?

DR. LO: Yes. I guess, I would like to go back and think through what the purpose is. I think one of the purposes I would argue is to recognize and respond to public concerns that given that this is such a controversial morally contested, as you said earlier, Harold, area of endeavor, we would like some assurance that people doing it are doing it in accordance with generally accepted moral and ethical standards.

I agree with Dave and Larry that for NIH funded proposals I have no question about scientific merit. They are going to be very meritorious projects given the peer review at the NIH.

I am more concerned that in deriving stem

cell lines for sure but maybe even using them there may be ethical issues that -- some of which we may not even foresee and that given that this is a controversial sensitive area, I think it would just be prudent to say, "Let's go slowly at first. Let's do it in a way that we could really assure the public that this is being done responsibly."

I must say that I would really want to include as best we can privately funded research. I think the issue that was raised earlier this morning about whether one of the compelling reasons to federally fund this was that we saw no other way of bringing privately funded work into sort of the gambit (sic) of public oversight. I think we need to question that assumption.

I think there are models out there and the very least we should say that from sort of an ethical point of view we would strongly recommend that a mechanism be set up by which privately funded research would come before a public oversight body to look at what is going on.

I must say I was very -- I do not know how to say this -- disappointed in the way Geron set up its Ethics Advisory Board. I mean, I do not think that meets standards that a thoughtful person would view as

appropriate. You do not set up an advisory board after you have decided what to do and say you have got a short time period to justify what we have decided to do.

I think it is that -- it is that kind of procedure that gives people who do not necessarily have, you know, fundamental moral and religious objections to this kind of research, it gives people a question of what is going on out there.

We need standards they would think are ethically appropriate so I would urge us to try and find some way of not necessarily bringing everything case by case but having some sort of oversight over what goes on in the private sector.

DR. SHAPIRO: Eric?

DR. CASSELL: Well, I am going to be the fourth commentator to really point out that what we are not addressing are some of the issues that came up in our previous discussions and that should be addressed by an oversight whatever, and those are the issues of respect for human tissue, respect for embryos, and issues of justice and use.

They are also the reasons why we want to make sure as much of what is done is done in the public sector as opposed to the private sector.

You establish, Bernie, an ethics committee

like that if you want to make sure you can go on doing what you wanted to do. That is why you do that. I mean, everybody knows that.

We would like to have one that is overseeing not the individual protocol, that is not our concern, other people do that very well, but in some way, which is hard to define, that is why all our comments have been so abstract, in some way of tracking what is this -- what is this protocol leading to? What came out of it and how does that affect what we are to do in the next protocol?

It is the kind of oversight on science that does not presently happen where science has simply been allowed to do its thing and then what happens is what happens.

But in this issue because of the use of human embryos, we thought there was a difference, our public commented the same thing, respect for the embryos, socially just use, and to make sure that the research progress as it goes on meets the need of the people who are actually paying for it.

DR. SHAPIRO: Other comments about this?

It seems to me we have some serious issues to address here and let's address what seems from just the comments that have been made, not necessarily my opinion, seems from the comment that have been made here to be an

issue, and that is the question of project by project review -- whatever oversight is up here -- vis-a-vis some other type of review. And there is also this distinction between use and derivation.

Let's just talk about the use for the moment since that is probably in some level a little easier. Is it the general feeling that whatever oversight mechanism we design here that you do not want, is what I am hearing so far, a project by project review? Is that -- am I listening correctly? Am I hearing what people are saying?

DR. CASSELL: Well, of the kind of presently exists. What we are saying is the NIH and so forth has the ability to do the project by project.

DR. SHAPIRO: The science, yes, I understand. In the typical way.

DR. CASSELL: That is right. But project by project review in terms of outcome and use, while it is not quite the same -- in other words, it is not so blanket that there is no control at all over individual projects but the area of control is not in the nature of the science, is it good or bad science, but what is happening with this.

DR. SHAPIRO: I just want to understand. I understand that point.

DR. CAPRON: What happens then if we are thinking this would be something that would extend to the private sector?

DR. CASSELL: Well, that is exactly -- I think you have no control over the private sector. Even if they registered every embryo that comes down the line and gives them all first and last names, you would still have no control over what is actually done with the tissues and you just do not.

DR. CAPRON: Well, I am not sure -- I am not sure as a rhetorical statement whether you are right. Certainly the British believe that their human fertilization and embryology authority has that control as to what is done with the embryos but I was not assuming that we were going to have an authority.

But suppose Bernie's comments led an organization like Geron to say, "You are right, this kind of ad hoc privately funded group of ethicists who we gather does not give us the reassurance that we are doing the right thing and does not reassure the public, and we want to have a very good reputation with the public. We want them to feel confidence that we are doing the right thing. And so if you have an oversight body, NSCORP, or whatever you are calling it, we will go before it and we will tell them how we are going to derive these cell

lines and what research is going to go on with them. Now we expect part of that meeting will be open and as is presently permissible with any federal advisory body, part of it will be closed when purely proprietary matters are around the table but we are going to go to them."

Is that -- and that group cannot say, well, case by case there is going to be the NIH study sections because they are not going to go to NIH study sections because they are not seeking federal funds. They are doing this with their own funds. Are we ruling that off the table?

DR. CASSELL: Can you clarify for a moment? Is there no regulatory force behind this body in your hypothetical?

DR. CAPRON: There are two questions. Whether the body would be available to organizations and whether the organizations would be required to come to them. In the case of the Recombinant DNA Advisory Committee, it did not have regulatory authority and yet in the early years, to the best of my knowledge, all the experiments, including ones which were being carried out by industry as they began to gear up, came to them and then after they got to a certain point those responsibilities were spun off to EPA and the Department of Agriculture as they related to different areas.

It is also true that the RAC operated by categories and so that as a category of research came to be seen as not problematic you did not need approval whether you were federally funded or otherwise but that was voluntary on the private side as I understand it and it was done for the same kinds of reasons that a Monsanto or whoever was going to do that work wanted to be seen as a good citizen and not to be doing something which the public had not had a chance to hear about and a knowledgeable review body said, "Yes, you are doing it in an appropriate way."

DR. CASSELL: That is categorical rather than this individual research project.

DR. CAPRON: No, they went with a research project. They went, you know, we are going to take this vector and that, and then -- and the body said, "Well, yes, this vector is still subject to our individual review of the circumstances and are you doing it in the right way. This other vector, no, we have approved it. You can do almost anything you want with that vector it is so safe you do not have to come before us for that one but you do have to come before us if you are NIH funded here and you are voluntarily putting yourself in the same category."

I gather that worked pretty well for a decade

or so. That is my -- I mean, we do not -- one of the issues that I hope we are going to study on this sort of revisiting the Asilomar conference a year from now, but that is a separate thing -- but that was without regulatory authority. It was not required for all that.

Now some of those things may also if they were drug related had to go to FDA and that is a separate issue.

DR. CASSELL: May I make one further comment?

DR. SHAPIRO: Sure.

DR. CASSELL: When I say not study by study, I do not mean what you are talking about. I mean, in the sense of the details of the science and did they do the right thing and the right reagent. You know, will it produce good science, I mean.

But what you are talking about is precisely the kind of control I think you should have. Yes, what they are doing project by project or categorically should come out in the open and project by project in the sense of this kind of project or this category of project should be in the open and there the openness is the regulation. However, there is a big difference between the science -- between private science of ten years ago and private science now in terms of its muscle and money and so forth.

DR. SHAPIRO: Trish?

DR. BACKLAR: Well, I am concerned about oversight in the private sector. If there will be -- how one can have oversight in the private sector to ensure that the people who donate the tissue or the embryos are properly protected. So that is where my concern will be.

DR. CAPRON: Again, I mean, as I understood what we were talking about at one point -- and the reason I tried to make the distinction between federal funding and federal regulation would be if there were standards established which had to be followed by the federal -- the funded researchers or NIH researchers, it would seem to me that if they are articulated in a reasonable way one could create the expectation that any legitimate researcher was going to adhere to them.

There may be people who would be willing to be outliers and take the wrath of people saying, "Well, we have got to now legislate because you guys are doing things. You are getting embryos without getting the woman's consent or the couple's consent and you are doing it at a stage where they have not decided what they are doing and you are pressuring them and offering them incentives to create more embryos, and this is really not fertility work, it is really disguised as the creation of

embryos for research." I think there could be a public reaction saying, "We will assert commerce clause authority in the federal government." I mean, the State of California and one other state legislated on the cloning issue. States would get into it.

But I would think that we could go into this with the expectation that the scientific community wants to behave in a way which will not subject individual companies, Geron or anybody else, to public criticism for doing something that falls short of a standard that was established for federally funded researchers.

So I would not put the emphasis right away on building the legal case for why this is subject to congressional authority. I would try to establish what we think are a reasonable set of standards as to the kinds of things that you just mentioned and put forward our expectation that researchers will follow those standards, whatever their sources of funding and recognize that if that is not the case Congress will face an additional question as to how or legislators more broadly face an additional question of how they want to deal with that if they think it is a serious enough violation.

DR. SHAPIRO: Larry, and then Rhetaugh?

DR. MIIKE: I hear two lines of discussion

here. One is about oversight over the uses and the actual research uses of stem cells. The other one is oversight over the derivation.

On the uses, I do not see, and someone can persuade me otherwise, I do not see different ethical issues and unique ethical issues in this area from other areas of research in the actual application of uses of stem cells. So I do not -- so I am convinced that we need an ethical oversight of whatever kind outside our current system of IRB's by institutions for those.

On the derivation side, that is all -- and I think the only way that we are going to be able to do that is to develop standards or best practices or whatever for people to follow, and then I would agree with Alex that the way to -- that is going to be practical to accomplish in the private sector is that you -- it is sort of almost like you get the standards and it is almost coerced they be able to follow them. Maverick researchers are not going to follow them anyway but the legitimate ones, I think, would.

DR. SHAPIRO: Well, let me -- I know I want to recognize Rhetaugh in just a minute but let me just try to raise an issue with respect to probably what is the easiest case, that is uses as you have indicated, Larry. And, of course, whether derivation or uses you

have, of course, a public-private distinction. You have kind of a four by four matrix here of issues that have to be addressed.

On the uses side, let's say publicly funded just to take what is the most straight forward case, it seems to me that if there is an argument for what everyone seems to be against, project by project review at some level beyond the scientific merit issue, I agree that scientific merit can be handled in some other -- at some other point but it seems to me the reasoning would be that we need some oversight to guard against promiscuous use of materials for which we are trying to show some respect. That would be the argument. It has nothing to do with scientific merit only. There is all kinds of things which have scientific merit.

But the issue of whether we think these materials and in some sense the over use when other -- for example, when other possibilities exist with economizing the use of these materials. It would have to be that kind of an argument. I am not sure it is a good enough argument. I am not suggesting it. But it seems to me that is -- I may have misinterpreted it.

I thought Bernie was sort of saying something like that but I may have misinterpreted what you said, Bernie, because I think everyone has been against project

by project review that I have heard speak so far but if that is not convincing then in that case, the use case, the publicly funded use case, then I cannot think of another argument. So I am just trying to respond to your question. What would be the argument? It might be an argument like that.

DR. CAPRON: Doesn't that -- I hate to take us back to the use/derivation thing again but if stem cells -- if a particular researcher were making what you were characterizing as a promiscuous use, that is to say was using human stem cells when she could use mice stem cells for an experiment, but she was using them from an existing established stock, and if I understand the technology here, the great thing about these stem cells is you can grow them up, they are immortal, they are stable, et cetera, et cetera --

DR. SHAPIRO: We do not know how long --

DR. CAPRON: -- I mean, that is -- hypothetically, that is what --

DR. SHAPIRO: -- as far as I am told.

Carol, you may --

DR. CAPRON: Is that --

DR. GREIDER: That would not be my assumption. I mean, I certainly know people that make embryonic stem cells from mice and after a certain number

of passages you have got to go back and make them again if you want to use them under certain conditions. They are stable for a certain amount of time and then you need to --

DR. CAPRON: They become unstable.

DR. GREIDER: Yes.

DR. CAPRON: Okay. Well, then the argument is stronger because thinking of what I thought the word "immortal" meant and what was different about these cells was unlike other cells which after 100 passages in the laboratory age and stop working, the idea was that they were going to be --

DR. GREIDER: That is not true.

DR. CAPRON: Okay. Then I think your point will hold because then you are forced back. But again it is really the derivation. You are basically saying at some point you are putting pressure on the derivation side and you going to make -- cause someone to have to make more of these unnecessarily as it were and that is ethically problematic.

DR. SHAPIRO: Well, I think there is that issue and I am just -- I am not exactly sure what my own mind is on this issue but there is also the issue, as I think about it, of not only the issues that you have outlined here but the symbolic issues involved here

regarding using this material about which one might want to be more careful. It seems like to me different material than just other material.

So that might cause -- I am just trying to make an argument -- one to look at even in the initial period at least on a case by case basis but I think what I hear around is that people do not find that persuasive but let's --

DR. DUMAS: Well --

DR. SHAPIRO: Rhetaugh, you are next.

DR. DUMAS: -- my comment is not on whether it is a case by case basis. I think that the approach is something that we need to think about a little bit more but I do think there should be oversight and I think that the oversight is on the use because that is the area that the federal government has jurisdiction over rather than over the derivation.

But I also believe that the derivation can be influenced by the type of oversight and the standards that are set for the use. For example, if as a part of the expectations of scientists who would be using these stem cells that they are expected to use cells that are produced by methods that are appropriate then through that type of expectation we can expect to have some influence although we may not have control over the

public -- the private sector.

DR. SHAPIRO: David?

DR. COX: So I would like to come back -- and this is to lobby one more time for an Institute of Medicine type of commission or committee to say and help us define what these indiscriminate or nonrespectful uses of the cells are because I believe until we define that, having a regulatory body in place that has people come before it to see if it is being respectful or not, will not achieve its goals.

The reason why I feel so strongly about this is that as I sit for myself asking what would be respectful or not respectful science with these cells, I have an extremely difficult time to coming up with what a not respectful experiment is.

DR. SHAPIRO: Well, let me give you an example of a category. I cannot imagine an experiment. I do not know enough. But it is something -- Alex gave the example of something that could have been done with cells from mice would be an example. I mean, you use one because you had them and you did not want to get others. It could be something like that. Whether it would be, I do not know.

DR. COX: So to have guidelines laid out by the committee that would allow scientists and lay people

to go before the IOM to have the discussion about what such things would be. The -- I have no problem once that is laid out and I also really like the idea in terms of guidelines for use of sort of having it publicly available what the uses have been. I think recording that is extremely helpful and that is an easy thing to do.

But I just think of having -- I just envision scientists or other people coming before a group to decide whether it is respectful or not of how to use these cells, if you do not lay some groundwork for that ahead of time, I think it is Emperor's New Clothes. It is going to be something that is set up to make people feel good and it is not actually going to be achieving that at all.

DR. CAPRON: But that panel has to set those standards itself. You cannot -- as a member of the Institute of Medicine I will speak against assigning this to the Institute of Medicine.

(Laughter.)

DR. COX: But, Alex, I am not keen on --

DR. SHAPIRO: They might choose Alex as head of the --

(Simultaneous discussion.)

DR. CAPRON: It is not just overworked. I

think it is inherently it is not subject to the Federal Advisory Committee Act. Part of the value of that panel working through that issue and articulating the standards would be that they are the ones who are going to eventually have to apply that and they ought publicly to go through a process for which they are accountable if I understand it.

DR. COX: But all I am arguing is that the standards should be set before people start getting judged by them.

DR. CAPRON: Yes.

DR. COX: That is all that I am saying. Right now we have --

DR. CAPRON: And in light of experience.

DR. COX: Absolutely. We have an ongoing assessment of what is happening and that we have standards set. That is the situation that we have right now with respect to the derivation with fetal tissue and that is where we have grounding. We have some way of proceeding forward. But if we did not have that first then it would be really very difficult to proceed forward.

DR. SHAPIRO: Bernie, and then Larry.

DR. LO: Let me follow-up with David's concern about whether you can articulate standards in

advance of sort of reviewing a series of cases. I would argue that it is sort of an iterative, almost secular process that to -- I mean, we would have a hard time as would any other thoughtful body have a hard time sitting down now in advance of very many protocols saying what do we think are the really impermissible uses that are disrespectful of embryos.

When the embryo panel -- the NIH Embryo Panel did it in 1994 we tried to take, you know, a really off the wall example.

But my point is that only when you actually look at some protocols that people are proposing do you start to get a sense of, yes, all of these are fine; you know, we do not have any problem with this one; we have some concerns; and this one we really have strong objections to.

So I think part of this is that you cannot always anticipate and because this is so new and so unprecedented you want some way of finding out sooner rather than later what some of the problematic areas are. That is not to say we cannot try in advance to try and define sort of the broad guidelines as to what is unacceptable. My sense is those will only take on meaning as we view them in the context of actual cases coming up.

I think the way we can do that in the fetal transplantation area is there is a lot of experience with informed consent, with abortions, and the kinds of pressures women are subject to and not subject to. Just as I think we can talk about guidelines for consent for embryo donation in the IVF context but when we are starting to get into areas where there is not a whole lot of experience we would need to kind of have this interplay between the actual cases and trying to set up guidelines.

DR. COX: Please keep the derivation separate from use because all your examples were derivation examples, not use examples.

DR. SHAPIRO: Larry?

DR. MIIKE: First of all, I would really object to any kind of a judgment that says you should do mouse experiments first before human experiments. I do not know how we can get into that area and make a decision on that.

But there are current mechanisms. If we are talking about a research proposal that has aspect of derivation then human subjects protection should fall in then there should be an institutional review. Our Human Biologicals Material Report is putting forth some other recommendations and we will be dealing with human

biological tissues. So it is not like it is going to be avoiding it and only the scientific panels at the NIH will be doing the review. They are going to have to go through the usual review process. So I feel comfortable with that.

My idea of the IOM was not to set standards. The IOM idea was that after the dust has settled out, there are some experiments going in, it is a review of the progress and the issues around the use of human stem cells in research. Are we moving along the line that everybody was excited about and that justified federal funding for it. That kind of review is the ones that are more classically within the IOM purview.

DR. SHAPIRO: Trish?

DR. BACKLAR: But the issue is that some of those oversights will not work if it is in the private sector. Isn't the point about thinking about some kind of oversight body is that it would look not only at what was federally funded but also what goes on in the private sector and I am not certain how those protections would be in place in the private sector.

DR. MIIKE: Only in the same way that current ones are in the sense that institutions that participate in such research if they are following federal guidelines and if they are publicly funded they would follow federal

guidelines.

DR. SHAPIRO: Arturo?

DR. BRITO: I want to second what Trish just said but this is a very specific and very special area that I think we have to be very careful with and I would feel very uncomfortable without the oversight in the private sector so I would be very uncomfortable relying strictly on what regulations exist right now for other types of research.

DR. MIIKE: But, you know, we are getting into sort of a funny area. We said that we are focusing on federal funding and that now when we come to the oversight we are trying to have a much more rigorous application of control in an area outside of federal funding.

DR. CHILDRESS: Right, that is exactly right.

DR. SHAPIRO: You got it, Larry.

(Laughter.)

DR. DUMAS: What I am suggesting, Larry, is that that control can be facilitated -- well, that control can be indirect by the kind of guidelines that we expect the scientists who will use the stem cells to abide by.

DR. MIIKE: I do not have a problem with that. I do not have any problem with that but there is -

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DR. DUMAS: But if we have some standards or conditions that, you know, that we would look at under which these cells are collected and the conditions under which they are forwarded to people to use then I think we would, in essence, have some mechanism for control in the private sector.

DR. MIIKE: As I say, I do not have any problem with that but I think Trish and Arturo does.

DR. SHAPIRO: Other comments and questions now? I want to move to public comments almost right away so we will continue our discussion on this issue.

We have really quite a number of distinctions to make here and we are going to have to start making them. There is -- first of all, where the oversight is to cover both the -- as I mentioned before, both materials derived from fetal tissue and embryos, whether that should be the same oversight mechanism that we have or whether we should leave the fetal one to the existing one amplified in some way. We have the public versus privately. We have the use versus derivation. And we are going to have to start indicating which parameters we want to sort of begin narrowing down on so we can actually articulate an oversight mechanism that makes sense but we will return to that as our meeting goes on.

I have two people who have signed up for public comment. I do not know if they are -- either, or both or one are here right now. But just let me remind everyone that public comments are limited to five minutes plus if there are any questions from commissioners in addition to that it could go longer in any individual case.

Let me see if Mr. Stan Khawan is here from Meadville, Pennsylvania, if I read the town correctly. He had wanted to address the commission on the use of misinformed human subjects in research. He may if he comes in, in the next short while, we will certainly still be available to hear from him.

Also here with us today is Phil Noguchi, who we have known before, from the FDA, who also would like to speak to us regarding the use of human embryonic stem cells in research.

I think -- either you can stand. If it is more comfortable for you to sit you are welcome to take a seat at the end of the table. Whatever is easier.

PUBLIC COMMENT

DR. PHIL NOGUCHI, FDA

DR. NOGUCHI: This would be fine.

I appreciate the opportunity to again to make a few comments about the FDA perspective on this

discussion.

The first thing I would just like to remind this commission is that you have many constituencies and certainly the FDA and I as the director of Cell and Gene Therapy, which would regulate the clinical use of these products, we take what you say extremely seriously and I feel that it is very important that should you have major reservations about any of the types of approaches being taken it would help us quite a bit to know that.

Now, second, I would like to follow up on some discussions about is there a mechanism to oversee both the private and public sector in terms of research. I am speaking now only for that which is used in clinical studies. However, one must admit that the primary reason there is so much interest in the use of embryonic stem cells is, indeed, for their clinical application.

We have had a lot of experience with gene therapy and with xenotransplantation. Two areas which, indeed, bring forth some of the similar concerns, that is gene therapy first being a possible genetic manipulation, permanent or otherwise, of a patient's own DNA. Xenotransplantation being the use of animal organ cells and tissues where the concerns are not only to the patient but to the public at large in terms of potential

zoonoses.

Now here we are faced with, I think, what is the even broader scale of public interest and concern, that is the possibility of being able to regenerate or to repair things that wear out, brains wear out, muscles wear out, things of that nature, and we have other clinical applications using less advanced techniques for this but what we have really found is that in order to get the very best clinical science in order to make sure that this is as safe as possible, public discussion, especially in controversial areas, has proven to be extremely helpful.

Now in terms of a model -- for example, the RAC, all companies and all sponsors who have ever done a gene therapy protocol have all submitted their protocols to the RAC. They are not all publicly reviewed and they are not always submitted in time but they have all been submitted there. The public suasion of that process is such that, in fact, it has become a de facto requirement.

Some of the advantages of that public discussion are, first, you know what is going to happen and FDA with the Office of Recombinant DNA Activities and the RAC are now starting to do this in a more proactive way such as whether or not to allow in utero gene therapy at this point in time, and actually there were several

conferences which concluded, no, not yet until more science is done and under these conditions and these would be some of the concerns in terms of informed consent. So that certainly in anticipation of something that may happen in the future was extremely valuable.

It can also help us to make those decisions. Should we do this and, if so, what are the concerns and, if not, why not? In a separate forum but for xenotransplantation we have now as a society decided that the use of nonhuman primates is not warranted in terms of any type of transplantation at least for the United States. It certainly helps to gauge whether or not the society is ready to move on into a particular area.

And then I think finally going back to the question of this particular area, should we not being doing the very best science, should we not be doing the very best clinical studies, and I can assure you that private funding being what it is, what can be imagined will be done but they are also subject to all the rigors of what is practical to do.

If a company, for example, embarks on a developing project that involves something that is not really acceptable to this type of a forum or to society in general they may waste five years and eventually not come up with a product. So I am pretty sure they would

be very interested in actually being able to discuss these sorts of things in public.

So with that I thank you for your attention and that is just FDA's point of view for this process.

DR. SHAPIRO: Thank you very much. They are very helpful comments, indeed. Let me just see if there are any questions from commissioners.

Yes, Carol?

DR. GREIDER: I had a question about the xenotransplantation. Am I correct that there was recently a conclusion that reversed earlier ideas about xenotransplantation in terms of the danger of viral transmissions?

DR. NOGUCHI: I am not sure what exactly you are referring to. FDA has issued a guidance document saying the nonhuman primates are not appropriate for use. There has been additional findings that pigs harbor an endogenous virus which can actually infect human cells and that there is some form of activity, retroviral activity, that can be found in some natural porcine products.

DR. GREIDER: So what is the reason for the nonhuman primates not being used? Is that because of the viral transfer?

DR. NOGUCHI: That is because of the -- of a

lot of burgeoning evidence but I would say primarily there is now good epidemiologic evidence that both HIV-1 and HIV-2 were transmitted from monkeys and that clearly is a risk that we are not willing to take.

DR. GREIDER: So that the dangers of xenotransplantation kind of get at the issues that we are addressing here in terms of autologous transplant issues of tissues.

DR. NOGUCHI: I believe so. All these stem cells, human cells you have looked at, are at this point in time essentially teratocarcinoma cells and while they may or may not really be cancer, they certainly look like it so the next step is to make sure they only go in one direction and they stay normal just as one example.

DR. GREIDER: Interesting.

DR. SHAPIRO: Are there other questions for Dr. Noguchi?

Well, thank you very much for coming here today. We appreciate that very much.

Has Mr. Khawan arrived?

Is there anyone else who wishes to address the commission who is here today?

If not, we still have -- let's -- there is no one else. We will end the public comment session but let's return to our discussion regarding oversight and

let's at least spend 15 minutes with it at the moment and then see how far that gets us, and that will -- we can continue this afternoon if that is necessary, which it may be.

I want to go back to what I thought was a simple question I was trying to ask. I probably asked it in an extremely obscure way. And that is, is there anyone on the commission who feels that we need project by project oversight beyond the local area review and study section, and the stuff is just out there in any case?

DISCUSSION CONTINUES ON DRAFT REPORT

DR. BRITO: For the use?

DR. SHAPIRO: For the use. Excuse me. Thank you very much, Arturo. I appreciate that correction. I was really thinking about use. Thank you very much.

So whatever the national oversight is in the judgment of the commission, it is not a project by project review regarding use. Let's just stick on use for a moment.

Let me ask another question. Whatever our system of national oversight might be in this arena, do we want to at the very least make it available and encourage private organizations to use -- to participate in the system?

(A chorus of yes.)

(Laughter.)

DR. SHAPIRO: A kind of --

DR. CAPRON: Amen.

DR. SHAPIRO: Right, amen. That is right. I was looking for the right word. That is it. Thank you.

Larry?

DR. MIIKE: But my question to the commission members then is that what do you about private research that creates an embryo to --

DR. SHAPIRO: Yes. We are going to get to that. I agree that is an important issue, derivation and so on. But we are just talking about these. I am just trying to get a few things straight in my head so as we begin to build structure we have some anchors to build it on.

Okay. So we are agreed that -- again we are looking at the use right now -- that whatever structure we develop and however we articulate it we want to encourage everyone doing research which uses these materials to take advantage of the oversight mechanism, so on and so forth. I do not have the language but that is very, very helpful.

Let me ask -- let me now go to derivation. Not that we have resolved all these issues.

DR. LO: I was counting Eric's phone calls.

(Laughter.)

DR. SHAPIRO: I think we ought to start charging him so much a call. I mean, AT&T is probably charging him and we ought to charge him so much.

Let me now just talk about -- see where we are and talk about it for a moment on the derivation, that is we have to get back to the issue because we have got to resolve derivation regarding whether federal funding is appropriate. But assuming for the moment that it is just as a way of dealing with this part of the conversation, what do we feel about oversight in this area or derivation, whether it is from fetal tissue or from so-called excess embryos? Is that a project by project review? For example, in order to certify that, in fact, the sources here are those that are deemed to be appropriate at this time.

(A chorus of yes.)

DR. SHAPIRO: Okay. So that is project by project. Okay.

Now let me ask the question -- and we would likewise in this case want to encourage everyone who is doing this to take advantage and follow the guidelines that are articulated and so on.

(A chorus of yes.)

DR. CAPRON: Could we put that a new way? It is not simply a matter of encouragement. The report would expect -- establish the expectation that anyone in this field would do that. It is a moral expectation. Whether it becomes a legal one is a --

DR. SHAPIRO: Yes. We are not going to recommend that.

DR. CAPRON: Just a slight difference in tone.

DR. SHAPIRO: I understand. I understand the issue. How do other commissioners feel about that issue?

DR. CAPRON: Strongly.

DR. SHAPIRO: Strongly.

DR. MIIKE: Harold, can I ask a question? We have not yet addressed the question about what mechanism we are going to use to --

DR. SHAPIRO: No, no, I understand. We have to design this. That is right. There are a number of different ways to do it. I am just trying to get some parameter set here so that as we set the design that we can think about it carefully.

So what we have -- what seems to be the preference of the commission is with respect to derivation, whether publicly or privately funded, that it would -- this is a project by project or situation by

situation review to which we expect everyone to participate under the guidelines that we lay out.

Now in all of this that we have been talking about I took it from what we said before or what other commissioners said before that we really want this oversight mechanism to encompass both the embryonic material and the fetal tissue material but we do not want to make that distinction for this purpose.

Okay. Well, that is extremely helpful. That is a series of at least tentative decisions which really will help nail down the -- and so, for example, if you look at the recommendations in chapter six right now, regardless of what one thinks about them individually, they would obviously have to already be rewritten if for no other reason than to reflect this.

Now could -- I am a little unclear in my mind -- what I would like to return to right now is the issue of -- all right, we do not have in the case of use now -- returning to use -- we do not have any project by project review beyond the local study section, et cetera, that is already in place.

What kind of review are we expecting? One possibility, which I think I have heard some people mention, is just that all projects would in some sense have to be registered and information accumulated, public

reports made once a year regarding what has happened, what the outcomes are and so on, and an evaluation made of the way the system is working. That is one kind of thought that I think I have heard expressed here.

Is that what -- is that the kind of national review again for use that people are thinking about and presumably this commission or whatever it is that is established would on the basis of this information develop ideas, develop guidelines and so on which you would expect IRB's over time to line up against but this would be, as Bernie said, an iterative thing that is very hard to judge all these things in advance.

Is that the kind of idea? I am not trying to detain (sic) a solution here. I am just trying to understand what people have in mind.

Yes, Tom?

DR. MURRAY: Very tentatively that seems to me one plausible function for this review committee. I want to direct a question now more to the scientists on NBAC. Is it reasonable to think that there will be discernible categories of studies that will be sort of identifiable as research begins to unfold that this review committee might, in fact, comment upon and make some recommendations about?

Is that reasonable or is it likely to be so

fluid and, you know, unsuitable for that kind of -- you know, sort of capturing the flow of where the research is going and being able to say something useful about sort of ethical cautions or such, or points to consider about different categories of research?

DR. GREIDER: I mean, I think that to some degree there will be research that will clearly fall under certain categories. You know, people that are specifically trying to do things to differentiate cells along the lines to treat certain diseases. But there will also be a category which will be miscellaneous where people are doing a certain amount of research. So I could easily imagine several broad categories but then some areas they would not be categorized at all.

DR. COX: I mean, that is what actually troubles me because most of the time I can always think of worse case scenarios of things I would not want to see people do but I am having trouble in this particular instance coming up with those and so -- because I distinguish the cells from embryos, I could think of lots of things I would not want to see embryos done with, but the cells -- it is -- I make that distinction.

So that is why I am very keen on accumulating what the uses are and having any scientist who uses these cells, you know, register what they are doing and then

let's look at it because it is what Bernie says. I mean, you want to do both. You want to think ahead what are the things you really do not want to have happen.

I would be open to having anybody tell me what they do not want to have happen. I am having trouble coming up with that myself but at a minimum register what people are doing so we see what it is.

DR. DUMAS: Would you also want to register how the cells were obtained even though that is not private -- you know, how do -- how do --

DR. COX: As distinct from derivation?

DR. DUMAS: No. As a part of derivation.

DR. COX: But I see use and derivation as very different here.

DR. DUMAS: Well, you made a statement about use. Would you not want to have the people who are using the cells have some intelligence about how those cells were obtained?

DR. COX: Absolutely but I would want that to be regulated under the derivation. I do not want any cells out there for anybody to use that have not passed what our derivation --

DR. SHAPIRO: Rhetaugh, I think presumably in this area I think that one way or another if someone is proposing to use cells they would have to find some way

of testifying or certifying or being certified that the use that the cells that they are using were derived in ways that seem appropriate. We have to have some certification process.

DR. DUMAS: Right. They are not -- I was just -- yes. I was wanting to make sure that in that survey list of information that would be collected and accumulated that that would be one aspect of the information that we would be getting.

DR. SHAPIRO: Right.

DR. CAPRON: Let me try to respond to David's request if I may.

DR. SHAPIRO: Yes.

DR. CAPRON: And it is the example I gave before that Larry ended up rejecting but instructed by you and Carol a few moments ago that we are not talking about inexhaustible stock. Once you create line X1, at some point the cells become abnormal in some way and are not useful and you have to go and create line X2.

It would seem to me that agreeing that these cells do not have the status of embryos and, therefore, the full blown concerns you would have about any use of an embryo did not arise. To the extent that they require a process of creation out of an embryo they ought to be used with a certain necessity.

After all, the whole argument here for altering the present framework which says you cannot use the embryos at all with federal funds, you cannot use the embryos at all is that, well, there are certain things which are scientifically very important where this technique opens the door that was not open before and there may be things for which they are not really important but absolutely essential.

If you get to a use which does not qualify in that way where you still have a great deal of preliminary work that could be done with a nonhuman stem cell line or where the science to use the findings does not seem ripe at all and a year or two from now it would be a much better time or a much more prudent time to do it.

Is that not something where purely on the use level you could imagine a committee helpfully and appropriately establishing a standard which says for the moment the following things do not qualify as ethically acceptable uses of this very precious commodity.

DR. COX: I will tell you the problem I have with that personally is that the -- we do not have such guidelines right now for human cells that are taken from living human subjects. All right. But what we are doing is that we are putting those guidelines specifically for cells that are derived from human embryos.

DR. CAPRON: But those cells, I would gather, are derived (a) with the consent of the individual, not someone else; and (b) do not require the destruction of the individual to derive them.

DR. COX: Yes. And those are the two criteria, that is correct.

DR. CAPRON: Isn't that true?

DR. COX: That is correct.

DR. CAPRON: And that is, after all, why we are having this whole discussion.

DR. COX: And that is what makes them --

DR. CAPRON: I mean, HELA cells do not raise these issues.

DR. COX: And that is what makes them different. That is correct, Alex.

DR. CAPRON: So that since they have -- I mean, part of what it seems to me we are saying, again to give you another analogy, and the difference between embryonic stem cells created out of embryos that were made for research purposes and those that were made from embryos that were otherwise about to be discarded, was that we did not think that the latter category, those that are going to be discarded, will create an industry and that we will open the flood gates and have people creating embryos just like they were anything else in

large numbers simply because they are -- it is easy to do and so forth.

We would rather be -- we are reluctant at this point to think that anything approaching that is justified. If, therefore, you have an experiment which could be done without human embryonic stem cells but the person says, "Well, I would just assume use them," they are pushing us in that direction because they are increasing the demand for those cells and, therefore, increasing the pressure towards having a process that is a comodification of embryos towards this end.

I think that is an ethical argument as to why we would want to say there should be a justification, a necessity of some sort for using it.

Now I also am cautious because I know that any particular scientist may have an argument, well, gee, it would be so much better to do this and I do not have to do it but, boy, the research would be so much better, and where do you cut that and so forth. But it is a matter of what presumption you go in with and then you -- I actually -- and this is as to categories because we have already decided we are not case by case --

DR. COX: The problem, though, is that what those categories are -- and see we could start but collecting what the uses are -- I take your point quite

clearly about the informed consent and the destruction of those -- of embryos in order to create the cells. That is what makes these cells special.

DR. CAPRON: Different than other human cell lines.

DR. COX: Yes. On the other hand -- and so I think the presumption comes in of people saying why they would want to use embryonic stem cells as opposed to some other cells. I can almost -- well, I hate to ever say I can assure you but I feel fairly strongly that most research scientists would not choose to use human embryonic stem cells to do anything with unless they had to because of the extra scrutiny that would befall them.

DR. CAPRON: But that is the question. Will there be extra scrutiny?

DR. COX: Yes. But how much extra scrutiny one needs right now in order to scare scientists away from using these cells I do not think is a whole lot. But I think having some insight here but particularly looking at what the uses are and then saying for those uses what is acceptable and what is not acceptable I am very in favor of and if we can think ahead of time of what particular classes are that we would not want to see happen, I am all in favor of that, too.

I am just saying that this group that is

looking at what is collected should come up with suggested classes and run it up the flag pole -- run them up the flag pole.

DR. SHAPIRO: I think that is right. I think it is going to be -- I think you are both right in a sense. I think there are some things we can say and there are some things as Bernie and others have indicated we cannot really know now and we are going to have to let this group evaluate and discover.

DR. CAPRON: I was not arguing against that. I thought at one point I heard David say, "I cannot imagine what those categories would be." And since we had earlier discussed one such category, that is to say research you could do just as well with nonhuman stem cell line, I wondered if you were also dismissing that as a category.

DR. COX: Yes, I am. Because the -- and I would say it in the following way: If I want to know what goes on involved dealing with humans and how human cells work, I will use human cells.

DR. CAPRON: Well, that is something -- in other words, you cannot do with a nonhuman cell line so the -- that standard or that barrier would not be a barrier to that research.

DR. COX: Yes.

DR. CAPRON: So that is not a problem. But I agree. I mean, it is not as though we would have pages and pages of all of these but if we illustrate and then say it will be up for this panel to work through that, which they are going to be doing in a kind of a points to consider mode, that is to say explain to us what you would be doing, and then in the process of reviewing those they will in a common law way have a creation of standards.

DR. SHAPIRO: Let me raise one other -- I am sorry, Arturo. I apologize.

DR. BRITO: Just a quick comment. I have followed this discourse here and I understand the logic and agree with it but I just want to make sure, Alex, that there was one comment you made that makes me a little bit nervous and I do not think it is what you meant when you said this and you were implying something else. But when we were talking about oversight for the use of stem cells, we are not talking about oversight in their uses for -- because there may be scientific advancement.

But we are really talking about the oversight because of ethical considerations, right? Because you said somewhere in there that when the science, we could advance -- I am paraphrasing here but advance

scientifically, that is where we need to be -- have the oversight. But that is not what you meant to say, is it?

DR. CAPRON: Well, I mean, the ethical concern is what motivates the need for the oversight.

DR. BRITO: Right.

DR. CAPRON: But I thought in all of this we were recognizing that it requires a justification and the President's letter, in effect, is asking -- our whole process is, is there now a justification in this particular area, and if we answered yes, I would say it is on the basis that this area offers an opportunity which is not available through other methods and they -- it is linked with important scientific discoveries and clinical applications.

We do not know all of those so we are not giving a green light to everything. We are recognizing that this will be an iterative process in which the question will be has the science advanced enough so there is a reason to do this.

DR. BRITO: Right. But the motivation is ethically based.

DR. CAPRON: The motivation is ethically based and it is a caution -- it is basically a caution to say do not just say, sure, there -- it is fair game now. Do anything you want with these cells.

DR. SHAPIRO: Let me turn to a different issue now because I think it is relatively straight forward and we will have to come back to this oversight issue, and we will naturally come back to it as we look at the recommendations.

And that is the issue I raised earlier on with respect to sources of either fetal tissue or excess embryos that might come from abroad.

I think my own view is we cannot write the report leaving that issue out as if it does not ever happen and, therefore, I do not have a detailed proposal but my general idea was that since we are talking about the oversight mechanism will have to have some certification regarding where these cells were derived from and if they were derived in ways that we think are appropriate from appropriate sources that the exact same set of issues ought to apply for issues from sources that come, whether country X, wherever that is, outside.

That seems to be relatively straight forward and simple and we can just put that in.

DR. CAPRON: We should be explicit about it.

DR. SHAPIRO: Yes, we should be explicit about it. But is there any concern about that?

DR. MIIKE: Yes. I do not know what to do about it but just the kind of information we had from the

anecdotes about the international studies, the informed consent issue is not going to be the same.

DR. SHAPIRO: It is not going to be --

DR. MIIKE: So we can have our standards but we --

DR. SHAPIRO: -- struggle with that.

(Simultaneous discussion.)

DR. SHAPIRO: We will try to -- I understand that issue and we have been struggling with that in other contexts as we all know.

DR. CAPRON: I am not sure that I accept the problem that Larry just posed for us. It is one thing to say that if you are developing a drug or a vaccine for use in country X and it is international research that that process ought to take account of the local norms about consent and so forth and so on.

It is a different thing to say if you are developing a cell line that wants to certified for use in this particular way in the United States that you can say, well, we go to Zambia an the chief gives consent for the use of embryos from anybody in the tribe and he takes payment for it up front. Uh-oh, no. I mean, it may be fine. We heard the bottles of liquor for this to the chief and so forth for that kind of thing. Well, you know, that is one set of issues.

But when you come to this I do not think we want to say, well, we are going to be very scrupulous in the United States and the human stem cell companies are going to go abroad and start creating the stem cells and shipping them to this country with meeting none of the standards and engaging in the very kind of comodification and industrialization of this that horrifies people.

So I do not accept the notion that it should be a separate standard. I think if they establish a standard --

DR. SHAPIRO: You are in agreement.

DR. CAPRON: Okay.

DR. BACKLAR: You are in agreement.

DR. CAPRON: Oh.

(Laughter.)

DR. CAPRON: I am sorry that I misunderstood you.

DR. SHAPIRO: Where is the amen?

(Laughter.)

DR. SHAPIRO: Okay. Jim, and then we are going to adjourn.

DR. CHILDRESS: This will come up again later but I think that there is a real question as to whether the informed consent model is the appropriate one anyhow for even talking about the transfer. There are at least

two different ones. One would be the informed consent model that we use in the area of research involving human subjects.

The other is a donation model and we -- it seems to me we confuse this a lot in talking about, for instance, in the last chapter, page 17, "...to allow the use of donated embryos in research informed consent is required." If they are donated that is already a statement that consent is present. Then the question would be how much information has to be involved and it seems me we have the two models there and we run them together without a good sense of how they may involve quite different implications.

DR. SHAPIRO: Okay. We will reassemble at approximately 1:15.

(Whereupon, at 12:09 p.m., a luncheon break was taken.)

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

DR. SHAPIRO: Colleagues, I would like to continue our discussion.

I have a brief note here from our colleague who runs the public address system, which says that we ought to talk at very least in the direction of the microphone. It would be helpful.

DR. DUMAS: That is a reasonable request.

(Laughter.)

DR. SHAPIRO: And I guess the closer the better but at least in the direction of. So if you would all do that I would appreciate it very much and more importantly he would appreciate it.

I think what I would like to do now is turn our attention to the actual recommendations in chapter six, recognizing that many of these are going to have to be altered in a very significant way even judging from this morning's discussion, and to go through some of these and to see where we stand on some of these issues.

They will raise some of the issues on which we could not agree this morning and we will have further discussion on that. On the other hand, some of these we might be able to resolve and put them aside for now as we deal with the issues that still seem controversial to us.

I think as we go through these, as you will

see, they raise pretty well all the issues one way or another, directly or indirectly. I am going to skip for the moment, except as it might come up as absolutely necessary, the actual text, not of the recommendation itself but the text that surrounds chapter six. As I indicated this morning, there is certainly some of the text here that needs changes and now more of it will need changes on the basis of what we have already said.

But I suppose you cannot say that too often but let's just go directly to the first of the recommendations here that I think, if I recall right, are on page eight of -- page 8 of chapter six. The first one being -- well, actually the first couple of recommendations there really have to do with the alteration of existing legislation in the fetal tissue transplantation area to clarify that these should be modified in some way so as to recognize and accommodate the embryonic germ cell research or the cells that are derived from the fetal tissue.

If you recall, our reasoning here was that although it was thought by many that the existing legislation really was adequate or at least covered this, if that is so then we thought, well, there ought to be no -- you know, no great difficulty just to make it clear. And so I look at these at the very least as clarifying

but some people might think they are more than clarifying. So I would be interested to know your views on those. Really the two that are on eight are similar in that respect.

Jim?

DR. CHILDRESS: I will start with the second one. I guess I am not convinced by -- and this is a case where the recommendation and the text, I think, have to be considered together. I am just not convinced by what appears in the text that the recommendation is warranted. It seems to me to be a stretch. We already have in the federal funding area a pretty strong prohibition on the recipient specific donation.

I guess I am not sure how this really works out in this particular area and the argument that follows is not convincing and goes also well beyond -- for example, when we get to the bottom of page nine -- well beyond what is involved in the recommendation. So this is a case where the recommendation to me does not seem to be necessary and the text does not provide the support for it in my judgment.

DR. SHAPIRO: Tom?

DR. MURRAY: Well, Jim may have precluded what I was going to say because I was comfortable -- we are talking now about the recommendation on page eight

that covers lines 18 through 21, I understand. Is that correct?

DR. SHAPIRO: There is two on page eight. Jim referred to that one.

DR. MURRAY: Yes. That is what I thought --

DR. SHAPIRO: Right.

DR. MURRAY: I was going to say that if we are going to keep it in and keep in a reference to revising or amending the Uniform Anatomical Gift Act we should add an encouragement to states to adopt the amended UAGA because I am not sure that -- a lot of readers will not be aware that the Uniform Anatomical Gift Act is simply a model act and it is up to each jurisdiction to decide whether it wishes to adopt it or not.

DR. SHAPIRO: I think -- it is, in fact, in the text here how many -- I do not remember where it was but somewhere it indicates the number 26 or something. I have forgotten the number that have adopted the new version -- newer version. Excuse me. It is not so new anymore.

DR. MURRAY: Yes. I remember that but I thought we -- if we really wanted it to take effect then states have to adopt it and that should be in our recommendation.

DR. SHAPIRO: That is useful.

DR. CHILDRESS: If I could follow up on that, and I am not convinced by the argument that appears on ten in that regard, that we have this terrible tension between what might be required on the federal level and what might be present in a revised Uniform Anatomical Gift Act or in its current version that it has the effect of undercutting any federal prohibition of designated donation of human fetal tissue.

It would if we go in the direction of a total prohibition but if we go in the direction of attaching it to the regulation involving funding it would not necessarily. And, furthermore, it -- let me just stop there. If it was attached to the funding part it would not.

DR. SHAPIRO: Larry?

DR. MIIKE: I have not had a chance to take a look at the revised versions but my impression of the way that this is written is that it puts too much emphasis on an interpretation of the statutes and the regulations, and we jump into it right away. I think this -- we should have a much more policy oriented report that tells what our recommendations are and our ethical reasons for doing that.

We should not highlight so much the legal

issues because, as the way I understand the thing as being written, we are also saying that we disagree with DHHS general counsel. So I think that it is much more sanguine to put these in terms of there are interpretive difficulties with the current laws and statutes that need to be clarified rather than coming out with something very, very prescriptive in this area.

DR. SHAPIRO: Tom?

DR. MURRAY: Just in reference to that. Larry asked the question that needed to be asked. I guess I had assumed incorrectly that some policy decision had been reached that our recommendations would include this kind of very specific language about specific pieces of legislation. If that is not the case then we ought to address the point Larry raised about whether or not we should work at the level of policy, maybe with a clarifying statement pointing out the different pieces and bits of laws that we need to change in order to accommodate them. I am in Larry's camp on that.

DR. SHAPIRO: We had made no policy decision on this issue. We have not made any judgments about the issue in those terms.

Bernie, and then Carol.

DR. LO: Yes. I would just like to strongly support Larry's position. I think this is a level of

detail that really is not the level we want to be hitting at. I think that we would do much better to sort of outline the general policy issues and leave it to someone that is much more technically able to look at these laws than this commission to recommend specific language changes.

I am also concerned that it gives an unfortunate tone and balance to the report. I mean, it sounds very legalistic. We are going to change this. We are going to change that. And I think we want to take this argument to the level of what are the big policy ethics issues, not what language needs to be changed in this law or that law.

DR. BACKLAR: Yes.

DR. CHILDRESS: I second, third, amen or whatever.

DR. BACKLAR: Yes, amen. Right. Absolutely.

DR. SHAPIRO: Let me ask about the first recommendation, which I take it is at another kind of level. The first one says that this should be clarified, right. Put aside what the text says for the moment.

And because this kind of work was not sort of in the minds of people as they were writing this at that time and it does have to be revisited -- in my view it has to be revisited -- does anyone have any objection to

that?

Okay. Now the question --

DR. MIIKE: Harold?

DR. SHAPIRO: Excuse me.

DR. MIIKE: I guess another difficulty I have is that I think the conclusion is the recommendation and then the recommendations are stated as --

DR. SHAPIRO: I think that is a problem. I agree with that.

And so what the

DR. KRAMER: It should all be recommendation.

DR. SHAPIRO: I beg your pardon.

DR. KRAMER: I said it should all be recommendation.

DR. SHAPIRO: Right. I think it has words like "should" in it and so on.

DR. KRAMER: Right.

DR. SHAPIRO: Carol, I am sorry. You were next in line. I am sorry. I forgot.

DR. GREIDER: I just wanted to offer the further suggestion I agree that the language is too legalistic as it currently reads and we should be directing ourselves at a higher policy level. But perhaps some of this can be put into an appendix as suggestions. I mean, a lot of thoughtful work has gone

into what specifically we would suggest changing. It could go as part of an appendix.

DR. SHAPIRO: Okay. I will have to review the substantive issue that Jim has raised as to whether, in fact -- whether two, for example, is needed anywhere or at all, which I take it is the issue you raised, Jim. This is something we will have to review. Could you say a little bit more about that, Jim? I was not quite sure. I was trying to grasp what reasons you had for --

DR. CHILDRESS: Well, the recipient specific fetal tissue donation, which the Human Fetal Tissue Transplantation Task Force recommended be prohibited and which is currently involved in -- which is currently the case in terms of federal funding at any rate. It is just not clear to me in this area that we are really talking about recipient specific donations when we are talking about donations for research and developing cell lines and so forth. I am not quite sure that it is something that really fits here but I would be instructed by David and Carol as to whether it is something that makes sense here.

DR. SHAPIRO: Okay. That is helpful to me because I was not exactly sure. That is certainly helpful to me.

Okay. Any other comments on this particular

issue? All these, of course, are interrelated and we are going to have to revisit all of these as a whole as we get these done.

Why don't we turn our attention then to the recommendation three or it is not numbered that way but it is the one that appears on page 12 at the bottom.

As I understand this regulation, this is subsection D of -- is -- and it may fall in the same category of the kind of things we have just been talking about as too detailed for us to worry about or to worry in detail about.

DR. CHILDRESS: There is one on page 10.

DR. SHAPIRO: Did I miss one?

(Simultaneous discussion.)

DR. CHILDRESS: Line 21, page 10.

DR. SHAPIRO: Oh, line 21. Excuse me. I did not -- okay. Let's deal with that one then.

DR. BACKLAR: Where?

DR. GREIDER: Page 10.

DR. SHAPIRO: Page 10, line 21. Comments or questions?

DR. GREIDER: It seems like the language is not as legalistic as the other language that we just felt was -- too direct and that really has -- this gets at more of the sort of global policy issues, I think. I

mean, I do not have any problem with this recommendation.

DR. SHAPIRO: Bernie?

DR. LO: Well, I think we get into one of the issues you raised at the beginning of this meeting as one of the -- whatever it was -- six you wanted to deal with where on page 11 the text that accompanies this --

DR. SHAPIRO: Right.

DR. LO: -- how we work that out and, in particular, the problem when Roman I, II and III are the same entity, how do you sort that out. I think we do not do a really good job here.

DR. SHAPIRO: I do not think we can sort it out. Certainly not sort it out but more importantly I feel we really cannot sort that out. We are going to have to leave that as one of the areas that people are going to have to worry about over time but that we really cannot sort it out because as I indicated before it involves assuming that I, II and III are actually carried out by independent entities and there is no way we can think through that. So I just think we are going to have to stick with the kind of material that is above that in the text and we are just going to have to eliminate that in some way because I am not comfortable with it as it stands.

DR. KRAMER: You are going to eliminate all

of that then, that text beginning on page -- line 11.

DR. SHAPIRO: That is my inclination right now. I have not thought it through completely but as a general proposition, yes.

DR. MURRAY: You would eliminate that?

DR. SHAPIRO: Well, I do not think we could -- I do not know if we want to -- I think we ought to eliminate the recommendations is what I think but that comes -- so to speak the recommendations that are down on lines 22 on because I do not think we can -- we have a way of implementing that. I do not think we have a way of even describing how to implement it. That is just my own view.

DR. MURRAY: Could we express our moral views about these things?

DR. SHAPIRO: Sure. One could certainly do that. We could certainly do that. Though I hesitate to say the whole paragraph is --

DR. CHILDRESS: And it might be possible just to use part of this to say in trying to make this recommendation more specific or trying to implement it one might need to consider the following sorts of things.

DR. SHAPIRO: Right.

DR. CHILDRESS: But this just simply would be a rough indication of some points that might be

considered rather than kind of a specific judgment we make that we believe categories II and III might be treated differently. We really have not gone through the process of working up what would be necessary to establish that.

DR. SHAPIRO: And it is really a great problem in principle here. It is not just a problem that we have not worked through well enough, which is also true.

DR. CHILDRESS: Right.

DR. SHAPIRO: So we can use it as an example of some kind to give some kind of indication of where -- what our thinking is. That would be entirely appropriate.

DR. BRITO: I have a question on this.

DR. SHAPIRO: Yes.

DR. BRITO: What about the sale of cell lines that are derived from the -- if we exclude all these things here -- derived from that fetal tissue? Is that our -- is it our place to address that here?

DR. SHAPIRO: People's views about that?

DR. MURRAY: The issue of comodification -- I think we cannot escape it. We have to address it. We addressed it in that recommendation on page 10, line 21, sale of fetal tissue for research purposes should be

prohibited. That is very straight forward.

Anyone who has struggled, as I know Jim Childress has, at some length with thinking through the ethics of recovering organs and tissues for transplantation, if they are just simply for clinical use, understands the complexities of trying to sort all that out.

And I thought actually the paragraphs -- the bulk of page 11 did a reasonable job of offering a kind of useful set of categories and analytical framework for thinking some of that through. So, you know, you prohibit the sale and purchasing fetal tissue from a woman who had the abortion. You prohibit the purchase of spare embryos from the couple who made the embryo. I mean, I think that is probably the right thing to do and probably well reflects the sentiment of most Americans who have given it more than a moment's thought so we need to say that.

But on the other hand it is -- there is not the same sort of moral approbation once that -- once the cell lines have been sort of worked on extensively and are now in the hands of a laboratory, developed, and they may be -- then, you know, people will sell them back and forth. Once cell lines have been transformed and worked on people -- they may, in fact, be sold. I mean, that is

a reality.

DR. BRITO: Right. The people there. That is my concern. Although we cannot foresee all the possibilities here that what we consider -- I know there has been a court decision already on this but then my impression is that the people who are going to be benefitting from this are going to be the scientific groups, you know, the commercial groups and people who donated the tissue initially --

DR. MURRAY: Do not get any more money. That is correct. That is correct.

DR. BRITO: We are okay with that?

DR. MURRAY: Well, that is a good question.

DR. BRITO: Trish seems to be.

DR. BACKLAR: I am.

DR. BRITO: I have to put a lot more thought into it but it is just something that occurred to me while reading the explanation here on page 11.

DR. SHAPIRO: Bette?

DR. KRAMER: Somebody correct me if I am wrong but have those cell lines not become a proprietary product at this point? I mean, I do not think there is anything we can do about it.

DR. GREIDER: I think that the -- right. You are talking about the patent that has been applied for

currently extant cell lines. I believe that the patent has been filed for and has not issued. That is my understanding of it but certainly we do not have any control over that.

DR. SHAPIRO: But whether a patent is appropriate or not, unless we want to propose legislation prohibiting the sale --

DR. KRAMER: Right.

DR. SHAPIRO: -- there is nothing we can do about it.

DR. MURRAY: If we pose such legislation I think people involved, both scientists involved and the biotechnology industry involved, would point out that this would effectively squelch a great deal of the sorts of development that would need to take place before any of these cell lines could be actually made into clinically viable entities. It costs a lot of money. It takes a lot of time to go through the various operations that would make it something that could actually be used as a therapy. And, you know, I have to say I find their arguments plausible on this.

DR. SHAPIRO: David?

DR. COX: So this comes up to an issue that I could raise in a variety of venues but this seems like an appropriate one to bring it up. It is in this context of

justice in terms of use of stuff as well as in the context of what you would lose if federal funding is not involved in generating these types of lines.

I think that I see that these lines, these cell lines, as not the reward in and of themselves. It is what the cell lines generate that is the reward. That is really what the patent system is for in my view, which is basically the therapies that are derived from these lines.

But access to these kinds of lines by a wide variety of individual scientists, private ventures, is essential, I believe, and is in the public interest. It is absolutely against the public interest not to have these lines widely available and widely disseminated.

Now I think that the money that individual people get back pales in comparison to what society loses if these lines are not generally available. I would liken them to availability of DNA sequence of the human genome. They are raw material which everyone, I believe, needs access to.

Now granted people that put resources into developing these kinds of lines should be rewarded for it but they should not be rewarded by a strangle hold on the availability of it and access to it to develop the therapies so some statement about this, I think, in many

different venues is important in our report because in the context of justice, in the context of just, you know, reward, and more importantly in the context of the public interest.

So I do not know what is the most appropriate here but this is a point that I feel very strongly about, about the general availability of these lines, and I think it is concern about not having federal funding is that it would limit the general availability.

Bette, that is actually why I come down siding on the fact that embryos really are used to generate these type of cell lines with federal funding for precisely this reason.

DR. SHAPIRO: Carol?

DR. GREIDER: I also want to sort of address what Tom just said and that is that in a lot of instances the biotech industry has argued that they deserve a certain amount of enumeration -- is that the right word? -- compensation for putting in a lot of effort and research into something and that is why they justify their compensation.

In this case I think, though, that the reason that this is done in the private sector is because it has been not allowed to occur in the public sector. It is not difficult to do this research. It is not something

that really takes years and years of input of raw material and brain power, et cetera.

The only reason is that it has not been allowed in the public sector and so if we are going to say that we are going to continue to not allow this in the public sector the idea is you are pushing it back in the private sector again.

DR. MURRAY: My comments about sort of the -- I was really referring to the -- that sort of last stage in the development when in order to have a clinical application where you have to go through the full FDA process, I mean that is a pretty big investment, and there the argument that the companies make is that -- you know, without giving them some proprietary interest -- it is in no individual company's interest to spend the whatever, tens of millions of dollars it takes to go through all the trials and everything.

I find that part compelling but the interesting --

DR. CAPRON: That is appropriate.

DR. MURRAY: Yes. The interesting thing, though, that you and David, I think, are highlighting is that it may not at all be the appropriate standard when it comes to sort of basic research and availability of these cell lines for basic research.

Now I am very -- I find that a very appealing and useful distinction in this context. I do not know if we can give it voice in our report or not but I think it is -- it is something that we ought to try to preserve if we can.

DR. GREIDER: It may take a million dollars to build a very strong edifice and to make a building but if you do not make the bricks available to anyone no one is going to be able to build that building, and that is what we are talking about. We are talking about having the bricks be widely available to anyone to build whatever they want.

DR. COX: Tom, if you -- we raised a question earlier. What do you lose if you do not have federal funding? I think this is what you lose big time.

DR. SHAPIRO: We are going to get in just a few moments to the issue of derivation and use. Here, if I understood the question we started off with here, is whether or not we should suggest a prohibition on the sale of derivative products if I could use that kind of a phrase, that is it comes out of working with the fetal tissue which the sale has been prohibited.

The discussion on page 11, whatever you might think of the transfer price problem, suggests a distinction. That is that the down stream products would

be available and people could sell them for whatever they could get for them.

I do not see myself that that is a problem. If as these things get -- you know, this will be taken care of over time as different cell lines get developed and people decide whether the price is worth it or not.

DR. BRITO: If it is available in both public and private sector?

DR. SHAPIRO: Right.

DR. BRITO: Right. Part of the point here is that I know we are talking about -- we are not talking about derivation.

DR. SHAPIRO: But we are coming to that in a minute and they are related in some way. I agree. I mean, it is not that these are unrelated. I am not trying to make that argument but we will come back to that in a moment.

Okay. Let's before -- we will be getting -- as soon as we get to page 15 here we will be right into the derivation versus use issue and see where our discussion takes us on this issue this afternoon.

The recommendation on the bottom of page 12 really might also deal with something which the commission feels might be more appropriately empaneled in some other way, that is it is a sort of detail with

respect to the current revisions under way in subpart B of whatever -- 45CFR46, whatever the right way to refer to that is. It is really an exhortation as opposed to anything else.

DR. GREIDER: Right.

DR. SHAPIRO: But it should be -- as people rewrite this, they should at least be thinking about the set of issues that we are now -- that is how I interpret that recommendation.

Now that may also be something you think we should sort of take out of the mainstream and put in some place where we are advising people to think about things but let me see what other comments there might be.

DR. HANNA: Harold, I would just ask when you think about it and also think about your recommendations about oversight, if you do not address this issue in some way I do not see how you can require IRB review if 45CFR46 does not apply. So just think about that when you get back to your review schema for who is going to review what, where. Currently it is not -- this does not fall under 45CFR46.

DR. SHAPIRO: Bernie?

DR. LO: Conceptually and perhaps organizationally it might make more sense to put all the legal recommendations to sort of implement our policy

recommendations at the end of the recommendations and I mean we have a huge recommendation saying the current laws and regulations ought to be changed so that the policy recommendations we are recommending take place and are not stymied by exactly the sorts of things Kathi mentioned. But I would sort of put it way at the end because sort of the carts are going before the horses here. We are talking about changing the regs before we are saying what it is we want to see happen as policy.

DR. SHAPIRO: Bette?

DR. KRAMER: But you know if you go and read the first paragraph of text following that recommendation, namely the paragraph beginning on line 1 of page 13, that picks up something that is very important to what is going to follow and that is placing -- I am sorry, acquiring oversight regardless of the funding source or jurisdiction. So we really need that before we go on to the oversight proposition it seems to me.

DR. GREIDER: Maybe the recommendation could read differently than it does now.

DR. KRAMER: Right.

DR. GREIDER: It could be something more -- I have not come up with language but something that addresses that issue more directly like the top of page

13.

DR. MURRAY: Carol, could I just clarify that? So the recommendation would then -- rather than making reference to a particular portion of the federal code, it would say the federal code ought to be redrafted in order to ensure that -- and then fill in the blanks -- are, in fact, covered and would be subject to review.

DR. GREIDER: And some suggestions for how this might be done is in appendix A or whatever.

DR. MURRAY: Okay. So the specifics about which piece of the code refer to our sort of technical document which contains our recommendations to drafters.

DR. SHAPIRO: Bette, and Arturo?

DR. KRAMER: It just -- perhaps it could add to the language at the end of the recommendation where it says, "Should be redrafted to account for human embryonic stem cell investigation and to provide areas not currently overseen."

DR. SHAPIRO: Arturo?

DR. BRITO: Should we all agree on, you know, making recommendations to adapt the federal code, to make an addendum to it, then are we saying that the Common Rule is going -- this part of the Common Rule is going to apply to both the private and public sector? Or are we still saying this is just the Common Rule and like it

says in here on page 13, the third sentence of that paragraph, "Regrettably the Common Rule is not universally or fully applied," et cetera. Or are we going to, like we did this morning, go through this later and say there is going to be oversight?

My confusion with this is it seems like, you know, the public and private sector are still going to be playing under different rules here and, therefore, we are not going to get to the problem of justice or distributive justice, et cetera. So if we agree that we are going to make the addendum to the Common Rule or recommendations to make and addendum to the Common Rule, is it going to be applicable to both the public and private sector?

DR. SHAPIRO: You want to say something, Eric?

DR. MESLIN: Just to be accurate, subpart B is not the Common Rule. Subpart A is the Common Rule.

DR. BRITO: Subpart B.

DR. MESLIN: Yes.

DR. BRITO: But if we make that addendum -- but it is still applicable to the public sector.

DR. SHAPIRO: That is right.

DR. KRAMER: Yes.

DR. SHAPIRO: That is right. And you still

have that issue. And as we discussed this morning, we would like to structure this to encourage others even to expect that they will -- might even abide by these kinds of issues of concerns and be part of the national oversight but we are not suggesting legislation to force that so that there still is -- if one looks at it that way there are two different moral universes here operating and we are trying to bring them together a little bit but we do not go all the way.

Okay. So I understand the changes that I think would be useful here.

All right. Let's go then to the recommendation that is on the bottom of page 15, conclusion/recommendation, the material that is at the bottom of page 15.

Now this goes right to the derivation and use so we might as well engage that issue which divided us this morning in some way again.

Obviously the way it is written here, we say that the derivation and use would be ethically acceptable for federal funding. That is what this says. And that being the case it would rescind or require that Congress rescind, in part, its ban on federal funding and so on. I mean, that is clear what it says whether one agrees with it or not.

And so I think we just need to come back to the issue we discussed this morning. Obviously it would be critical for this recommendation or anything that replaces it to be clear on this issue.

While I certainly understand the other perspectives on this, I think there is more than one interesting perspective on this issue. As I said just before lunch or so on, I still feel that this is appropriate. I am not arguing for language here particularly but that idea but let's discuss that further. Obviously there is disagreement.

DR. BRITO: There is a lot of disagreement on the issue.

DR. SHAPIRO: Yes. Carol?

DR. GREIDER: In participating in the discussion this morning I did not really hear that there was that much disagreement on the issue that one perhaps should consider these are separate areas but then the question about whether we come down differently in the derivation and use is another issue.

DR. SHAPIRO: Right.

DR. GREIDER: But I thought I heard a consensus that it seemed appropriate to use language that said that derivation is one thing and use is another thing.

DR. SHAPIRO: That is correct.

DR. GREIDER: So if we all agree on that then at least I am not feeling like we are not --

DR. SHAPIRO: No. I think we all --

DR. GREIDER: Okay. I just wanted to get that clear.

DR. SHAPIRO: -- agreed on that.

DR. GREIDER: And we could then change the language "appropriate" because it does not always say that in the report.

DR. SHAPIRO: Right.

DR. GREIDER: And I think I would appreciate it if that could be changed.

DR. SHAPIRO: No, I think that has to be changed.

DR. GREIDER: Okay.

DR. SHAPIRO: It has not been very helpful but in any case that is right, there is a difference as Tom and others said this morning between the distinctiveness, et cetera, et cetera. It was a threefold distinction which I think is quite correct and quite useful.

But nevertheless one has to come down to what are we going to say regarding what is eligible for federal funding. Eric?

DR. MESLIN: Well, we are agreed already about use so the real argument comes about derivation. I think in our previous discussion we did not weigh heavily enough on that justice issue. If we do not come out in favor of -- positively on derivation then we have no control over what happens to these tissues. They will be used -- they are going to be in for profit corporations and if they are anything like IVF they are going to be distributed in a way that is not just and equitable, and we will have no control over that. We will have no way of seeing that.

So while at first glance one might say, oh, if you come out on derivation, you open yourself up as though you are insensitive to the embryo. It is not at all the sensitivity of the embryo. It is quite the opposite. It is a social sensitivity that unless we do that we cannot respond to it.

DR. SHAPIRO: Tom?

DR. MURRAY: I want to thank Eric for that because I think that was -- that moves us in the direction we needed to go. I want to make my comments in two steps and I am going to ask for -- see if there is an ascent after my first step. My first step would be suppose that the first conclusion, which should be recommendation on lines 22 through 24, read, "Research

involving the use of stem cells from embryos..." and then continue to read on "...is ethically appropriate for federal funding. Would there be a consensus about that, the use of stem cells?

(Simultaneous discussion.)

DR. MURRAY: Pretty much. Okay.

So the issue is really whether derivation should be appropriate for federal funding.

I articulated a crude principle before, namely that as a moral consideration when you make public policy if you can get the same -- whatever it is -- goals, the same goods, benefits to public policy aimed at in a way that did not offend the moral sensibilities of even, you know, a small minority of Americans, you get the same results by not offending them or by offending them then you should choose the course that does not offend. But the "if" is do you get the same results.

Eric is now raising the question that I think we need to ask. What would happen if we recommended that there be no federal funding for derivation? What, if anything, would we lose? And that is the question that I would like to hear addressed by any member of the commission who feels they have insights on this.

DR. SHAPIRO: Rachel?

DR. LEVIN: I would like to point out that at

the public meeting of Ad Hoc Advisory Committee that NIH put together in April they discussed a possible mechanism whereby oversight could be exercised for federal grantees but where there are not funding derivation.

And that would be simply that they would have requirements that ethical standards would be observed by the deriver and that would have to be certified by the person who is applying for federal funds to use the cells. So they described a possible reach back mechanism that would address some of the concerns that you are talking about.

DR. CASSELL: I mean, to reach my concerns they would have to be nonprofit cells and that would be pretty difficult, wouldn't it?

DR. LEVIN: No. The deriver could be a for profit.

DR. CASSELL: Yes. But the cells per se -- if the deriver is for profit and they are ethically wonderful but they sell those cells then the distribution of them begins to have problems.

DR. LEVIN: But this would simply be for federally funded research using the cells. All federally funded research using the cells that they would have to --

DR. CASSELL: Well, how about the research

that is not federally funded that uses those cells?

DR. LEVIN: Then absolutely not. Then that still goes by the market.

DR. CASSELL: Right.

DR. SHAPIRO: David?

DR. COX: Carol was first.

DR. GREIDER: Well, just to address the issue that we came up with before just in terms of the number of people that would be available to do the kinds of research if it were federally funded as opposed to two, three, four biotech companies would I think be greatly enhanced. In order to determine whether or not we would lose anything or whether there is any difference between embryonic germ cells and embryonic stem cells, one has to do research and more research gets done if you open it up to, you know, thousands of researchers a opposed to three or four.

DR. MURRAY: Is the research on the use or we are just focusing on derivation?

DR. GREIDER: But when you use cells -- right now if we just say what is in use right now, there are two different cell lines. An embryonic germ cell line and an embryonic stem cell line. As a scientist, I would not want to compare exactly what the difference is between those general types of cell line are with just

two extant cell lines. And they can change. Cell lines can change over time.

One needs to, you know, understand what really are differences and you cannot just use two examples. So that is one scientific argument but I think the argument of justice and pushing this into private sector funding is really an even larger one in terms of the moral issues that Eric raised.

DR. COX: That is exactly the context I would put it in as justice and one can use whatever analogies you want, Carol. You use an analogy of bricks in wall and use an analogy of clay for sculptures to make the statues. You know, if somebody ties up all of the clay or restricts the clay, you do not end up with any statues. That is certainly not to the public benefit because it is the statues that the value comes out of, not the rock clay sitting there in a mound.

So it is -- we are not talking about individual interest, we are talking about the public interest and that is the real issue here. That is what really drives this.

So you are not talking about do you have any source of stem cells for researchers. As I pointed out earlier, you do. You can use the fetal tissue as a source of stem cells. It makes the research a little bit

harder to do but I do not find that a compelling moral argument that would sway me to say, well, you know, I just want to use the embryos because the research is hard to do. I do not find that compelling.

I find the social justice argument extremely compelling.

DR. GREIDER: I do, too.

DR. SHAPIRO: Larry?

DR. MIIKE: If I understood your question, Tom, what you are asking was if you allow federal funding for use research but not derivation research, what is the harm. I am not a scientist but I would guess that there would be more cell lines available because if it is the attitude that we will not see where it came from but once it showed up we would do research, you would have more cell lines. However, they would all come with strings attached. I think that is happening outside this area right now when publicly funded researchers use commercial products. There are strings attached.

I would guess that there would be a dampening factor where you would not get as many researchers involved so that it -- but it would not -- we would not be limited to these current two. But I think that there is enough of a dampening effect on the research if we do not fund derivation research and that it would affect the

public interest.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I guess, I am still struggling with whether we would lose -- that is whether what we would lose would be so significant in terms of the numbers or even in terms given the limitations of our own system the distribution of -- obviously it is to the advantage of these companies to make these materials available. The only question is how much they will charge for making them available.

So the question would be whether given those two factors for this area of research to go forward, whether those costs are so heavy in terms of the numbers and the cost of proceeding that we should then be willing to accept the considerable offense that would be created in the society-at-large for funding the derivation involving the society and its taxpayers more directly in that enterprise.

It seems to me that is the kind of -- since we are asked to consider the balancing, it seems to me that is the kind of balancing we have to face if we are going to get these issues on the table and then come to some resolution.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: It seems to me that if you buy

the cells you are, in effect, supporting the enterprise that produced them. I come down on the side of wanting to provide the direct support so that there can be some broader distribution and greater oversight.

DR. SHAPIRO: Carol?

DR. GREIDER: Just to address something that Jim just said in terms of if the companies are deriving these that certainly you have to pay for them and that is part of the cost but an additional cost is -- I do not know how these things actually read but certainly I have been in the situation where I have tried to obtain things from companies and the agreements that one had to sign were so onerous that my institution refused to sign it. So that would make it unavailable to me. Just the strings that are attached can be greater than just monetary strings that you just cannot collect enough money to do it.

Not in all cases will institutions sign agreements that certain companies write.

DR. SHAPIRO: Tom?

DR. MURRAY: I am going to reaffirm the challenge Jim, I think, has laid down. Namely if we were to make the case for federal funding of the derivation of embryonic stem cells, we should be clear that there is an interest on the other side and that we have got to come

up with some very strong arguments as -- that would over weigh that other interest and concern. I am hearing arguments of the following type: I am just going to try to enumerate them.

Number one that the science would be poor and/or slower to develop.

Number two, as a consequence of that, whatever therapies might be made available that would ameliorate suffering and prevent premature death will come later so that we will have -- there will be death and suffering that would have been avoidable otherwise.

Number three, and this is where it gets a little fuzzy, there are concerns about justice. Now when David talked about justice, actually what I heard you say was benefit, not justice. At least when you try to fill in the blanks. My ethicist ears did not hear justice considerations there.

Perhaps -- I do not know if this is separate or if this is identical to three -- there would be something on the order of kind of equitable access to the new therapies derived from stem cells.

DR. COX: That is what I meant by justice, Tom.

DR. MURRAY: Okay.

DR. COX: Because that has nothing to do with

benefit. The people that are rich will not have any trouble being able to get this.

DR. MURRAY: What makes us confident that it would be any different if we were actually to have federal funding in derivation versus just private funding?

DR. CASSELL: Our oversight.

DR. MURRAY: Our oversight.

DR. CASSELL: You put the two together and you have some chance of doing it. Now we all recognize that it is difficult to understand how that oversight functions because, in part, it is doing something that people have not previously done with science or at least not worked it out.

But the fact that it is difficult does not take away from the importance of the issue that it is trying to address. And to say, well, because it is difficult, we are going to go back a step, I think is not wise.

DR. CAPRON: How much does it cost to get a liver transplant in this country today? How much of that research was privately funded rather than federally funded? I do not think the justice argument is one that we can make out as to the access to the eventual therapy. The fact that it is publicly funded does not necessarily

make it more accessible. A great deal of the drug developments that exist in this country basically go back to federal funding. They are -- some of them extremely expensive.

DR. CASSELL: That is why our oversight --

(Simultaneous discussion.)

DR. CAPRON: I do not know of any oversight mechanism that will reach to the eventual cost of those therapies.

DR. COX: Yes. But, Alex, if they are not available at all --

DR. CAPRON: No, no, that is a different argument. That was point number two on Tom's list.

(Simultaneous discussion.)

DR. CAPRON: I am just very skeptical about that particular argument.

DR. SHAPIRO: Carol, and then Arturo.

DR. GREIDER: Well, I think one way to address this is if you throw the playing field open to a much larger number of people, the likelihood of it being particularly in the hands of any given two or three companies is much smaller. Where exactly will those discoveries come from?

If you throw it open you widen the playing field and I think all of the things that you talked about

there was certainly a wide open playing field in terms of, you know, who could make a contribution.

DR. CAPRON: But it did not mean that the eventual thing was accessible to all people. You have got to show up at the University of Pittsburgh with a check in your hand to get in the door to their transplant program and yet most of the research that went into that was public funds.

DR. SHAPIRO: Arturo?

DR. BRITO: This is not what I see on a day-to-day thing about distributive justice. I understand your point, Alex, but my fear is that there is not the same amount of money made available for both the derivation and the use of these stem cells in the private -- I mean, in the public sector as there is in the private sector. I really think the focus may be really different.

An example of this is like minorities -- there are certain minority groups in this country that are more likely to be in the lower socioeconomic classes and those minority groups may be more prone to certain diseases and, therefore, if it is only available in the private sector more money is going to be utilized to study those diseases first and not the ones that are affecting minority groups.

And that would be one place where we start.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I think the point that Alex is making is very important and that is that even with public funding we may not have the justice that we would want to see but it is still a goal to which we aspire even though it is not operating the way it should right now with federal funding. There are still inequities. There are still injustice. But I think we have a better shot at it, Alex, if we have public funding than if we only have private funding. But you are exactly right, there is not justice right.

DR. COX: There is no guarantee.

DR. SHAPIRO: Larry?

DR. MIIKE: I just have to respond to Arturo's scenario because I just sat on an IOM Committee on Minority Cancer Research and our argument was NIH was doing exactly that, not paying attention to minority needs but saying that cancer is cancer and we were trying to change the mind set. So it does not guarantee that. The public side can be just as biased as the private side.

DR. SHAPIRO: Well there are -- like in most areas there are no guarantees, including all the ones we have --

DR. CAPRON: We just do not have a very good history here.

DR. SHAPIRO: Yes, I understand the issue and accept that. I think -- Bette, I have a few comments to make.

DR. KRAMER: No. I was just going to say -- I mean, let's not lose sight of the fact that if it is federally funded, the NIH is going to apply for that patient just as quickly as any private company would. It is going to be held by a public body but it will be patented.

DR. CAPRON: They are under a congressional mandate to license those out which mostly end up being licensed to private companies.

One thing that was not on Tom's list was the point that I heard Larry make and then Carol underlined, and that was the inability of certain categories of people even to do research in the area because their university will not accept it and, of course, the point that we have had a dozen times, which is the entire National Institutes of Health may find itself at a huge disadvantage for the same kinds of reasons.

DR. MURRAY: I had meant that to be included under the poorer science, slower science category.

DR. CAPRON: Okay.

DR. MURRAY: But it is a very good and specific point that I think we ought to make forcefully. Thank you.

DR. SHAPIRO: Larry?

DR. MIIKE: To end this discussion on derivation versus use, I know we are focusing on only one aspect of it all but remember there are ethical differences in the IVF embryo -- excess embryo arguments. It is not as though we are saying -- I mean, there is an ethical distinction between creating -- at least on my part -- creating an embryo for research purposes versus using embryos that would have been discarded so it is not just that. That has to be factored in.

DR. SHAPIRO: Tom?

DR. MURRAY: I am afraid I have to share Alex's view that we are not going to sort of necessarily advance substantially access to therapies by making sure that the basic research is funded publicly. I think that is the track record. His report of that is accurate and really indisputable.

But I -- there was a part of Arturo's argument that I think we can pick up and actually I think it is right. Namely that in the basic science phase if the support is going to be all directed towards -- if it is going to be funded privately and not through public

funds then -- you know, companies that are basically motivated by profit maximization are going to pursue even at a basic research level those things where the biggest profits lie and they may not lie, you know, where -- you know, impoverished segments of the American population are.

A wrinkle cream might be much more lucrative than, you know, a life saving line for some subgroup of Americans just because there is a lot more money in wrinkles than there is in saving the lives of poor, and fill in the blank.

So I think you can take a piece of Arturo's argument and say, look, it probably -- and I think it is plausible -- probably having public funding of derivation to the extent that derivation determines the lines of basic research may, in fact, have longer term outcomes that are more disposed towards justice than -- towards distributive justice than if we left it totally in the hands of private industry.

It is still going to cost money at the end to buy the products but at least the basic research is more likely to happen.

DR. SHAPIRO: All right. I think we have talked in some sense enough about this issue and some very good points have been made, which will certainly

enable us to articulate the arguments in a more effective and sophisticated way as we come down to this. Again let's talk just about derivation now, the uses as we have said we were all agreed on.

Each one of us can balance this in their own way and there are interests on all sides. There are important interests on all sides and there is no way to accommodate all of them. And so we will just have to make a decision.

I would like to take -- I mean, I do not want people to make a final decision until we have articulated the arguments in some appropriate way and so I am not asking for that because these things are related to each other. But just -- I would like to get a feeling just as to where the commission is -- where their views are at that moment pending seeing the final arguments here -- on whether or not we ought to make derivation also eligible for federal funding assuming the sources are appropriate and so on and so forth, and we have the regulations and oversight in place. That is all a part of it. Let's not go into details now.

I, myself, as I said all along, still favor that and making it eligible. Let's see who else feels that way at least currently just to get a sense of the commission.

(A show of hands was seen.)

DR. SHAPIRO: Okay. Again we will come back to look at this more carefully when the time comes but it seems that there is, you know, an extremely substantial majority of the commission that feels that way.

DR. BACKLAR: I think there is an important liberty issued embedded in that.

DR. SHAPIRO: Yes.

DR. BACKLAR: That I do not want us to -- do not want to have it escape before there is some thought given to it.

DR. SHAPIRO: Right. For any -- you know, we -- as we begin to write our final recommendations here, any suggestions such as this one, issues or arguments which you think we ought to mount or issues we ought to articulate please let us know. We will definitely include them but you have to write them down. That is the rule. We have got to write them down because otherwise we just cannot keep track.

Bette, I am sorry.

DR. KRAMER: No. I have a comment and a question. First of all, the first page of chapter three, in the second paragraph, the text spells out a lot of the arguments that could support federal funding of derivation. Although I think there have been additional

arguments made today that could flush that out even more so but I wondered is it possible to ask -- I do not want anybody to kill me but is it possible to ask that the staff draft the two strongest arguments on both sides of this issue and put them out for commissioners? I mean, I would like to have something in front of me as I consider this and make a decision.

DR. MURRAY: Good idea.

DR. SHAPIRO: I think we may try something like that. I take the point. We are going to have to see just what things we have to get accomplished between then and now and only take on those things we can actually do.

DR. CAPRON: Between now and tomorrow morning?

DR. SHAPIRO: So we will see what we can do. We might need to put a group together to really -- we may need to put a group together to think about this. I do not think -- my own reaction was to the number two -- because I think different people would weight the different arguments as more important than others. I think the attempt to lay out the arguments on both sides is important.

DR. KRAMER: Right.

DR. SHAPIRO: And that is what we will try to

do but I would not want to limit it to two because what I think is the most important someone else might think is the least important, and so on. But to lay out the arguments, I think, is important. And in our report as well.

Okay. Thank you very much. I think that was helpful.

Now we can -- there is a section that begins on page 17 and I know that we are skipping some pages here and again I know I, myself, have some reservations about a good deal of the text in here but I have tried to note them down for the staff. If everyone else would do the same that would enable us to reflect any particular issues that you have in mind.

But there is also, I guess, associated with what we just were talking about was a recommendation on the top of page 16 and that is just maintaining local review and national oversight. I am going to go by that for right now. We all agree there ought to be some local review and national oversight until we come to actually articulating what that is. I think that is not a controversial issue but just what that national oversight is has to be articulated carefully and that we have not done yet so we will come back to that as appropriate.

There then is a section on informed consent

which begins on page 7 and there is then a recommendation on page 18 which talks about consent.

Comments or questions with respect to that recommendation?

Bernie?

DR. LO: I would urge us very strongly with regard to informed consent to say a lot more about the problematic nature of informed consent in the assisted reproduction setting. The 1994 panel had an extensive discussion of about how dependent women and couples are in that situation. I think not to at least refer back to that and reaffirm that -- I think would -- it is de facto a weakening of protections for women and couples who are donating these.

I also think that because this is likely to be a controversial issue, we should really err on the side of demonstrating that we are aware of the potential pitfalls.

Finally, I think that some of the concerns that were raised in the memo that was circulated at lunch regarding special concerns that before consenting women and couples be explicitly informed of the option of donating embryos for implantation be part of at least the supporting text.

I think that how the consent is done in this

setting with particular care for the things that make this kind of consent even more problematic than consent in other settings is important to try and spell out because I think it is one of the things that will tend to reassure people that this will not be misused or abused.

DR. SHAPIRO: Trish?

DR. BACKLAR: I agree because I think this is the area where we have to show very precisely how we respect the people who are giving and donating and that these are -- this is the -- these are the subjects that I am concerned about protecting.

DR. SHAPIRO: Bette?

DR. KRAMER: I think that there is another corollary to that and I think one of the recurrent themes when we were doing the cloning, and it keeps coming up again, is the damage that is done by the fact that the IVF industry is not regulated nor overseen. I mean, just -- it was interesting that we could not even get statistics, valid statistics, to cite.

I think that this is an opportunity to capture in the text some reference to that and to the fact that it is -- for that reason it is all the more important that the informed consent is perceived to be really spelled out quite carefully.

DR. SHAPIRO: Thank you. Other questions or

comments? Alex?

DR. CAPRON: Yes. I think we ought to, as part of that process, entirely agree with the points that have been made. Also draw an analogy to the staged process with fetal tissues that is already part of the law that we are recommending be extended for fetal transplantation into this area because it seems to me that the strongest argument we have at the moment for the analogy is the analogy between the already aborted fetus and the decisions that will be made about its disposition and the embryo which is not going to be implanted by this couple as part of their own fertility effort and as to which there are several options.

It seems to me that we might even -- and I do not know whether this is at a discussion level or a recommendation level -- say that the real branch is the decision between donating for implantation with another couple and discarding or allowing it to be used in research because once the decision has been made not to allow implantation then the embryo is in a condition which is closest to, although not identical to the one which is already permitted for the fetal tissue.

I think drawing that analogy would be strengthened if we said that the consent process, the decision making process, should be staged in that

fashion. And I do not think -- I mean, I agree with Bette that there is not much of a handle yet on the fertility field but it would seem to me that the case that we are being morally scrupulous and think that the process should be a morally scrupulous one is increased if we spell that out and suggest that the regulations or whatever that would come out to govern the process actually require that step-wise process.

DR. BACKLAR: So may I ask something? In a sense then what you are saying is that people should be asked what it is they want to do. Do they want to donate or do they want to discard? And then you ask when they once say they want to discard then you ask for research -- if you can do research on them because in a sense at that point the embryo is doomed. So that would be the next step. You would not say discard or research at the same time.

DR. CAPRON: Right. That is right. You would be you donate for fertility purposes for implantation with another couple or not.

DR. BACKLAR: Yes.

DR. CAPRON: And if not --

DR. BACKLAR: Right.

DR. CAPRON: -- discard, allow for research on fertility, allow for research with embryonic stem

cells.

DR. BACKLAR: I would go for the discard. I would not go for the research. I would say another couple or discard.

DR. CAPRON: Initially.

DR. BACKLAR: Yes.

DR. CAPRON: But if --

DR. BACKLAR: And then after --

DR. CAPRON: -- they say discard --

DR. BACKLAR: -- then you can do it.

DR. CAPRON: Yes, that is right. That is what I am saying.

DR. BACKLAR: Okay.

DR. SHAPIRO: There is a couple of people -- is it right on this point, Bernie?

DR. LO: Just as a point of fact, the options are not those at all. The options are either to keep it in deep storage for another year by paying your annual storage, which is what most couples elect to do.

DR. BACKLAR: I agree.

DR. LO: But I think we really have to round off the options to say that either you donate it or you discard it really does not do justice to --

(Simultaneous discussion.)

DR. BACKLAR: I agree. I just did not want

to ask for research until you had established that it was going to be doomed.

DR. LO: But I think it is exactly this kind of shorthand that we use, very understandably, which tends to give the impression that we are not even supporting what, in fact, is the option most people would -- most people make.

DR. CAPRON: I agree with you. The phrase that I was using was once their own fertility project was over, they had -- they were done with cells, the embryos, the question that Carol raised a long time ago when we were first talking about this, I believe it was Carol, was there can be times earlier in the process when any particular embryo is found to be not usable at all for anybody's implantation but it is an open question as to whether it might still be successful as a candidate for other forms of research.

Now I am not clear whether the kinds of barriers that existed for implantation were ones which we strongly believe are not barriers for the other. If it is a question of the cytoplasm of the egg, it does not look like the egg will implant. I mean, is that the kind of judgments that are being made? Am I right to say that you brought this up?

DR. GREIDER: I think it was Kathi.

DR. CAPRON: Oh, Kathi. Excuse me, Kathi.

DR. HANNA: I understand. When we talked to IVF providers they said that there are certain indicators that they look for. Once the fertilization has occurred in vitro, they then monitor the -- what is going on and there are certain things that they can tell that give them a good indication of whether this is going to be a good embryo to transfer.

They are doing this because they obviously want to increase their success rates and so they are developing a lot of techniques that help them to predict which will be the most successful. They then discard those that they do not think meet their criteria for implantation.

DR. CAPRON: And did they answer the additional question of whether the things that make them not good candidates are ones which mean they are not likely to replicate even to the blastocyst stage successfully?

DR. HANNA: Well, we asked Dr. Sander Shapiro that question in Chicago when he came and he said that it is hard to tell. The things -- obviously we know that viable embryos do not implant. We know that that happens all the time and it has something to do with the implantation process.

So his answer was that it is very possible that some of those embryos would produce stem cells that would be useful that has nothing to do with their ability to implant in the uterus.

DR. CAPRON: I understand that but that is sort of -- those are two answers. That is to say we know that many -- in the state of nature as well as in the infertility clinics, many embryos that are inserted do not implant. Now the question is are the techniques which are now being used to sort out the ones which they regard as eligible for the process of an implant attempt, are those ones which mirror that so they are making good predictions or do they just -- they just do not know at this point.

DR. HANNA: I do not think they know.

DR. SHAPIRO: That is the impression I got. They just do not know.

DR. CAPRON: Well, I think we ought to take account of that category which is separate from the -- we are in the middle of our fertility project and we have these eggs which are -- the doctor does not think we should use. What do we do with them? I mean, these embryos. And then where at the end of the project we have made the decision that we are not storing these anymore because we do not want to use them. We are now

confronted with the issue do we want to donate them for fertility purposes; no, we do not. Do you want to discard them or would you donate them for research purposes at that point becomes the question.

DR. LO: Or preserve them.

DR. CAPRON: Well, I was taking the end of our fertility process being already that question. So, yes, that is a prior question.

DR. SHAPIRO: Bernie?

DR. LO: What about the scenario of you are going through an IVF cycle, you are told there are seven IVF embryos in the lab, of which four are A's, two are B's and one is a D and probably would not implant. There are concerns one needs to think about, about how free and informed is a consent that is given in that context.

First of all, you may be extremely unlikely to say no to your IVF doctor because you are so dependent on that doctor for how soon you get in for the next cycle, all kinds of little extra things on how flexible they are going to be to adapt to your schedule. So there may be even more of a sort of implied or whatever sense of not being able to say no than there is in any other clinical investigation where the principal investigator is also the personal physician of the patient.

Then there is also sort of the time factor

that, you know, typically these decisions get made in a matter of hours to a day and at that time it seems to me that the woman and couple are very vulnerable to how many of these are the ones do I implant, is this going to work.

So there are lots of concerns here about, yes, you may be able to use some of those embryos but the nature of the consent you would get are so problematic that you would not want someone later on to say, gosh, if I really had known all that I now know a year later about what this all involves I would have made that same decision I was called upon to make in a relatively short period of time. So that is the kind of complexity of getting informed consent in that situation. I think we need to just be aware of it.

DR. CAPRON: Well, I mean, the notion that there is more information that one gets about one's past choices is not unique to this area and from the familiar experience of buyer's regret and onwards, we all have situations like that. But I think the concern you raise is a real one.

If I were trying to deal with that as a practical matter I would say that IVF clinics ought, if they use a process of sorting the A's from the D's or whatever, to tell people up front that they use that

process, to tell them the kinds of considerations and why they believe in their clinical judgment that they would not feel comfortable implanting a D in this couple or anybody else.

And then tell them we will notify you when we are in the middle of this process how many embryos have been established and we will tell you if there are any that we are not planning either to implant or to freeze for future implant because we think they are not -- and at that point we will ask you several choices that you can make. We think you ought to be thinking about those now and ask us questions about them, the kinds of things that would go on.

Frankly, I would be -- I would think it would be less coercive if the research the person was being asked to consent to was research unconnected with the fertility center for which the fertility center and the couple will receive no compensation whatsoever than if the fertility center says and by the way we can learn a lot about infertility and we would like to use these for research. At that point the sense of obligation and of saying, yes, of course, you can use them to your own doctor when you want that doctor to be a better fertility doctor, et cetera, et cetera, would be greater. So in a way this category of research could be less problematic.

But I agree that -- I think that we ought to say something about that and my suggestion about how to do it would be advance preparation for the thought process so it is not something you would first hear of and by the way we have to know in half an hour because the embryos will not, you know, be good after that or something, which I do not see why that should be and we could not just freeze them and unfreeze them to discard them or to research them.

DR. SHAPIRO: Jim, and then Trish.

DR. CHILDRESS: The points I was going to make have already been made better than I would have made them so that is good.

It seems to me that this has been a really rich discussion and connects well with the overall concerns we have about voluntary and informed donation or consent in this area. But I guess if we are thinking about this overall area of what to do with the embryos remaining after infertility treatments and we had the initial discussion of derivation and use that went through review and then informed consent.

It seems to me that we still are not addressing in this area some of the concerns that were raised in previous sessions about the -- some way to deal with the difficult question of the -- perhaps the

incentives that centers might have in fertility clinics to try to get -- increase the number of spare embryos to be available.

Is there any way we can address that under this heading because it seems to me to have been one of our constant concerns.

DR. BACKLAR: I am not going to answer you exactly but one of the concerns that we have not dealt with here is that actually it is these couples who are going to be funding this research because they are paying for their infertility treatment and so it is costing them and we are going to benefit from what they have paid for. And I am not certain -- I just want to lay that out on the table because I do not have any solutions. I just want us to be aware that that is going to be another factor in here.

DR. SHAPIRO: That does not really -- well, I want to get back to Jim's question, also, which is the question of whether there is anything we can do to eliminate excessive production of embryos, which I think is an important issue.

The issue you have raised, Trish -- I mean, this is all going on now and there is no use for this material and they are still paying for it.

DR. BACKLAR: Right.

DR. SHAPIRO: Whatever the charges are. I do not know what they are. And I do not think there is much reason to believe that the charge would increase with this. So it does not strike me as a -- I understand the point you are making but --

DR. BACKLAR: I do not want it to go under the rug because somebody else is going to pick it up and --

DR. SHAPIRO: That is all right.

DR. BACKLAR: -- and maybe what is important is the charges do not increase for this. I mean, it may be as simple as that to deal with it.

DR. SHAPIRO: Jim, on the other question you -- excuse me.

DR. CAPRON: Could I address Jim's point?

DR. SHAPIRO: Yes. Okay. Go ahead.

DR. CAPRON: Jim, I think that we ought to discuss the issue. I do not think we have any very ironclad answer for it. If there were clear standards in the fertility field as to appropriate numbers of eggs to bring about through super ovulation and through harvesting then we could say that presumptively those should be followed and when they are not followed presumptively the person is doing it for an illegitimate reason. There is not any such.

As far as I can see, we only have one thing we can say, which is that if there is no financial remuneration or other valuable consideration, as the law likes to say, to the fertility centers for doing this, at least we have removed that kind of incentive for someone to produce extra embryos as a way of increasing his or her business.

If the harvesting of additional embryos not only puts a financial cost on the couple if there is a greater cost of creating 30 embryos than there would be 20, but that puts an extra medical risk on the woman through the process of super ovulation, that you have to be more super ovulated and have more follicles stimulated and so forth, and I do not know factually whether that is the case but if that is the case then we could note that that, too, is a deterrent to anyone who is practicing medicine in an ethical fashion will not do something for the benefit or to add risk to his patient's situation.

What more can -- you know, this is not something where we can absolutely guarantee that no doctor is going to do this. The incentive is removed and the opposite incentive not to do anything risky through the woman is there if that is a risk. There are the considerations that we can set forward.

DR. SHAPIRO: Larry, and then Diane.

DR. MIIKE: A couple of things in addition to what Alex has just said. I am assuming that the people who are interested in doing the stem cell research are not the IF clinicians themselves. They are just the source. So there is a disjunct and so there would be less of an incentive there.

My only comment -- I am sorry I stepped out for a second but the way this recommendation reads it says after the infertility treatment has ceased and then I came in at the tail end where we talked about what about those less than perfect eggs. Don't we really mean when the couple no longer has any use for a particular embryo? That would seem to then more or less finesse the issue about the interim steps where you might have defective eggs which research may later on show that they are not viable as babies but they are good sources for stem cells.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I have some concerns about the subtle coercions that could exist for individuals or couples undergoing infertility treatment because if you just look at the language that we use, we talk about being given the opportunity to consent to research. We talk about altruistic motives that deserve recognition as well as the intent for procreation. I think there is

just enormous possibility that people might be subtly or not so subtly coerced into donating embryos or perhaps into thinking that it is a good thing to create excess embryos so that they could be donated for research because you might help us cure cancer or other disorders.

So I think there are enormous problems that perhaps we should acknowledge even though there may be nothing that can be done about them. You just have to trust that people will be fair and that people will not use these tactics to coerce others. But I think we should acknowledge more the possibility of subtle coercion in that process.

DR. SHAPIRO: Well, it is clear that we need in this area to have some expanded text here to cover all the various issues that come up here. I am not going to try and summarize them at this time. There is -- I think some of you, if you have not looked at it already, might want to look at it again.

There is an interest in a segment of the points of consider document that is at the back of this thing on informed consent which really highlights a lot of other issues that have been raised here and what this discussion tells me is that we have to find a way to organize that and the comments that are made here and put it in the text to make everyone who reads this somewhat

more sensitive to these various issues that have come up.

David?

DR. COX: So, I mean, I may well be way off base here and I certainly appreciate the kinds of coercions that can happen but I do not really see that being the main issue.

I mean, I think that there are so many embryos in storage right now and so many embryos available that unless there was some theme or economic reason for an assisted reproductive technology professional to do this, I do not see that the motivation is going to be there to drive them to do that at all. So I think there are many other reasons to do it and many other concerns that I would have about getting embryos to establish stem cells.

So the -- again it is putting where the priorities are, where the greatest risks are, and my point is I do not see this as the greatest risks or harms to people.

DR. SHAPIRO: Alex?

DR. CAPRON: One more point. At our first session with Harold Varmus about all this, he put forward the suggestion that we consider that the moral status of certain embryos would be different if they had been created for research, and we have not gone with that and

I think wisely so but there is a flip side of that.

And that is that where people have created embryos for the purpose of trying to create children I think that one of the safeguards on all of this if they are at all part of the consent process that is at all informative and not unusually coercive, and I agree with David's comments, is their own attachment to the potential that they thought those embryos were going to be.

And I do not think that the people are going to lightly make the decision to discard those embryos in the first place and I think that they are not likely if they decide they are not going to use them to go to the point of not offering them for implantation for others but for people who think that is not the course they want to go I think in a conscientious way they are the greatest safeguard against abuses here.

I think we should talk more about that and acknowledge it. It is a reason why and a way that the so-called excess embryos, which kind of has a certain awkwardness to it as a phrase, goes back to the point that these were ones that people are going to make, I think, very conscientious and cautious decisions about, and I would like to see us say that.

DR. BACKLAR: Yes. And this is one of the

real areas. This is a liberty issue. That is going to be a group of people, who if they wish to donate and have thought it through very carefully, offset the group of people who think this should never occur.

DR. SHAPIRO: Okay. We will produce some material here reflecting these issues.

Let's go on just before we -- we will break in a few minutes.

I do want to say also a word about the issue that Jim raised, that is can we do anything about the IF and any incentive they may have to excessively produce embryos. I took it that was your concerns. And I also have a concern in that but I do agree with Alex's response. I think the only thing that will reach that is professional standards and openness.

We have made some -- not we, that is the country has made some progress in this but not enough. And that really is, I think, the place and, in fact, I would see nothing wrong in the text with acknowledging that fact,and without making a specific recommendation, to just highlight this fact in some way that this is something that at least deserves attention because I think it is a real issue. I think we should find some way to reflect it.

All right. Let's go on. Also on page 18,

something which is raised as a conclusion but in any case I am not going to read it out loud. You all have it before you. But are there any comments or question on that? All this is going to be restructured so that I think this should state something -- restate it.

Yes, Carol?

DR. GREIDER: Well, this gets back to something I discussed this morning. The first sentence there simply states as a conclusion, "At this time there are not persuasive reasons to provide federal funds for the purpose of making embryos solely for the generation of human embryonic stem cells."

I would feel much more comfortable if we separate the issue of somatic cell nuclear transfer from in vitro fertilization to create embryos as two completely separate topics here and deal with them separately because I think that there are some very strong arguments for the somatic cell nuclear transfer possibility.

We can make those arguments and then maybe we do not agree with them but I think to simply state at the outset that there are no persuasive arguments, I disagree with that.

DR. BRITO: Second that.

DR. BACKLAR: Yes.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: As I read the sentence that Carol was just referring to and I go back and reread the sections that just preceded that it seems to me to be very inconsistent because we have just very persuasively that there are altruistic motives that would cause people to want to contribute to knowledge about infertility, cancer, genetic disorders. We have talked about research -- participating in research by donating embryos as being an opportunity and then we turn around in the next sentence and say we are suggesting, although not saying it outright, that there is something wrong with making embryos solely for the purpose of generating stem cells.

It seems that we have just completed our statements about the altruism involved in donating embryos to research. Those seem to be very inconsistent and I do not know what my own view is about this particular issue. You know, I have thought about it quite a bit but I think at the least we need to have more consistency than there is between these two parts of the report.

DR. SHAPIRO: Larry, then Arturo, then Eric.

DR. LO: I am sorry but I do not see any inconsistency between the two positions. In the first

case the couples are trying to have babies and in the failure with some of the ova, the fertilized ova, to have a baby or in succeeding in others, they have excess embryos that would be discarded. The question becomes what is a use for that that is to the public good in which they can -- that they would give their informed consent.

In the other case you are asking them to produce embryos not to have babies but for research purposes. So I do not find them at all inconsistent to have them stated this way.

DR. SHAPIRO: Arturo?

DR. BRITO: Yes. The inconsistency is in the way it is written so it makes it sound like it is an inconsistency but I think the key here is to emphasize what we are talking about is a balancing benefit, you know, to society versus wasting embryos that are left over in excess.

But the way I read this is that what we are saying here is not to make embryos just for the research itself but if the embryos already exist and either through electively aborted -- well, the stem cells through electively aborted fetuses or IF then, therefore, those are okay to use but let's not go making new ones from somatic cell nuclear transfer or from encouraging

people to have excess embryos made through IF.

So I think it is just the way it is written. I think it is just the wording and I do not think it is inconsistent.

DR. CASSELL: Harold, let her make her next comment so I can answer both of them.

DR. SHAPIRO: Mr. Cassell yields his time to --

DR. CASSELL: Temporarily.

DR. SHAPIRO: I was going to say the gentleman from New York but I did not know if that was an oxymoron.

(Laughter.)

DR. CASSELL: Now I have several comments.

DR. SCOTT-JONES: I would urge us to think about this again. If you have a procedure that each time it occurs results in excess embryos that need to be discarded or saved for implantation in another couple or in the donating couple at a later point in time, if every time that procedure occurs there are excess embryos then you have to admit that we always have the possibility of doing what we are saying is not acceptable and that is that embryos are created with the goal of contributing them to research because the one procedure each time it occurs results in those excess embryos.

And if you have a situation where people are told that it is altruistic to give those for research then you are already doing that, and I think that we are not being honest in what is occurring here.

DR. SHAPIRO: Eric, and Carol afterwards.

DR. CASSELL: Well, first of all, we might use, Alex, the word "remaining embryos" and that would solve that excess problem because they are remaining embryos. There may be an overlap. In other words, somebody may produce so many and you say, well, listen, we always have remaining embryos, and that was really underlying that was done for research purposes.

But, number one, that is not necessarily true and, number two, you can have good reasons for having the embryos but also good reasons against them. So it is not simply that, oh, well, those couples ought to be able to as altruistic in the promotion of research as they were in their promotion of fertility. But on the other hand there are objections to the research and the embryo produced for research that are not as -- that are much stronger than those for remaining embryos.

So it is not just one factor. So you are not being inconsistent at all to allow that there are some things that are against you doing something where in another situation because things are different they are

not against it. I do not see that as a problem.

DR. SHAPIRO: Carol?

DR. GREIDER: I tend to agree with Diane.

DR. CASSELL: That was gentlemanly, wasn't it? You know, we can learn. We can come to Washington and learn how to be a gentleman in Washington.

DR. GREIDER: I yield the first 30 seconds of my comment to the gentleman from New York.

(Laughter.)

DR. GREIDER: Since he took the mike away.

(Laughter.)

DR. SHAPIRO: You almost made it, Eric.

DR. GREIDER: I agree with a lot of what Diane said that if we are talking about altruism and people doing things for research, it starts to lead you down the path that makes me reconsider why I, and I know other people are uncomfortable with the issue of creating an embryo for research purposes. So that is why I divide these into two categories of the in vitro fertilization or the somatic cell nuclear transfer.

And I ask myself the question if we are talking about, for instance, the somatic cell nuclear transfer with the aim of making particular tissues from embryonic stem cells, what is it that makes me uncomfortable about that research. What if there were

conditions for doing that transfer such that this embryo is not ever going to be a viable being?

What if you have culture conditions where you have a particular factor that will cause it immediately to differentiate down a particular pathway so that it actually is not capable of becoming a person? Would I feel differently then that I am, you know, creating a person that then would be used solely for research?

And I am not sure exactly where I would come out here but I can see the arguments are not a cut and dried kind of argument, especially if you get back to what Diane was saying about people's reasons for donating for research purposes.

So I would just like to sort of revisit this issue about what exactly the distinguishing characteristics here are about this category and are they really one category or two categories.

DR. SHAPIRO: Let me just make a few comments before -- there is a lot of people who want to speak and I will recognize everybody as soon as I can.

One, the word "solely" is very important in that recommendation. Whether we like the other words or not is another matter but the word "solely" is in my view an extremely important aspect of this which certainly serves to distinguish this class from others regardless

of what one feels about it. At the end this obviously is a separate class. We discussed this morning, and I will not want to repeat again, how we came to make this distinction between solely and not. I will not -- you know, ditto whatever I said this morning on that issue.

But the issue which Carol is raising now I want to make sure I understand. And the issue as I understand it, Carol, is that we are not quite sure what it is that somatic cell nuclear transfer may generate so we do not know quite what to call it. We are sure in the IF case what it is that is generated. That has been studied. We know what it is. We know it can be implanted in a certain percentage of cases. It makes some sense to that word than the actual process.

Whereas, it may turn out that we do not know and there is a good deal that we do not know about somatic cell nuclear transfer, it may turn out that whatever it is that is produced is useful for embryonic stem cells but not for anything else or not for even -- can never grow into -- can never go to term and so on and so forth under any conditions, and that is true.

And I understand that difference and I think there is some usefulness in pointing out in here those differences because I think -- but it also highlights another difference, and something we do not know a lot

about, period.

That is we just do not know what it is and that raises an issue which, at least as my recollection of our discussion, Fletcher raised first of all that we know so little about it, it is not quite responsible to proceed down this line yet in view of the other kinds of concerns around the issues.

So where I come down on this is I certainly understand the distinction you are making and I think it ought to be reflected somewhere in here in the text or somewhere. I have not really thought that through carefully yet. I have not really thought about it before you raised it. But it does not lead me to come to any different conclusion at the end of the day. It just puts down a flag that says, you know, as we revisit this issue over time we will want -- as we learn more about somatic cell nuclear transfer, we may feel differently.

Now is that inconsistent with your own feeling about this?

DR. GREIDER: I certainly would be very happy if that is how the report ended up coming out. At least I would be a lot happier than I am now because I think the issue is as we or other bodies revisit this issue to separate these out as two different areas, which at this current time of understanding, we maybe cannot

distinguish between but we recognize that there are certain criteria which would then lead other people in the future or us in the future to distinguish between them. But if we at the outset lump them together it is much harder -- it will be much harder later on to separate them out.

DR. SHAPIRO: I am just speaking for myself now, not anybody else here. I am not talking about completely reasonable.

DR. BACKLAR: Yes.

DR. SHAPIRO: No amens, please.

DR. BACKLAR: Me, too.

DR. SHAPIRO: I have got a lot of people on the list. Larry, you are included. But, Trish, you are first.

DR. BACKLAR: No, it is okay.

DR. SHAPIRO: Larry?

DR. MIIKE: Just to answer Carol, I think there is another aspect which we talked about earlier which I will mention and see if you agree. I think that the reason why we feel uncomfortable about recommending somatic cell nuclear transfer is that they need to create stem cells, is that there are a lot of people who believe that what you create is an embryo, and there is no difference between that and an embryo created by a

natural means.

DR. SHAPIRO: We simply do not know.

DR. MIIKE: Regardless of what we actually know about that. That is one.

The second point is that, yes, there is a distinction between embryos -- at least the end pathway that you are looking down with somatic cell nuclear transfer because of the autologous issue but that is a use issue and we do not even get there because we are worried about the embryo issue in the first place.

And then the third part is the heading on page 19 needs to be changed because there is the possibility that somatic cell nuclear transfer can occur into a stem cell where you bypass the embryo and we certainly do not -- we are certainly not saying in this report that we want to prohibit that but the prohibition is to create the embryo to create the stem cell, not --

DR. SHAPIRO: That is a very good point. I completely agree with that. I completely agree with that.

DR. GREIDER: That is not clear currently in the report. We need to clarify that.

DR. SHAPIRO: Yes. I agree.

Okay, Arturo?

DR. BRITO: I will pass right now.

DR. SHAPIRO: Alex?

DR. CAPRON: I wanted to reply to Diane and in a way, I guess, I am doing the same thing that Arturo and others did in reply to say you are probably right that it is not well enough presented here but the arguments about choices that we are characterizing is well justified clinically, therapeutically, altruistically, not carrying over. I think is carrying over to the category of embryos made from research is true. Let me try the following argument:

To the people who are most concerned about the creation of embryos there is no justification for creating human life except the possibility that that individual embryo will be given a chance, will have a chance to become a human life, which is why some couples going through the process insist upon all the embryos that are created in vitro being implanted either in themselves or in someone else.

That is -- that can be a fact for some people who take that view but who then say if you get to the point in the process where we are not going to implant those embryos we started off in good faith hoping that each of them could become a life. Now for whatever reasons we cannot establish any pregnancy, we are giving

up on the project, we are going to adopt or whatever, and we do not want other people having our children.

It is like people who are at a stage in their illness where obviously they never wanted to get cancer. They hoped that the experimental treatments they were undergoing would be successful. I mean, the conventional treatments would be successful. And they have now gotten to the point where they say, altruistically, I will let basic research go forward and you can do studies on me because I hope that somehow that will be -- some good will come out of this.

That is meant by embryos that are created for research because at the first point that commitment and that sense that we were doing it for a reason which is beneficially potentially to that embryo is absent from the beginning and I think to the extent that we are making a distinction it is mostly the distinction which appeals to people who would draw that difference.

For people for whom that difference does not exist and that embryos -- that there is nothing wrong with creating the embryos in the first place, that you do not need a special justification to do that as long as they are not going to get to say the fourteen day stage or so forth, then that argument does not exist.

But to the extent that we are drawing two

categories, I think it is mostly to address that sensibility and that view and there is that distinction. I do not know if that is helpful to you or not because it just never exists for the embryo created for research purposes. You can never say that you did it for that embryo's own sake, the creation process.

DR. SHAPIRO: Bernie, I have got your name here but I do not know if I have got it correctly or not.

DR. LO: I will pass.

DR. SHAPIRO: You will pass.

Trish?

DR. BACKLAR: Well, I agree with you, Alex, and that is why I think that I want to keep a category that we look at and in a sense talk about purposely making embryos for research and I think that we need to address it because I think there are lots -- a great deal in that package that one would want to look at. I certainly hope that we will have a little bit of discussion about it.

DR. SHAPIRO: About? Would you say again?

DR. BACKLAR: Purposely making embryos.

DR. SHAPIRO: Research embryos so-called?

DR. BACKLAR: Yes.

DR. SHAPIRO: Well, it has been quite clear where the bulk of the commission has stood on this issue

now for quite a long while. Namely that we would not make those eligible for federal funding.

DR. CAPRON: At this time.

DR. BACKLAR: At this time.

DR. SHAPIRO: At this time, right. Okay.

Let me suggest that we take a break for about 15 minutes and let's try to reassemble roughly at 3:30.

(Whereupon, at 3:15 p.m., a break was taken.)

DR. SHAPIRO: Colleagues, we have about one hour left to discuss things this afternoon.

Let me tell you where I would like to turn our attention and that is I would like to revisit the oversight issue, not to argue out the same issues we clarified this morning but to try to just understand in a little more detail what you think would be an appropriate -- characteristics again, we will have to flush all this out so I cannot describe it all in detail right now but let me try to look, first of all, at publicly funded research in these areas and let me try to deal with uses first and then derivation second, and then we can come back and think about just how we want to -- or how we would hope to expect the private sector to be involved with this.

But just for purposes of clarifying my own thinking and for us being able to articulate this in a

way that would be acceptable to you, let me just try to look at the publicly funded uses part of this.

What we had decided this morning is that that would not be -- that whatever national oversight we have this was not a project-by-project review. That would take place at the local IRB level and all those other levels that are currently established for review of things regarding scientific merit, informed consent, and all the other things that are involved in IRB approval.

Therefore, the national group or the group that we are thinking of is kind of a group that might very well issue guidelines for IRB's to live within in this area as it accumulates experience. It would handle the registry, that is keep the information regarding what it was that was going on and make sure it was publicly distributed.

It might even have an audit function of some kind to ensure that things were going on as anticipated but it would not be an approval step as I understood this from our discussion this morning. That is they are not approving individual projects. That would -- if it is not going to take place there that would just take place in the normal way perhaps subject to guidelines that this group might issue as it saw appropriate over time.

That is what I -- my -- I am just

rearticulating something I think we decided this morning if I understood it correctly.

Now if you then transfer over in our minds to think about the derivation issue rather than the use issue, there we wanted both local and national approval on a project-by-project basis so that in the case of derivation we would require approval in the normal way in the local IRB's, et cetera, and other funding agencies if it is publicly financed.

But, also, expect this national group to look at materials that have been presented to it and see that it has gone through its appropriate local reviews and also approve this on a project-by-project basis. So it has additional functions in the derivation area that it does not have in the use area.

Now I am just trying to summarize the things I thought we said this morning, not to introduce any kind of new ideas here at the moment. Have I sort of reflected our conversation correctly?

DR. CASSELL: Correct.

DR. BACKLAR: Yes.

DR. CAPRON: Amen.

DR. SHAPIRO: The amen corner over here.

DR. CASSELL: As the project-by-project goes on that this group begins -- this agency begins to be

able to issue further guidelines so that it might not have to do project --

DR. SHAPIRO: That is right.

DR. CASSELL: In other words, it is -- project-by-project is not the same as the IRB. It is to ensure that this kind of research is --

DR. SHAPIRO: Okay. Because I just think as we begin to articulate this in detail, I just want to make sure that we had in mind -- what the commission had in mind for the use of this national organization. It sort of combines the registry, audit, oversight, guidance functions in some appropriate way and at least for the time being in the derivation side would do it by a project-by-project basis so it has approval authority. It does not have approval authority in the use side.

DR. CAPRON: And when you say "registry," this is some kind of a certification that the cells derived -- any -- if you establish a stem cell line from this approved project it will be certified as an approved line for --

DR. SHAPIRO: Yes. I have -- in the case of derivation that is exactly right. In the case of uses what I have in mind is just accumulating knowledge and characterizations of what it is that is going and they may, in fact, publish reports once a year or something of

that nature to characterize what it is that has gone on and what has been achieved and so on and so forth over time just accumulating information about it.

Now so that part, I think, is relatively straight forward from our discussions this morning. What I would like to revisit now is the issue of how we expect private organizations or research protocols that are funded -- not funded by the Federal Government to participate in this process.

DR. CASSELL: Just a step before that.

DR. SHAPIRO: Yes.

DR. CASSELL: It occurs to me following our discussion -- our justice discussion and the impact on private and so forth that one of the ways in which those ends of social distribution are met is by public education by people knowing what is going on because that brings to bear on private companies something that they otherwise cannot do and it can open up a field and again AIDS research is one of the classic examples of public pressure had a lot to do with the way that ended up being done so I think that should be part of its function so that the world knows what is going on in this kind of research.

DR. SHAPIRO: All that, at the level we are talking about right, seems really quite clear to me in

the case of publicly funded worth either on the uses or derivation side. What about -- I would like to hear a little more about how people would anticipate or would like this work with respect to privately funded work in these areas.

Now one of the expressions we had this morning is that we would like to encourage privately funded efforts to participate in this process in some way and at the very least provide information regarding what they are doing, at least nonproprietary information, so this I would like to hear a little bit more about.

DR. CAPRON: I threw out, and I heard a lot of agreement, to the notion of it would be our expectation -- it is not merely a matter of encouraging.

DR. SHAPIRO: Right.

DR. CAPRON: It would be an expectation that people in the private sector would avail themselves of this process.

DR. SHAPIRO: What does that mean in your view?

DR. CAPRON: To me -- and I think it can be stated again with an illustration of what happened in the early years of recombinant DNA work that an exercise of responsible private corporate behavior that to ensure that their protocols are, indeed, meeting the same

standards that apply to publicly funded research, corporations, private sponsors, whatever they are, would submit those protocols for whatever process would have existed if they were on the public side.

As to the derivation issue, and this is why I asked -- and I do not think it is covered -- Eric pointed me to the materials on pages 26 and 27 -- I do not think it is covered by the notion there of registry or the way the certification process is described here.

I thought that the oversight process would, in effect, assign a number. I mean, if you create -- if you run a derivation process and create a cell line and you want it to be available for use you are going to have needed to go in the first place to this panel, submit the protocol and show that it meets the ethical requirements as to consent, et cetera, et cetera.

And if it does then the panel will say at the end of that process if you are successful you will be issued a number indicating that you are in category A, B, C, whatever type of cell line it is, dash zero, dash one, dash two, dash three, whatever the -- in effect, saying this is now one which fits into the process which is described on page 27 where IRB's reviewing protocols involving the use of stem cells from existing sources have determined to be ethically acceptable and certify in

writing that the protocols will use such sources.

Well, we have to have a list of such sources. That is all I am saying. And the expectation would be that if you do not do that you will not be on the list and people cannot use your stem cell lines if they want to behave ethically.

DR. CASSELL: So, in essence, you are registering the onset, the start of the cell line, like a cell line birth certificate and then it is followed from then on and if you do not use one of those then you are not going playing the game.

DR. CAPRON: That is right. And you are presumptively out of bounds. What you do is presumptively out of bounds for anybody who in the use process wants to behave according to this expectation that they will only use stem cells from a certified pool.

DR. DUMAS: Who would certify them?

DR. CAPRON: This panel. The panel would certify the list and then the IRB would certify that the person doing a use experiment --

DR. DUMAS: On that list.

DR. CAPRON: -- is going to use one of the certified --

DR. SHAPIRO: Kathi?

DR. HANNA: I just was following up on things

Rhetaugh had said earlier, whether -- if you wanted to put more teeth in it you would actually require that federally funded projects could only use cell lines that were in the registry.

DR. CAPRON: Well, I thought that was -- I thought it --

DR. HANNA: I just want to clarify that.

DR. CAPRON: Yes, I think that is what we want to do and the thing on 27 -- the first recommendation there is not strong enough to make that clear. I would agree to strengthening it.

DR. SHAPIRO: I think my notion here is it is required for people using federal funding and we -- whatever the appropriate language of expectation is that we can work out that would encourage and make it most likely that people who are privately funded would also adhere to these standards, although not absolutely required to.

DR. CAPRON: I think we could say in that regard that if it turns out that this expectation is not being met then Congress or state legislators if they are concerned that such research is going on privately funded, which does not meet the standards or has at least not been reviewed for meeting the standards, may wish to formally require that. I would think it not a valuable

use of our time to get into the question of whether there are particular difficulties on the commerce clause level with Congress having that authority. I think probably it has it but right now the authority of Congress over the activities of states much less over private individuals is --

DR. SHAPIRO: Questionable.

DR. CAPRON: -- questionable.

DR. SHAPIRO: Newly questionable somehow.

Okay. That is very, very helpful.

Let me ask a more particular question. In my mind, as we have been thinking about this, one of the criteria I kept going over in my mind is I imagine people applying for either the -- let's say the use of stem cells, whether so-called embryonic germ cells or the embryonic stem cells. One of the criteria was that, in fact, one needed those cells to do whatever the project was and that this was not just a mere matter of convenience, that they actually needed it and the sense that it could not be performed by using some alternative scientific procedure.

Now I thought it was probably a good idea to build something like that into the recommendations at some appropriate point and it is not in there -- at least it is not in there that specifically in any of the

current recommendations, at least that is my recollection.

I just wanted to make sure as we go through this and try to refine all this that either there is or is not agreement on that issue.

DR. GREIDER: Agreement.

DR. DUMAS: Agreement.

DR. CASSELL: Agree.

DR. BRITO: If there is no alternative, that is the only time --

DR. SHAPIRO: That is right. And it goes along with the general idea of -- or we can phrase it in different ways of not wanting promiscuous use, wanting to show respect for this kind of material, and so on. It is that kind of motivation that is at stake here.

DR. CAPRON: I think just to put language on that, respect for the process by which this material is derived would be the emphasis.

DR. SHAPIRO: Right.

DR. SHAPIRO: Now are there any other issues of that nature that you think we should be specifically dealing with in these recommendations? Obviously this area, the oversight area, has to be completely rewritten.

DR. CAPRON: Can I ask about one that is here which I just wanted to have --

DR. SHAPIRO: Yes.

DR. CAPRON: On page 27 --

(Simultaneous discussion.)

DR. CAPRON: -- as of the date of publication of NBAC report, et cetera, et cetera --

(Simultaneous discussion.)

DR. CAPRON: -- cross that one out.

(Simultaneous discussion.)

DR. CAPRON: No, I understand the thrust, which is to say these people -- we have looked at what these people have done. They behaved in apparently a conscientious fashion and attended to the kinds of things we are concerned about and they ought to be, as it were, grandfathered if you can grandfather an embryo in.

(Laughter.)

DR. CAPRON: I do not know whether this is kind of a bold-faced recommendation or a commentary type recommendation if you know -- that it would follow from that the major recommendations are that research which precedes the effective date of any -- not of our report but of any implementation regulations ought to give consideration to qualify as legitimate cell lines that would fit within the certification. Sort of 01 of category A and 01 of category B, these two pioneering protocols. That strikes me more comfortable than putting

it up in the bold face.

DR. DUMAS: It just struck me -- I wondered where it came from and how it got there. It seems so inappropriate because if these two enterprises are, in fact, whatever, they will not have any trouble qualifying by whatever standards have been set up and I do not think that this group is a certifying body so I think it is entirely inappropriate. I do not think there is anything we can do to it to dress it up. I think it should come out.

(Simultaneous discussion.)

DR. CHILDRESS: I think that is probably the best way to handle it. I mean, there would be -- I mean, is it a case, for instance, that we have looked at it carefully in terms of all of us --

DR. CAPRON: Yes, I adopt Rhetaugh's view on that.

DR. SHAPIRO: Okay.

DR. DUMAS: Amen.

DR. CHILDRESS: I thought you were presenting the other view, though, that --

DR. CAPRON: No. I was --

(Simultaneous discussion.)

DR. KRAMER: A point of information. A question was raised earlier, did either or both of those

protocols go through the IRB process at their institutions?

DR. SHAPIRO: I believe so. I know it is so at Wisconsin but I do not -- I believe it is also true --

(Simultaneous discussion.)

DR. KRAMER: So would it be necessary for privately funded research taking place at an institution that had a federal assurance, whatever the term --

DR. SHAPIRO: Project assurance.

DR. KRAMER: Right. Exactly. Would any protocol that was going to be conducted under those circumstances at such an institution have to go through the IRB process? You are saying yes and Rachel is saying no.

DR. LEVIN: You mean the deriving or the use after they have been derived?

DR. KRAMER: The deriving.

DR. LEVIN: Deriving, yes.

DR. KRAMER: It would. Okay.

DR. SHAPIRO: Absolutely.

Okay.

DR. CHILDRESS: Is that really clear that this counts as research involving human subjects?

DR. KRAMER: Well, that is the question I am asking.

DR. CHILDRESS: A lot of people nodded yes and I am just not sure that that is the case.

DR. KRAMER: Where does it say so?

DR. LEVIN: You said in institutions receiving federal funds?

DR. KRAMER: Right. If -- well, that is why I asked the question about these two particular pieces of research. If a piece of research is going to be done and it is totally privately funded --

DR. LEVIN: No, totally privately funded, no.

DR. KRAMER: Even if it takes place at an institution --

DR. CAPRON: It depends on what the institutional's MPA --

DR. SHAPIRO: That is right.

DR. CAPRON: If they are multiple project assurance says, as at many of the leading institutions, we will review everyone regardless of sponsorship and hold them all to the same standard, yes.

DR. KRAMER: But that is not -- okay. That is not uniform.

DR. CAPRON: No, and it is not required either.

(Simultaneous discussion.)

DR. SHAPIRO: Eric?

DR. MESLIN: This is why we drew to your attention the recommendation relating to subpart B in a letter that we wrote to OPRR asking for clarification of this issue. The answer was not as clear as we would have hoped because the definition of what counts as in vitro fertilization is somewhat ambiguous with respect to embryo stem cell research and it is for that reason that we put the recommendation relating to subpart B in there so the answer -- the reason that you heard yes and no is that the answer is it depends. It depends on what the nature of the MPA is and it depends on whether an IRB would consider that to be human subjects research, whether they would read subpart B in that way or not, et cetera.

DR. KRAMER: So does this impact at all on what we are doing here?

DR. MESLIN: Yes.

(Laughter.)

DR. KRAMER: Okay. Are we capturing it?

DR. HANNA: If I could just help clarify here. You remember in subpart B it used to be the requirement that if you are going to do this kind of -- do research, IVF it says specifically, it had to go to the EAB. Well, EAB did not exist in 19 -- I forget what date it was, 1993, I think. That section was deleted

from the regulations so the regulations in subpart B are now silent, in effect, about whether, in fact, if you were using embryos remaining from infertility whether there is a human subject involved.

Now OPRR would like to --

DR. CAPRON: No, it is -- they struck out the EAB --

DR. HANNA: The EAB part but --

DR. CAPRON: -- but there is a super IRB process.

DR. HANNA: But there is -- the question of who a human subject is, is still up for grabs, I think. We asked OPRR specifically whether the Common Rule and as Eric said the answer was --

DR. MESLIN: Whether subpart B applied.

DR. HANNA: -- whether subpart B applied. The answer was it depends.

DR. MESLIN: In fact, the answer was -- and we can circulate this to the commission -- was -- I do not know if anyone from OPRR is here who could correct me, I do not have the document in front of me but we will get it faxed and circulated tomorrow -- that they routinely advise IRB's who have this question to consult the regulations. I do not mean to misquote or paraphrase inappropriately the letter but we asked for some specific

guidance and they have not had, I suppose, sufficient time to clarify that.

DR. HANNA: It hangs on what you would call IVF research. So that is why earlier on I had said remember this when you come back to talking about IRB review because it is not clear whether IRB's would absolutely be required to review these protocols.

Now every institution can, you know, go beyond that and say we do not really care whether it is required or not, we require it as an institution.

DR. SHAPIRO: But my sense is, at least speaking for myself, is I want to require that.

DR. DUMAS: I do, too.

DR. SHAPIRO: And it seems the easiest way to do that is to go directly to the subpart B and provide appropriate -- I do not know what the language is. I do not have any language proposed but I think that our recommendations ought to be structured so that it is required. However subpart B or some other regulation needs to be modified, we ought to suggest it be modified.

DR. CAPRON: And that is pages 12 through 15?

DR. SHAPIRO: Correct.

DR. GREIDER: But perhaps that should come under here where we make this recommendation where it comes up. Actually just move that recommendation.

(Simultaneous discussion.)

DR. SHAPIRO: Now, we have got a similar recommendation made before it so just move this page further down.

Other comments or questions regarding the issues that -- excuse me.

DR. BACKLAR: It will not affect the private sector.

DR. SHAPIRO: That is correct unless they choose to have an impact on this or unless -- it depends on how -- it depends on how this works out in people's minds and how compelled they feel to want to come under the umbrella of these kinds of standards and approaches. I think there very well might be a difference between large companies and small companies and other kinds of distribution.

I do not think even the private sector here can be thought of as one simple homogeneous unit. There is all kinds of units operating here and I think no matter what we writhe someone will want to sign up to this in spirit and others will not. I think that is just the reality. There is nothing much we do about it.

Carol?

DR. GREIDER: Just to address that. It seems like the way that we discuss this in terms of having

someone to be certified that the private sector wants to sell its cell lines to somebody -- the vast majority of people out there would more likely to be federally funded researchers. If the federally funded researchers are required to get certified cell lines then it kind of pushes them in a direction of wanting to make their cell lines so that they are certifiable.

DR. BACKLAR: And we say that in some way?

DR. SHAPIRO: Oh, yes. That is going to be -- that is going to be in here.

DR. CAPRON: We talked about that a moment ago.

DR. SHAPIRO: That is right.

DR. BACKLAR: Right. But I mean make sure that we are addressing those people who may not come under that umbrella. The advantages to being there.

DR. SHAPIRO: I think for those people that are doing this in order to sell them to --

DR. CAPRON: To others.

DR. SHAPIRO: -- privately -- publicly funded work at academic health centers and so on, they will certainly want very eagerly to do this.

DR. BACKLAR: Right.

DR. SHAPIRO: For those that do not have that market in mind at all but are doing it for other reasons

all together there will be a mixture of responses my guess is.

DR. CAPRON: You know, there is really -- isn't there a second derivative issue then here because suppose you are running a company that is a biotech company. You are doing the stem cell work in-house creating your own lines but in the end the product of your process is something that is going to go to the FDA.

And there the question would be will the FDA, Dr. Noguchi, will the FDA establish any requirements that something which ends in a product just as it has to meet human subjects regulations and standards now, would have to meet this standard that it be performed with a certified cell line so that even if you are not selling them your incentive in-house is the same.

DR. SHAPIRO: If you are -- I think that is correct. If you are involved in a process which is now coming under the FDA's jurisdiction and the only part that does not is, if course, very early on research which may or may not end up in that area and I do not know exactly how that works out but --

DR. CAPRON: I mean, I have a sense just from the recombinant DNA experience that there gets to be kind of a standard in the scientific profession here and if people are saying, well, the right thing to do is to go

and do it and we are all under equal burden to do it, there is no selective advantage here, we all want our field not to get a black eye. Because all it takes is a couple of people doing something wrong and Congress will come down on them like a ton of bricks and it hits the whole field. So the incentive not to do that is there.

DR. SHAPIRO: Okay. Other issues that surround this oversight function over which there is a series of recommendations here. I do not want to get into specifics but there might be issues that have come up there that you want to address such as those we have looked at in the last few minutes.

Okay. Then we will as our next --

DR. DUMAS: Can I raise something about the last recommendation?

DR. SHAPIRO: Sure.

DR. DUMAS: It does not seem to deal with oversight. It is the last one on page 28. It says the federal government should dedicate a part of their investment to the study of stem cells from sources other than fetal tissue and embryos remaining. To what, for example?

DR. SHAPIRO: Well, that is not part of oversight at all. It was not intended to be part of the oversight so you are quite correct there.

DR. DUMAS: It does not belong there but even -- no matter where you put it, I do not understand what it is driving at.

DR. SHAPIRO: Well, the issue is -- I think what it is driving at -- I will see if I have got this right, I will turn to Eric in a minute to see if I have got this right -- is that there has been the assertion that at least in some cases you might be able to achieve some of the same results by using more differentiated stem cells, stem cells -- so-called adult stem cells.

DR. DUMAS: Okay.

DR. SHAPIRO: But that might be for some particular purposes a useful alternative and would avoid the use of embryonic stem cells.

DR. DUMAS: Okay.

DR. SHAPIRO: And that has been discussed and referred to here today a little bit. David, for example, said before that this was not the real thing as far as he is concerned and --

DR. DUMAS: It was not what?

DR. SHAPIRO: It was not the real thing. It was not --

DR. DUMAS: The adult cell is not.

DR. SHAPIRO: -- really a good substitute but that is an open issue we have to learn more about. So

one of the recommendations here was that that is another area for research in understanding which we might benefit from knowing about. That is the basic idea.

DR. DUMAS: Right. And it seemed to me that the place where this would probably fit better but it needs to be reworded so it will be clear is at that point where we are going to talk about not using embryos if there are other sources that will achieve the same purpose and then maybe the recommendation that adult cells might be considered if that is what this is intended to do.

DR. SHAPIRO: Okay. Larry?

DR. MIIKE: I do not think it is just a simple matter of whether adult cells can replace. I would guess that just as part of the research investigation one would want to try to do reverse engineering with adult stem cells to get at to see if you can get them to a more undifferentiated state. So it seemed to be a natural part of the whole package of research in the stem cell area.

DR. SHAPIRO: I agree. Any other comments? Questions?

DR. DUMAS: Can I just -- there is no concern from this group about the eligibility of adult cells, stem cells for research or is there? It seems like the

controversy surrounds the use of embryos and fetal tissue. I think we ought to settle that issue up front and say that there is no -- you know, that we would encourage -- if that is what we would want to say. We would encourage the use of adult cells and that they would be eligible and get that out of the way and that they are eligible, and get that out of the way so it does not get confused. Coming at this end, it is rather confusing.

DR. SHAPIRO: Okay. Alex?

DR. CAPRON: You keep saying any other comments, any other comments, is it possible on chapter six to make a comment about sort of the framework of the chapter?

DR. SHAPIRO: Yes. Let's -- I want to move to that in a second and, indeed, some other chapters.

DR. CAPRON: Okay.

DR. SHAPIRO: But I guess there seems to be nothing else on this oversight issue.

Please?

DR. CAPRON: Well, I will turn in to the staff some things but I thought I would raise the general focus of them to see if there is any consensus on this that could be expressed through the staff about it. I found the beginning of chapter six hard going, in part,

because -- for two reasons.

One, there seems to be to me too much of an attempt to paint with a broader brush than is needed and to pain the picture as kind of highly polarized instead of talking about what seems to me comes out of the early chapters which is that there has been a prohibition on federal funding in an area. There are now reasons to think that certain kinds of research ought to be able to go ahead and the judgment of that falls within the realm of what most people would regard as consistent with the special respect that is owed to any human embryo and that it is not just a group of cells.

The second reason I found it hard going is related to that and that is the self-referential quality. There is all this NBAC has reached the conclusion, that NBAC recognizes and so forth, and it is my sense that it is much easier to read a document which is written by NBAC if we do not say NBAC recognizes that. If we just recognize it, state it out, and reach the conclusions. And all this other -- it is as though we are writing -- I mean, it sounds like politicians who talk about themselves in the third person all the time. Nameless politicians who talk about themselves in the third person.

It makes it harder to get to what is a fairly

widely, I think, supported group of recommendations. I mean, we are going to have a lot of people, I am sure, who are upset with our recommendations but we do not help that process by these illusions to the moral status of embryos here and then this is, you know, highly polarized here. I would like us to just get to it and not have the sense of wheels spinning. I am not being very articulate about this I will give you. And it is just me -- I raise it now rather than just turning it in because if it is just me -- if other people have that reaction I want it to be expressed.

DR. SHAPIRO: Some others do.

DR. CAPRON: Some others.

DR. MURRAY: I think Alex made two very valuable, somewhat distinct, points. On the first point, namely sort of the tone of chapter six, in particular, which is a very much -- it is on the one hand and on the other hand, and spread your arms as wide as possible because it really is sort of the two extremes, the tone of it.

We need to acknowledge those arguments. We need to make sure that they are articulated well but in the end we are probably not really addressing the document that people who are here or here, we are really addressing the argument to all the people who are

somewhere in between.

So it may be more a matter of tone than of, you know, new arguments per se. But really let's focus it on the leader who is not yet absolutely decided one way or another. I mean, I think that is our leadership and I take it that was part of your first one. You are not alone. Another member of the commission expressed to me exactly the same concern and I think that is right.

DR. SHAPIRO: Jim is first and then Eric.

DR. CHILDRESS: I agree with the points that have just been made and we also emphasized this morning that this chapter is too legalistic but I would also note that if we follow Alex's earlier suggestion of relocating the chapters then I hope we can get rid of a lot of the repetition in this chapter. This is hard going because it is also repetitious and if we have the revised chapter three on ethics moved up next to it then I hope we can move in more quickly to the recommendations and get rid of some of the verbiage that is here.

DR. SHAPIRO: Eric?

DR. CASSELL: That is what I was going to say.

DR. SHAPIRO: Arturo, did you have your hand up.

DR. BRITO: Jim just expressed my views also.

(Simultaneous discussion.)

DR. SHAPIRO: Bette?

DR. KRAMER: Just to follow up on what Alex and Tom were saying, particularly on the first page of chapter six, that second paragraph, and it does -- it paints -- the second paragraph on the first page of chapter six -- and it paints the debate as an insoluble debate and I think that what we really need to do is give recognition to the two extremes and then say but there is a huge number of people out there in the middle and they are the real audience. They are our audience. Let's face it.

DR. SHAPIRO: Thank you.

DR. BACKLAR: The overlapping opinions.

DR. SHAPIRO: Okay. Other comments?

DR. GREIDER: Is this on chapter six that we are having comments on?

DR. SHAPIRO: Any part.

DR. GREIDER: So there were two issues in chapter three that really stuck out to me and I apologize again, I have not read the one we just got yesterday but this was very much in the one we got a few days ago. Chapter three read to be very legalistic to me. It read like a legal argument rather than sort of a lay person's argument and so that -- and that is really throughout the

whole of chapter three.

And the other -- there is a number of places, and I have marked it up in my copy, where we use language that seems to be extracted directly from the Human Embryo Panel to justify use of either spare embryos or any other source of stem cells as infertility research, that research that would use these sources of embryos to create stem cells will somehow help to permit fertility of couples in the future. And I do not think that that is the issue that we are getting at here at all.

We are getting at stem cells for research for a variety of different diseases not at all limited to fertility research and it comes up again and again, especially in chapter three, this reference to helping more people by having them overcome their fertility problems. I think that it is partly just because it is extracted from earlier reports or something.

DR. SHAPIRO: Okay. I thought you had another point.

DR. GREIDER: Those were the two points.

DR. SHAPIRO: Other comments or questions? Jim?

DR. CHILDRESS: It seems to me that chapter three, and I may have made this point earlier this morning, is actually too abstracted from the current

debate in the sense that -- and Bernie made this point in an e-mail message -- that it does not really engage the actual language of a number of the participants, particularly those who would perhaps be most vigorously opposed to the position we are addressing here, and I would urge that the revision take account of the actual written comments, oral testimony, including the testimony at Georgetown in the religious spokespersons' discussion in order to be as clear and as nuanced and as contextual as possible relative to where the discussion really is.

I think, for example, if we do that then there will be some other issues that we would need to attend to a bit. Several of those who -- at least a couple of those who spoke at Georgetown, for instance, were concerned about the burdening of conscience in terms of use of taxpayer dollars in this area. A form of complicity that is not really addressed here. And for them that was a justice question. The imposition of the burden on conscience.

The justice discussion needs to extend in terms of priorities as well. And it seems to me that some of the oversight points can -- as a matter of general concern -- also be raised toward the end of this since procedural issues are also important from an ethical standpoint.

DR. CAPRON: Could I ask for a clarification on that, Jim? I recall the argument that was raised, which I think you were correct, was framed in justice terms. Are you suggesting that we discuss that argument and respond to it? Because as I recall the argument, it was if therapies are developed through this means, which we regard as an illegitimate means, we will be in a position then of facing the hard choice of whether or not to accept those therapies if they are the only ones available or forego them, which is obviously a very difficult position of conscience to be in. It certainly is not unique to this field and I think it is an argument that should be acknowledged.

I do not think it is an argument that is persuasive.

DR. CHILDRESS: Right.

DR. CAPRON: That it is such an unjust position to put someone in that it is wrong to (a) through federal funding the creation of therapies that some people will find unacceptable.

DR. CHILDRESS: No, like you, I would disagree with the position but it seems to me that --

DR. CAPRON: But that was -- when you referred to it as the justice argument, was that the one you were thinking of?

DR. CHILDRESS: That was one part of it, yes.

DR. CAPRON: Okay.

DR. SHAPIRO: Tom?

DR. MURRAY: I have reconsidered. The point I was going to make I can make better in writing, particularly in light of the fatigue which I see evident in the room so I will just do that.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I think that we have a responsibility to describe the various points of view that have been expressed by the people who came to present their testimony. I do not think that we ought to endeavor to either support or refute their positions, or even necessarily to over interpret them.

I think that what we should do is based on all the things that we heard in our deliberations is make our recommendations and support those recommendations by the conclusions we have reached on the basis of all that we heard. And that is a little bit different than taking -- than putting the focus on the arguments pro and con that people presented.

Does that make sense?

DR. SHAPIRO: No.

DR. DUMAS: I started out being clear and ended up with a puzzle.

One of the things that I noticed about the -- the feeling that I get in reading much of the report is that we make -- we try to make a strong case for what we are about to recommend and it seems somehow that our pace that we are making is intended to refute some of the positions that people have taken in relation to this. I do not think that we need to do it that way. I do not think we need to refute anybody's position but rather to state clearly our recommendation, our conclusions and recommendations and support that, and say what our position is to support what it is that we have recommended.

Now there might be a thin line between that but there is something that has been kind of gnawing at me for a long time and I have not been at a point where I can really fully verbalize what my concern was and it has to do with -- and this is an overstatement -- this arguing against the points of views that have been presented by various individuals and groups in order to make our point. I do not think we need to do it that way.

We need to describe what they think, what they said, the conclusions that we came to, the recommendations that we made, and support those recommendations.

DR. CAPRON: But it does seem to me a fine -- I think it is a stylistic -- there are certain ways of writing that are more condensious (sic) than others. I would agree with you that we ought not to be argumentative in and of itself.

But if someone says that a particular course of conduct would amount to a grave injustice and we say we are going -- we recommend that course of conduct, we have some obligation to state our reasons and our reasons are --

DR. DUMAS: That is right.

DR. CAPRON: Yes. But if I can --

DR. DUMAS: But you do not have to say --

DR. CAPRON: But our reasons are, in effect -- in effect, but not stylistically perhaps, a refutation of or at least a statement as to why that position is not convincing.

DR. DUMAS: Well, yes, to us.

DR. CAPRON: Well, yes, it can only be. I mean, we have --

DR. DUMAS: You are right. It is -- it is saying that -- I can describe what other people's points of view are and I can respect those and not make it appear as if I am not sympathetic to their cause. It is just that when we put all the facts together and all the

things we know, this is where we come out, and this is why we are recommending this.

DR. CAPRON: But people are not making these arguments simply to let us know that they have moral views. They have a belief as to what the outcome ought to be and by reaching another conclusion we have to at least have enough, as you put it, justification for our conclusion to say why we are, in effect, not persuaded by their position.

DR. DUMAS: And what I am saying is a statement that we are not persuaded by their position made five or six different ways is not to me justification for our recommendations. That is my point.

DR. CAPRON: Yes, I would certainly agree with that.

NEXT STEPS

DR. SHAPIRO: Other comments?

I will just take the last few minutes here to review our agenda for tomorrow. The morning session, the first session in the morning, deals with federal oversight and we will have -- as you know from your agenda -- a number of -- I think almost a dozen representatives from various agencies to come and share their views on that issue and how the interagency process is working. It is part of an ongoing important activity

we have to look at the overall effectiveness of the system of federal regulation in the areas of concern to us. That we will start early tomorrow morning. We will be starting at 8:00 o'clock and that session will be chaired by Alta Charo.

I will probably not be here for the first hour or so not because I am sleeping late but because I am talking to a group meeting here in town, psychiatric researchers, dealing with our previous report with respect to mental disorders and so on. So I will join, hopefully, as close to 9:00 o'clock as I can get back here.

Then we will also have a report later on in the morning from the Advisory Committee to the Director, NIH, from the Office of Protection from Research Risks Review Panel. That is the OPRR location issue so to speak. So that will take place at 11:00 o'clock.

So we have a busy morning but it does not deal with the issue we have spending most of today on. We will then go and see what other issues we want -- we will save the afternoon or that portion of the afternoon we would like to use for dealing with any follow-up issues on the stem cell issue so that we can give the staff and ourselves as much direction as possible in producing the next version of the report, which happens

to happen, roughly speaking, within a week. So that is what we will do from approximately 12:00 on.

I am toying with the idea of having a working lunch here tomorrow so that we can finish early. I know there are many people that have to leave early whether or not we have a working lunch and so in order to keep as many people here focused on that issue it may be that we will pass around a list and see what kind of sandwich someone wants to have tomorrow if that is acceptable to people. I think that is preferable and giving us an opportunity to finish a little earlier.

Okay. Thank you all very much. We are adjourned.

(Whereupon, at 4:50 p.m., the proceedings were adjourned.)

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