33RD MEETING

OF THE

NATIONAL BIOETHICS ADVISORY COMMISSION

UNIVERSITY PARK HOTEL
JEROME C. HUNSAKER ROOM
20 SIDNEY STREET
CAMBRIDGE, MASSACHUSETT

July 13, 1999

EBERLIN REPORTING SERVICE
14208 Piccadilly Road
Silver Spring, Maryland 20906
(301) 460-8369

I N D E X

P R O C E E D I N G S

OPENING REMARKS

DR. SHAPIRO: Colleagues, I would like to call our meeting to order.

All right. Let me try to outline how we are going to try to proceed today.

First of all, I would like to welcome everyone and thank everyone for interrupting their summer activities in order to be here today. I think we are expecting all members of the commission here today although not everyone is here at the moment.

Let me begin, first of all, by thanking the members of the staff and many members of the commission for the enormous amount of work done in the last couple of weeks on various aspects of the report. I mean, quite a few of you did an awful lot of work and an awful lot of writing.

Jim, Carol, Eric, Alex, Steve, as you all got the e-mail yesterday, those of you who are up-to-date on your e-mail, and others. I mean we just -- Bernie has provided some really interesting material now which we will put in a couple of the chapters, little boxes which illustrate the possible uses and eventual benefits of research in the area that we are discussing. So that I really am very, very appreciative of the committee's

work.

My only -- most of the work that we did since our last meeting in Washington really focused on what is now chapters one through four, that is all the introductory chapters, and chapter six, which we were waiting to do at the last minute trying to get the materials together which aim towards chapter six. Well, it was chapter six, now chapter five, excuse me, the recommendations and conclusions chapter, is the one that probably needs most of our attention here today.

I intend to work as we have at other meetings to discuss particular issues, which I think we need to resolve yet to be resolved and then accumulate a few of these issues and to the extent that we want to sit down and rewrite things we will just break up while staff and a few associate commissioners rewrite things that we think need attention right now because I do want to get through a discussion of all the recommendations. We decided in some sense quite a few things last time but there are quite a few things in front of us that need our attention.

I would like to begin today's discussion by going to -- again in chapter five. If I say chapter six just think chapter five. I am probably not fully adjusted to the fact that we have renumbered these

chapters yet -- to, I believe, what is recommendation eight.

THE ETHICAL USE OF HUMAN STEM CELLS IN RESEARCH

DISCUSSION OF DRAFT REPORT

DR. SHAPIRO: Recommendation eight currently appears at the top of page 19 of chapter five. It reads in this current form as follows: "Current human subjects regulations require clarification and review to make clear the role of institutional review boards in the review of research using human embryos and requirements for consent," and so on. That is what it says.

There is a -- that is not an adequate recommendation in its current form and there are a series of very substantive issues that lie behind that and that is where I want to focus our initial discussion.

Subsequent to that discussion we can then look at the revised recommendation nine, which deals with the actual activities of the national review board or whatever its name is going to be. I do not have the name quite correctly.

And I think we might break at that time just to make sure we have those aspects of this tied down before proceeding to work on other aspects of our recommendations.

First of all, a logistical issue before we launch into this particular recommendation. The way this microphone system works -- I mean, we discovered that every venue we have is a different type of microphone. There is no end. There is an infinite number of possible arrangements apparently. All our microphones are on. If you want to say something really secret, press the mute button and you can tell yourself or your closest neighbor what it is you want to say. All our microphones are live, so to speak. The mute button is at the bottom of this pad and you press that if you want to say something really that is not relevant for others and not relevant for the discussion.

PROF. CAPRON: Boy, this is boring.

(Laughter.)

DR. SHAPIRO: There ought to be something -- I ought to have a hook here where I can mute anybody --

(Laughter.)

DR. SHAPIRO: -- here when I do not like what they are saying but I do not have such a facility. Not just yet anyhow.

DR. CASSELL: Not just yet.

DR. SHAPIRO: Not just yet. That is right. You know, that phrase we use "not at this time."

PROF. CAPRON: We ought to try some other

hotel until we finally get one.

DR. SHAPIRO: That is right.

PROF. CAPRON: Then we are staying in that hotel, right?

DR. SHAPIRO: That is right. We will finally settle down into a single venue.

PROF. CAPRON: Are we writing a separate report on all the hotels we have been in?

(Laughter.)

DR. SHAPIRO: That is right. We can have folders of special listening for all our experiences.

Well, let me recall first of all -- let me begin our discussion of this recommendation eight with the -- reminding you what we decide last time.

The principle thing we decided was that derivation required national review, however we structure that national review. Use, e.g. ES cells, required local review. That was really the decision that we made. National in one case and local in the other.

Now I think what we need to discuss is what do we mean by local review. Now I think we sort of talked in a kind of informal way about local IRB review and, indeed, if you read recommendation number nine, revised recommendation number nine, it sort of refers to the local IRB's.

There is, however, as quite clearly from reading what is currently chapter three that Alex has taken a leadership in helping us redo that the question is are we dealing with human subjects review here. Is that what we are saying? Or are we saying, "No, this is not human subjects review. It is just that we want some kind of local review and we may want to use a mechanism that is in place here for that purpose." And we need to discuss exactly what we mean in this area.

Then we can go to the issue of derivation and national review where I believe our thoughts are somewhat more clearly defined. This is really, I think, an important issue to decide in principle whether we are going to declare that this is human subjects research, which I think is not what we said. I believe what our thought was that -- I am talking about use now -- that this -- that we wanted to use the local mechanism that happens to be in place but how we decide that will determine how we have to rewrite this and what we have to say about subpart A and subpart B, the so-called Common Rule, and so on.

Alex, would you like to address the question? You have probably thought about this more carefully and what -- we will see what your judgment is on this issue.

PROF. CAPRON: Well, my judgment would be

that we are going to run into a lot of resistance, and understandably so, if we were to recommend a construction of a parallel set of review bodies at the local level to look at work with human stem cells and to make sure, for example, that if there is a registry or certification of cell lines that are fundable; that they be -- that they be met.

And on the other hand IRB's do not clearly have jurisdiction in this area because unlike research with embryos where there is some argument, I suppose, does subpart A apply simply because subpart B applies. And, indeed, does subpart B apply if you go back, which I did not even discuss in chapter three because I thought it was too arcane. If you go back to the preamble of the subpart B it talks as though research with embryos is not going to be covered but HHS has, in fact, treated it that way.

But once you are dealing with stem cells you are dealing with what are research tools at that point. Nevertheless, because of the desire to make sure that this area is going forward in a fashion which the public can be confident is getting oversight, it seems to me appropriate to expand on it and explain what we mean by the present recommendation eight and, in effect, make use of a group -- the IRB's that are familiar with the

research process and where no additional administrative machinery has to be established for them to take on the role that is suggested for them, for example, under recommendation nine in the rewrite that we got from you and Kathi.

Is that responsive to your --

DR. SHAPIRO: Yes, it certainly is.

Again, now we are talking about -- I want to distinguish between use and derivation here. I am trying to make sure that we agree on what we think the appropriate review mechanism is for use and there will have to be a rewritten recommendation eight in order to accommodate this more clearly.

But how -- do you feel -- if I understood what Alex said, and it certainly coincides with my own feeling about it, is that we do want local review of use. Okay. That is what we decided last time. And that we want to use an existing system not because it is covered legally by that system but we are recommending that we use that system, which is in place and well understood and so on, to give the kind of local review that we would feel comfortable with regarding use of EG/ES cells to talk loosely.

Jim?

DR. CHILDRESS: This recommendation also

includes as many of our other comments that we have about the twin protections of IRB review and informed consent. I guess I would be interested as we are thinking about this exactly what we are bringing into play and I think from my standpoint we are not bringing into play all those requirements about informed consent so at least that part would have to be dropped out of the recommendation.

And then exactly what do we expect of the IRB? What does this review constitute? Exactly what sorts of things do we want them to deal with and by what standards?

DR. SHAPIRO: Well, I will just -- there is a lot of people who want to respond. The things that I had most in mind myself, Jim, was: One, that the cells come from, so to speak, certified source. And, two, the other issue that at least was in my mind was to avoid the extravagant use of these materials. Those were the -- it was not -- those were the main things that were on my mind but others could speak.

Alex, and then Larry?

PROF. CAPRON: I agree with what you just said, Harold, and I actually did not think that some of the introductory language on pages 17 and 18 was appropriate for that reason. I do not think that this is

the report in which we ought to be rehearsing our larger project of the extension of the twin protections, as it were, or the extension across the Federal Government of subparts B through D or revisions in the Common Rule and so forth like that.

I mean, this, it seems to me, gets us off on the wrong foot. We ought to hone right in on what Harold just said.

DR. SHAPIRO: Larry?

DR. MIIKE: My recollection of the discussion at the last meeting about local review was that it was going to be whatever local review is now. So it is new to me that we are now talking about something in addition to human subjects research. That is where we seem to be going.

DR. SHAPIRO: I am sorry. I did not hear the last part of your --

DR. MIIKE: I thought we had concluded at the last meeting that local review would be local review as currently conducted so that if these cases of use are not human subjects they would -- we would not be extending the review to this area.

Now it seems to me that one way to get around the -- I guess, we do not want to be arguing about this -- is that I thought part of the oversight board was that

they would be doing -- looking at derivation and certification of that and eventually would develop some standards and then the local boards or somebody at the local level could actually look at individual projects and follow that process.

But to -- I do not think there has been any controversy about the actual research of ES and EG cells themselves. It is the source of the material and I look at this as just another part of the basic research area.

DR. SHAPIRO: Well, I think there are really two possibilities here if we want any oversight at all of this. Maybe that is an exaggerated way to say it but one is to use the local mechanisms that are available and not because they are defined as currently in the federal regulations but just to use an existing mechanism if we want some oversight on a case by case basis of the use side.

The other possibility, which I think Steve ad I had at least a brief discussion about just before the meeting, is to give that authority or give that oversight to sponsoring agencies. In which case what you have is case-by-case review but you have it at the sponsoring agency level. Now to not have any review of the use but just overall assessment as time goes by the national -- through the information that is collected in the national

registry -- is -- clearly that is possible but I did not think that is what we had decided but maybe that is my interpretation.

DR. MIIKE: Can I respond to that?

DR. SHAPIRO: Yes.

DR. MIIKE: That is not what I was really saying. I think that there would be a registry and that we would need to know what projects are getting done but I thought that we had decided at the last meeting that the normal peer review mechanism would make the scientific assessments of the research projects.

DR. SHAPIRO: The scientific assessments, that is correct. That is right. So the local review that we are talking about now would not be for the scientific -- overall scientific merit of this proposal that would be handled at the agency. The question is whether you want some additional local review to look at two things, certification and what I call extravagant use or -- but I think you could -- Steve probably wants to speak to this point -- put that at the funding level agency.

Steve?

DR. HOLTZMAN: So I would suggest as an alternative precisely because IRB's are not in play, because human subjects are not in play when we are

talking about use of -- as you said, Alex, it is a research tool or reagent -- that the two goals you articulated, the national looking over the derivation, a certification process with respect source -- the national could take care of that. And the other thing you mentioned was how do we have preventions against extravagant use.

I would ask the question how do we currently have protections against extravagant use of fetal tissue? And the answer is each agency looking at a protocol by protocol review of the submitted grants makes a determination as to the scientific validity of the worth in virtue of the material being used and that we could recommend or we could recommend that the oversight agency say to the agencies that the review of protocols using embryonic stem cells or other embryonic and fetal tissue that due consideration be given to the respectful -- that the scientific project merits the use of these materials.

DR. SHAPIRO: Clearly another possibility.

David?

DR. COX: So I really support what Steve is saying.

First of all, the two criteria that you mentioned, Harold, are the prime ones. I support that first.

But the problem with the local review is that, as Steve said, that the IRB's are for human subjects, they are not for this, and how are they going to collate this information to sort of keep track of who is using what? There is no way to funnel it back in ultimately to keep track of how many people are doing the work with the cell lines and what the results are. So that is better for the funding agencies and the funding sources.

I do not think it will be any less of a review but that it just seems onerous with presently existing local structures.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I would underline those points as well and it seems to me that given the problems that we have already talked about with the IRB system that it is -- it would be unfortunate to load something else on it when, as a matter of fact, what can be accomplished can be accomplished as well if not better at another level. So I very much support the direction this discussion is taking.

DR. HOLTZMAN: I also have a major pragmatic point. I do not know for a fact that every institution conducing biomedical research has an IRB because not all of them are conducting human subjects research.

DR. SHAPIRO: Eric, and then Alex.

DR. CASSELL: I think I want to reiterate these last few points. I think we would be adding a burden to IRB's but more than that it is not something that is part of their expertise. You know, what would they actually do and they would be finding themselves doing things they never did before and they do not have consent forms to argue about endlessly. Instead of that they would be looking at something that I think the funding agency should be and also at this next mechanism we are going to discuss in a little while which accomplishes some of the other things that we were looking for.

DR. SHAPIRO: Alex?

PROF. CAPRON: I think there is a lot of merit in Steve's suggestion. The question that I have is something which David and others can respond to. My impression from the study section approach is that they also do not have any experience with what we are asking or what Harold has put as the central question, which is, in effect, a question of justice, appropriateness and so forth.

Deciding on the scientific merit as a relative basis among and giving a priority score to a range of protocols that have come in is something that

the study sections are familiar with. But this notion that there are a set of social concerns about "extravagant" use I think will strike many of them as being as odd as you all -- and as Eric Cassell has just suggested, is for the IRB's to get off their familiar turfs. The irony, of course, is the IRB's have justice as one of the three principles under the Belmont Report that they are supposed to be implementing. Maybe they are no better at it.

So I am not -- I do not oppose it. I think there is a lot of attractiveness. It -- Steve's idea springs from the same motivation as the other suggestion that I had put forward, which was let's make use of existing mechanisms. Let's not create a whole new set of review bodies. It is a genuine question. Do you really think that if you were sitting on a study section and imagine the people who would be sitting around the table with you, would they feel themselves equipped to, ready to, comfortable with the process of saying, "Well, does this amount to an extravagant use," to use the Chair's question. That is really -- it is just --

DR. SHAPIRO: David, Steve and Larry?

DR. COX: So my answer to Alex is yes because the reason is that study sections are not your father's Oldsmobile any more and the scientists may not be ready

for it but the staff at the National Institutes of Health makes them ready for it because whether they are ready to step up to the plate or not that is part of the job. So it is already in place.

It is in place with the -- the human subjects that are being used, are males and females represented equally? Congress took care of that one. Now whether scientists want to address it or not, in every study section that gets addressed, okay, when you have human subjects.

How about different ethnic groups? How about children? That is the mandate from NIH now. Every grant that you review you have to look at and basically say, "Have children been appropriately considered?" So that it may be viewed as a burden by some scientists but that is tough because now that is part of the job and I think that in my view this is the best possible scenario because scientists get drug, if they are not -- they are not willing to do it themselves, kicking and screaming into the real world.

DR. SHAPIRO: I just want to point out, Steve and Larry, that whichever one we choose here, they have an additional set of considerations to work on. Our points to consider and things like that will help them, whoever it is, but there will be some additional burdens

no matter where we put this.

Steve and then Larry.

DR. HOLTZMAN: I guess, I would say yes as well, Alex, for the following reason or two reasons: The first is there is an experience now with approving protocols which use in research fetal materials. If you look at the statute and whatnot and then regulation or whatever, you get a whole lot of discourse to the effect that this should not be used gratuitously, that moving to the use of the human material should be if there is not available animal materials equivalent, et cetera, that you have moved to the point where this makes sense. So I think there is some precedent. I have heard scientists here talking about how they only move on to the human source material when the alternatives are not available.

The second point is, again, I think we can provide guidance and the new review body can provide guidance to the study sections that say, "Take this into consideration."

DR. SHAPIRO: Larry

DR. MIIKE: I am having trouble with some of the offered criteria for review. For example, on page 24 in chapter five there is five and six. And maybe the scientists here can correct me if I am wrong but I thought we were talking about really basic research so

that I do not know how one can begin to make these kinds of estimates about the potential benefits when it is going down a particular track, who is -- you know, whether the wealthy was going to get the benefits of it over others.

And it seems to me that we -- if -- I am having trouble seeing -- once the decision has been made that stem cells ought to be used in research as basically some materials to be used -- I am having trouble seeing what kinds of ethical issues we have to deal with -- and we continue to be concerned -- on the individual protocol basis.

DR. SHAPIRO: Well, first of all, Eric.

DR. CASSELL: Well, Larry, after all, one of the reasons that -- one of the justifications given in the first place for using human embryos at this time is that the potential reward from research is much greater now than it has been before. You cannot both say that on the one hand and on the other hand say, well, this is just basic research, you know, they do not have any end in view. For one thing, I never met anybody that did not have an end in view somehow.

DR. MIIKE: But, Eric, I think you can. I think you can.

DR. CASSELL: Their own vanity.

DR. MIIKE: That is what the -- that is what the proposed review after several years ought to be taking a look at. I am just having trouble with deciding how one would go about reviewing individual protocols by these criteria.

DR. CASSELL: Well, we would like them to tell us what they are doing this for.

DR. SHAPIRO: If I could just say that the issues you are -- I believe, Larry, excuse me if I have misinterpreted -- the material on page 23 and 24 really deals in the national oversight level. Point aside from whether it is the right material or not. It does not deal with the case by cases, at least it is not meant to, that we are talking about now.

Let's see if we can reach some conclusion -- I am sorry, Rhetaugh.

DR. DUMAS: May I just make a statement. There has to be some consistency and some link between the motives for the oversight and the initial review so that whatever we are going to propose to look at in the oversight we must ensure that attention is given to it at the earlier level.

The concern that I have in trying to separate this is whether or not we mind end up having a layer of criteria for oversight that has not been sufficiently

incorporated in initial reviews.

DR. SHAPIRO: I think that is an important point. I think that the way I would like to see recommendation eight be written, regardless of whether we put that burden on local IRB's or on funding agencies, so that it refers to criteria, for example, that are in the points to consider document, which is, I think, quite complete right now and other things which we really will incorporate. Those things at least will be on their minds as they go through and think about this.

Let's see if we can reach a conclusion. I do not know if we have anything further to say or to add to this discussion on what is a small but important point, namely where this case by case review takes place. There have been at least two options presented here. One is that it should take place at the sponsor's level, whether it is NIH or DOE or whoever it is that is sponsoring the research if it is federal funds. And, second, takes place locally. I think we -- so let's just say that is a well defined point and let's settle it.

How many favor, as Steve said, using the analogy from the fetal tissue case to have this case by case review at the sponsor's level? Obviously it has got to reflect the points to consider and so on.

PROF. CAPRON: Could I have just one question

before you --

DR. SHAPIRO: Yes.

PROF. CAPRON: -- because you stuck in the "as is the case for fetal tissue." Do we have any evidence despite the sensitivity on the subject that the study sections do anything on the fetal tissue issue? Because you threw that in, Steve, and you said scientists talk about this, and I am sure they do, and some write in journals about it. I am sure that is true. But do we have any evidence that the study sections have ever done anything about this? Do you know, David, or Carol?

DR. SHAPIRO: I cannot speak. I had not meant quite as much by that --

PROF. CAPRON: Yes, but I think what -- my reason for raising it is I do not think we can with either of these ideas simply say this is business as usual.

(Simultaneous discussion.)

PROF. CAPRON: I was almost ready to vote for it, you see, and then you put that in and I thought, wait a second, are we fooling ourselves saying, oh, they are familiar -- they do this already with -- under the fetal tissue --

DR. SHAPIRO: I think whoever does this will have to read this material, read the points to consider,

educate themselves some, whether it is the local IRB or someone else.

PROF. CAPRON: Okay.

DR. SHAPIRO: I think that is -- we cannot -- yes?

DR. LO: If I can just make a friendly suggestion that that text, exactly what you say, be part of the commentary that leads up to this so there is no confusion on the part of anybody implementing this.

DR. SHAPIRO: Yes.

DR. LO: That it is not business as usual.

DR. SHAPIRO: Yes.

DR. LO: It is a new challenge. They may have been doing it and they may not but they have got to meet it.

DR. SHAPIRO: All right. With that understood, how many would favor the review at the funding agency level?

(A show of hands was seen.)

DR. SHAPIRO: Okay. Clearly that is the overwhelming view of the committee if not the unanimous view.

DR. LO: Can I ask a question which has been bothering me as I read through the last chapter, chapter five? So much of what we are doing is obviously directed

at the issue of federal funding, federal oversight. Do we want to say anything at all about what we would pose as best practices or ethical ideas for research outside federal oversight in the private sector? So that is there some room some place to say that if you are going to sponsor such research outside federal auspices privately that you should have some comparable system in place to look at these issues when you are doing use?

DR. SHAPIRO: I think this is a very important issue and I want to come back to that as a separate issue if you do not mind, Bernie. It is a very important issue. We have discussed it from time-to-time. It is not adequately reflected in the current materials and we have to decide what it is we want to say in that respect so thank you for raising it. We will definitely bring it up as a separate issue.

Okay. So we will have to rewrite recommendation eight to reflect the discussions we have had here today and I think on reflection in hearing this discussion there are some very distinctive advantages to having this at the sponsoring level, not least of which does not confuse what the IRB's are about, and so I think that that is, you know, a way to do that. We will break after a while and see if we cannot get one or two of us to rewrite eight to reflect those issues and reflect that

discussion.

I would like now to turn to item -- recommendation nine, which has to do with the -- we are now talking about the National Review and Oversight Panel or whatever other name someone wants to recommend, I do not want to focus on that, which is described in recommendation nine. I think you all have copies of revised recommendation nine.

PROF. CAPRON: Before we go to nine, I am confused about one thing. What are we doing with the text and the recommendation -- the present recommendation eight, which is not exhausted by our previous discussion for the last twenty minutes?

DR. SHAPIRO: It is not exhausted. I thought that your recommendation was entirely appropriate myself, that is that we try to take on too much just prior to eight.

PROF. CAPRON: No, that is -- I am sorry, I am not clear. The first two paragraphs prior to eight I think basically should disappear. But then the next paragraphs, and the recommendation itself, asks for clarification of the role of the IRB vis-a-vis derivation. I thought -- in other words, the division that exists here is local versus national.

DR. SHAPIRO: Right.

PROF. CAPRON: The division that we have just been talking about is use and derivation. We are sort of going in nonchronological order. I mean, perhaps we ought to talk about the Seinfeld --

(Simultaneous discussion.)

PROF. CAPRON: Anyway, but on the derivation side there is a whole -- there is need for clarification of the role of the IRB's because some of the question goes to --

DR. SHAPIRO: I agree.

PROF. CAPRON: Okay.

DR. SHAPIRO: I agree.

PROF. CAPRON: And I was not sure whether we were --

DR. SHAPIRO: I agree with that.

PROF. CAPRON: -- aligning and sort of saying, well, we have gotten rid of eight because we have done this peer review thing now.

DR. SHAPIRO: No, I quite agree that it is not -- it is because we have changed local/national to use/derivation.

PROF. CAPRON: Fine.

DR. SHAPIRO: And this has to be adjusted to reflect that. So if we could look at recommendation nine. Now I do not -- obviously if you just look even at

the revised recommendation nine it refers -- under item (a) it already has to be changed because item (a) just refers to 9(a) refers to what role they have with respect to use and that refers to IRB's which now, of course, will no longer happen. That has to be rewritten.

I just want to -- without trying to give my own view of nine or revised nine right now -- to see whether it is captured in any way the kind of issues that we were concerned about as to what this role and function of this group ought to be.

Rhetaugh?

DR. DUMAS: I do not think 9 is clear at all. I found myself trying to add on to the recommendation as it is stated. It is not clearly stated in my conception what the oversight panel is going to be looking at. What function does it serve? What are we trying to ensure by that panel? And I do not think it is clearly enough stated in that section.

DR. SHAPIRO: May I just make -- is everybody looking at revised number nine? They may both be very unclear.

DR. DUMAS: I do not have that.

DR. SHAPIRO: I am not trying to defend either the currently --

DR. DUMAS: Oh, I am sorry.

DR. SHAPIRO: -- the first or the second version but let's all at least work from a single version.

DR. DUMAS: Oh, okay. I do not have that one. I have not looked at it. Scratch that.

DR. SHAPIRO: Your comments may very well apply in any case.

Steve?

DR. HOLTZMAN: But to Rhetaugh's point, even if rewritten, maybe if we took a moment for ourselves to say in a bullet point form what are the key roles with respect to derivation which I believe -- my understanding -- with respect to derivation protocol-by-protocol review. All right. With respect to -- let me call it -- registry functions. All right. Maintaining a registry of certified cell lines which can approve the -- approve protocol-by-protocol review and a registry of protocols using -- all right.

And then the last I am going to call the -- I would not call it review because I think it is confusing but rather public education, oversight of use where what you are doing is getting mandatorily the protocol-by-protocol for the federal agency and voluntarily from the private sector of use in order to, for example, provide an annual report on the state and progress of the

science.

DR. SHAPIRO: If the latter part -- the latter bullet that you described includes a periodic overall assessment of what is happening and perhaps some guidance to the sponsoring agencies regarding this. If it includes that -- I understand you were making shorthand bullets -- that -- those are the characteristics that I thought about in this. Nothing more than that. So --

DR. HOLTZMAN: And I think Alex actually added importantly providing guidance to the agencies with respect to nongratuitous uses or at least paying attention --

PROF. CAPRON: I think we can call that -- the principle of parsimony is actually what we are talking about, making parsimonious use of this particular resource.

DR. SHAPIRO: Right.

DR. DUMAS: See then my statement still pertains somewhat, and it has to do with the way that this is written, the A's, B's and C's describe what this body would do and the last one, I think, addresses -- the last one has -- addresses only, in part, what this is being done for. So the statement you made, Harold, about the basic function of this, what the advice and

recommendations and what have you, I think needs to be succinctly stated up front and then the A's, B's and C's is just telling them what they need to do in order to fulfill that.

DR. SHAPIRO: Any other comments? Yes, Tom?

DR. MURRAY: Yes. Apologies for being late. I had not counted on rush hour traffic beginning about 25 miles from Boston.

This discussion seems to presuppose that we have decided and the commission has already decided to recommend public funding for derivation of stem cells and I am reading recommendations that seem to -- not all of us are on board yet. I am not on board yet. And I do not -- I would like -- I am a little uncomfortable talking about the details of the recommendation language, which presupposes a point which I am not yet prepared to accept.

DR. SHAPIRO: Well, that is right. We are not all agreed on that but we did vote on that, not for perhaps the last time but we did vote on that the last time and there was a very large majority of the commission in favor so I do not think it is inappropriate to discuss this but we will come back to that issue as we go through the other recommendations.

Yes, Bernie?

DR. LO: I like the way Steve laid out sort of the new bullets in recommendation nine. It might help actually to separate into a derivation -- what is this new panel going to do with regard involving derivation and what is it going to do involving use.

You know, we have had very bad luck with tables but at least conceptually it seems to me there are columns in the table, use and derivation and derivation and use. And then protocol-by-protocol review, it is one but not the other, maintain your registry of what for what purposes, oversight and education, and I just think it would be nice to clarify this as much as possible so that everyone knows what we are really suggesting.

DR. SHAPIRO: Eric, and Steve, and Carol?

DR. CASSELL: Just a point of information. As this recommendation stands now, is it to be followed by the text we have in here that clarifies what we mean by it or is this meant to be instead of that text?

DR. SHAPIRO: Be followed by text.

Steve?

DR. HOLTZMAN: When I think of the model of the RAC and how it intersected with the private sector, I think that this could fit very well with how we were now structuring this oversight board because with respect -- if for federally funded projects would do protocol-by-

protocol, mandatorily protocol-by-protocol review, it will also provide a certification function of the cell lines that came from an approved protocol.

The private sector then can choose whether or not it wishes to have its cell lines derived -- which it derives get so certified by submitting a protocol. It need not. All right. But the cost of that, if you will, is those cell lines will not be able to be used in federally funded research and that is much like -- conceptually like the structure of how the RAC worked.

DR. SHAPIRO: Carol? Any other comments on this? Obviously we are going to have to sit down and get a few of us to rewrite this to reflect the recent comments.

Let me make a recommendation. I would like to take a break in our session right now and actually get two or three people in each case to lend their hands at redoing eight and nine just to make sure that we have that really pretty well set out. I think this is a critical aspect of this as far as I am concerned. There is the issue that Tom raised just a few moments ago. Obviously that is a very critical decision also. But the -- I would feel much better if we had these kinds of recommendations straightened out. So let me make a few suggestions.

Steve, would you and Kathi, and Eric, want to work on nine? And maybe, Alex, if you and Eric, and whoever else would be interested, I am interested, work on eight. And let's see if we can over the next 15 or 20 minutes get some new recommendations to put before the committee as a whole. We will circulate it all around obviously.

(Whereupon, a break was taken from 9:29 a.m. until 10:40 a.m.)

DR. SHAPIRO: I would like to call our meeting back to order.

Okay. Colleagues, please.

Colleagues, you should have available to you now what is being passed around a revised recommendation eight, a revised recommendation nine, which we will discuss momentarily, both of those, and a revised recommendation one and I and Donald just revised, and there is also copies of an additional recommendation which some commissioners have asked that we discuss.

My proposal is that we will go through eight and nine. We will then discuss this proposed additional recommendation and then start going from one through all the other recommendations. If we go in that way I think we have some chance of really feeling pretty good about where we are and making pretty good progress.

So let's begin now with revised recommendation eight. Does everyone have a copy?

Who needs a copy of eight? Okay. Who is in charge? Has everyone else got a copy of eight? We will produce an additional copy. Okay.

This is recommendation eight. Now if you recall -- let me try to get -- the original recommendation eight was on page 19. We discussed before why that was not adequate and we had a pretty good discussion which has resulted in this new recommendation eight.

Eric, or Alex, or Jim, which one of you would -- Alex, do you want to speak to this one?

PROF. CAPRON: Okay. The first one is the point that we had that show of hands on this morning and we did not use the term section and so forth because we are talking about agencies and different review processes. Let me just read it out and we will probably discover typos as we read along as well as thinkos (?).

DR. SHAPIRO: That is a new word which I just learned from you yesterday.

PROF. CAPRON: Thinkos.

DR. DUMAS: Thinkos.

PROF. CAPRON: Which you are sometimes trying to claim are just typos but you are pressed and you have

to admit, no, I messed up.

"When reviewing research proposals utilizing ES/EG cell lines, all federal agencies should ensure that their review processes comply with any requirements established by the National Oversight and Review Panel paying particular attention to the adequacy of the justification for using such cell lines."

The thought is that our points to consider are really a draft document, a working document for the use of this oversight panel, and that document itself talks about the adequacy or the necessity of using the cell lines and there are other points that come out there. Under the commentary we should really have bulleted -- these are reminder notes. These are place holders really -- that we would give an example of the study section process at NIH and the ways in which the institute has made sure that its study section members attend to issues beyond the narrowly scientific as part of the review process.

DR. SHAPIRO: Thank you. And the only question I have about this is that this reference to the requirements established by the National Oversight Review Panel assumes that the -- I guess that comes out in recommendation nine, which we are coming to -- that certification is taken care of, that these are certified

cell lines.

PROF. CAPRON: Yes.

DR. SHAPIRO: Okay.

PROF. CAPRON: I mean, I thought that was going to be explained in nine.

DR. SHAPIRO: Okay.

PROF. CAPRON: And that is the reason for the --

DR. SHAPIRO: Let's assume that is the case.

DR. COX: Should we have nine come before eight?

DR. SHAPIRO: When we get to nine let's discuss that. That seems reasonable.

Any comments on the first part of this? So that seems responsive to our discussion? All right. Let's go on to the second part.

PROF. CAPRON: That is the using part. The derivation part, which we broke out and actually is closer to the old eight and would rely in large part on the last two paragraphs of the commentary before the old eight states:

"Current human subject regulations should make clear that protocols involving the derivation of ES/EG cells must be reviewed and approved by an Institutional Review Board prior to consideration by the

National Oversight Review Panel. The IRB should ensure compliance with any requirements established by the panel, including confirming that institutions in the U.S. or abroad which supply embryos or fetuses have obtained them in accordance with requirements established by the panel."

The reason for that second or, excuse me, the final clause with the second sentence is the chart, which we have talked about which now appears at the end of chapter five, highlights the need particularly with embryos or fetuses supplied from abroad that there be some process that would say that they have been obtained in a way which is compliant with the gist of these regulations -- of our recommendations, which we see the national panel as being the body that will implement those recommendations.

There is now no real regulatory framework apparently. Eric reported to us that John Gearhart had asked the FDA -- Jaime Thompson, excuse me, not John Gearhart. Jaime Thompson had asked vis-a-vis the embryo -- using embryos, I guess, from Canada; is that right? Or Israel. Whether there were FDA regulations about that and was told, no, there are not as I understand it.

And so we want to make sure that it is not just the processes that occur at the institution but a

reminder that the requirement would extend to making sure that if there is an institution in Israel or wherever that is sending embryos that they have obtained them using the same requirements about separation of the process of getting consent for the research from the process of making the decision about whether to use them for fertility and discard and so forth.

DR. SHAPIRO: Thank you. Are there any comments? This does seem to reflect our discussion in my own judgment but any further comments?

All right. We will assume that -- thanks to the panel, subpanel or whatever we call it, the subgroup for drafting that.

DR. COX: Actually, Harold, I will come back to this issue, though, because I think the primary meat of all of this is in nine, not eight, so to have that up front and then --

(Simultaneous discussion.)

DR. COX: -- so eight is almost like an addendum.

DR. SHAPIRO: Yes. That is fine. We can certainly reorder this and I think there may be a lot of sense to that but we will see.

Yes?

PROF. CAPRON: As we were playing around with

the language of this, we actually -- we had -- it should be clarified, and that -- in the first sentence, and in that context the word "current" made sense but I think the present wording where we have said, "Should make clear," that what we really want to say is simply human subjects regulations without recurrent -- and maybe what we mean is should be revised as necessary to make clear or something like that.

MS. FLYNN: Can I say something? Can I just --

DR. SHAPIRO: Laurie, I am sorry.

MS. FLYNN: I just want to ask sort of an informational point that perhaps was discussed at the last meeting. Can we get some examples of ways that we would know that IRB's were able to confirm some of these things that we are believing are important safeguards here? Do we have a sense that there is some kind of a framework out there that is being developed or that there is some kind of ability for us to get that information in the case of embryos that may be coming from other nations?

PROF. CAPRON: Well, my understanding is that the panel that has already been established and that has, as of April, put together its draft guidelines for Dr. Varmus and NIH, which I do not think have been publicly

released at this point --

MS. FLYNN: I have seen nothing of their work.

PROF. CAPRON: Right. Those guidelines actually have an elaborate provision which is that if the -- if embryos from fertility are going to be used then at the beginning of the fertility process an IRB will have to review the process, meaning the consent and so forth, to ensure that at that point the couples are only making the decision to create embryos for fertility purposes.

So you have a research body making sure that no research is now contemplated and that at the point in which research comes into the picture it will only arise after the couple has decided that they do not intend to use the embryos themselves or to store them for future use but are ready to give them away or discard them and that there are going to be specific requirements then for the consent and the information that are given.

Now what that would mean to me is once those are put forward, if you're thinking that you are going to derive stem cells from embryos and you have a collaborator abroad or you have someone who you know is a source, a potential source, you would be in contact with them and say, "Here are the guidelines I have to work with. My IRB is going to want to see certification that

your IRB has engaged in this process."

Now I do not know that we have any way other than the good faith of IRB's to know that they are going to do that job any more than they do any other job and that is always the issue with this kind of deputy/sheriff model that we have for IRB's that they are out there doing these things on the promise that they will do it but they are not directly reporting to the -- any federal agency step-by-step that they do it.

In this case when we are talking about derivation, their paperwork is going to have to go forward to the National Oversight Panel. In that case I think there is greater likelihood, Laurie, that all the paperwork on the paperwork level will be in order. Now what that will reflect of what communication there was, was it an Israeli couple or a Croatian couple, or anybody else, as to what they thought they were getting themselves into, we are kind of trusting to people doing what they said they have done.

MS. FLYNN: The paperwork process that we do think may become more regularized would include the oversight of the paper going on in the foreign country?

PROF. CAPRON: According to this --

DR. SHAPIRO: They certify. That is right.

MS. FLYNN: That there would be some

standards that would then be applied against a variety of these foreign documents that would assure the appropriate informed consent and so forth.

DR. SHAPIRO: I do not know how else it would get certified. Okay.

Let's -- we will come back to this. Diane, did you want to mention something? Sorry.

DR. SCOTT-JONES: Yes. I just wanted to say that I worked on recommendation -- on new recommendation number five and it now includes one of the points that Alex just made that the couple needs to have decided to discard remaining embryos before being asked to contribute them to research.

DR. SHAPIRO: Recommendation five, if some of you do not recall, deals with the informed consent process for ES cells and we will get back to that shortly but I asked Diane to work on that because I did not think the current recommendation set it out properly but in any case we will get back to that as we go through all these recommendations.

Let's turn our attention now to recommendation number nine. Which one of the deputy sheriff's wishes to speak to this?

Steve, do you want to speak to this, or Kathi, either one? Steve?

DR. HOLTZMAN: Certainly.

DR. CASSELL: You just have to read them first. What we are trying to do with this is to make it possible to know where cell lines come from, to know where they go, to have a history of them, and to see what they are ultimately used for to make sure that we -- that we satisfy one of the things that was put forward by the theologians when they discussed it. The equitable use and outcome of cell line research.

I guess one change that -- my other deputy sheriff over there changed what I wrote so I want to find out if it would be all right with him if we put it back to a different way.

DR. HOLTZMAN: That was done with the consultation of the chair and our faithful scribe over there.

DR. CASSELL: These protocols will be -- and four, the last sentence of four, "These protocols will be entered into the registry rather than enable the correlation of protocols and outcomes with the cell lines used..." But do not take offense but I do not know what that means. "...to enable a record of the history and ultimate outcome of any line of ES or EG cells." All right.

DR. SHAPIRO: Steve?

DR. HOLTZMAN: Just in terms of some of the logic of what we did here, we thought the first thing you had to do was say that this panel has certain authorities so that is what we are actually in the first one saying that it has a certain kind of authority, namely to approve and certify cell lines. Approve protocols for derivation and certify the cell line. Then we get into what is in the registry.

The third point, we have been giving guidance as opposed to requirement so that we will have to harmonize that with what we say in the previous recommendation -- what was just discussed. Are these requirements or are they guidance, okay, to the sponsoring agencies?

And then four and five is the basis for getting a variety of information and publishing it and making it available.

And the last point in five is it is not just about the state of the science but as it were the state of the quality with respect to the science.

DR. SHAPIRO: What about Eric's?

PROF. CAPRON: Would you mind just having someone just read these aloud? I mean, it helps, I think, in our process.

DR. SHAPIRO: Fine. Who would like to -- I

will read them aloud.

This is recommendation nine. It is revised from what you have before you. "A National Panel should be established within the Department of Health and Human Services to provide review and monitoring of ES/EG research conducted or supported by the Federal Government as well as ongoing education, guidance and reporting on a continuous basis.

"One: The Panel shall have review and approval authority of all federally funded activities proposing to derive ES or EG cells. Approved cell lines are certified and entered into a registry. See below..." and so on.

"In addition, the Panel should review for certification purposes all cell lines submitted on a voluntary basis by nonfederally funded individuals or organizations.

Two, the --

PROF. CAPRON: Can we talk about --

DR. SHAPIRO: Yes, absolutely.

PROF. CAPRON: -- any of these?

DR. SHAPIRO: Any of these at all.

PROF. CAPRON: Okay. The second sentence, "approved cell lines are certified," can we get a subject in this sentence with an active verb? There is not -- I

mean, are we saying that the panel shall establish a list of --

DR. CASSELL: Will be certified. Will be.

PROF. CAPRON: By whom? I just want to be certain of this. I mean, around, shall we say --

DR. HOLTZMAN: Cell lines approved by the panel will be entered into a registry.

DR. LO: Will be certified and entered into a registry.

(Simultaneous discussion.)

DR. LO: Certifying cell lines and enter certified cell lines into a registry.

DR. SHAPIRO: I would prefer Bernie's.

(Simultaneous discussion.)

DR. SHAPIRO: What is your modification again, Bernie?

DR. LO: The panel will certify cell lines and enter approved cell lines into a registry.

DR. HOLTZMAN: Certify approved cell lines and then enter them.

(Simultaneous discussion.)

DR. DUMAS: Who approves the cell lines?

DR. HOLTZMAN: We have approval authority in the previous sentence.

PROF. CAPRON: But, frankly, that is why we

need an active voice. Is it in the panel, the secretary? Who is going to do it?

DR. SHAPIRO: It is the panel.

DR. DUMAS: The panel.

PROF. CAPRON: The panel will certify --

DR. LO: Approved cell lines.

PROF. CAPRON: -- cell lines derived from approved experiments. Is that --

DR. BRITO: The panel will certify approved cell lines.

(Simultaneous discussion.)

DR. BRITO: And enter them into a registry.

DR. SHAPIRO: Well --

DR. DUMAS: The panel will certify and approve.

PROF. CAPRON: Isn't it the panel is certifying cell lines derived from approved experiments?

DR. DUMAS: Right.

PROF. CAPRON: The previous sentence says they will approve --

DR. SHAPIRO: Okay.

PROF. CAPRON: I am trying to be careful about this.

DR. DUMAS: It is having approved the cell

lines the panel will certify them and enter them into a registry.

DR. HOLTZMAN: Alex is technically right. What we have been doing is approving protocols as an activity.

DR. SHAPIRO: Right.

DR. HOLTZMAN: We are now going to talk about certification and registration of the product of that activity. Right? So we are giving another authority or responsibility to the panel that the panel shall. All right. Certified as having arisen from an approved protocol cell lines and register said cell lines or whatever. I do not think we have to get into that detail at the moment.

DR. SHAPIRO: That helps.

DR. HOLTZMAN: In the following sentence we need a minor modification in that we are really talking about what is being submitted on a voluntary basis are protocols, cell lines, which resulted from nonfederally funded activities as opposed to nonfederally funded organizations because there can be --

DR. LO: Yes.

DR. HOLTZMAN: -- I think -- again I think that wordsmithing can be done.

DR. SHAPIRO: Yes.

PROF. CAPRON: Thank you.

DR. HOLTZMAN: Continue reading.

DR. SHAPIRO: "Activities would replace both individuals and organizations."

DR. HOLTZMAN: Yes, that is right.

DR. SHAPIRO: Okay. Let me continue with item number two. "The panel should maintain a registry of certified ES/EG cells. The registry will contain all protocols proposing stem cell derivation that have been approved and certified by the panel as well as a list of all certified cell lines."

PROF. CAPRON: Why do we have -- it seems to me that the first sentence suggests what I thought we were originally talking about, which was the registry of the certified cell lines. To throw in that it will contain all protocols proposing stem cell derivation that had been approved and certified --

DR. HOLTZMAN: The logic of keeping a record of the protocols, Alex, was that one can envisage a day in the future where it becomes fairly routine potentially and that just as we saw with the RAC that after you had a number of protocols of the same kind of form you could, say, issue a guideline that says so long as it is according to the following protocol it may go ahead, all right, and then provide the number and they could have a

certification. So we thought it was useful to get a registry of the protocols as well even if that day I just described never came, that they wanted to review them all the time but nevertheless have a record of them.

DR. SHAPIRO: Carol?

DR. GREIDER: Also, I would think from a scientific point of view knowing exactly what process the cells went through would be really important for any scientist that wanted to use the cells that were in this registry.

PROF. CAPRON: Could I suggest then that the recommendation number two be revised to say the registry established by the panel shall consist of two parts. The first will contain all protocols proposing stem cell derivations that have been approved by the panel. The second part shall -- in other words, make clear that --

DR. SHAPIRO: That is great.

PROF. CAPRON: Okay.

DR. GREIDER: But they have to be linked to each other. You have to know cell line X came from protocol Y.

PROF. CAPRON: Right. That means we want to have a sentence saying the relationship of the two parts shall be made transparent. But in the process I want to be careful that we do not do what the second sentence

says now, which says the protocols which have been approved and certified, let's use approval vis-a-vis the protocols and certified vis-a-vis the cell lines. Okay.

DR. GREIDER: Yes.

DR. HOLTZMAN: That is a great idea.

DR. SHAPIRO: Is someone getting all this?

PROF. CAPRON: Because I am not writing it down.

(Simultaneous discussion.)

DR. LO: Actually if I could follow up on what Alex is suggesting, which I like a lot, it seems to me one and two, provisions one and two, could be made a little more harmonious. I mean, one -- I mean, we are throwing several things here. One, it seems to me, is reviewing protocols, approving them and certifying cell lines. The second thing is a registry which is part A, as Alex pointed out, a registry of cell lines and, B, a registry of experiments linked, as Carol suggests, and sort of have the registry pop up in both one and two is a little -- it is not as clear as it could be.

PROF. CAPRON: And probably not as economic as it could be.

DR. GREIDER: Yes.

DR. SHAPIRO: Any other comments on two? Very helpful. Yes?

DR. DUMAS: That is two.

DR. SHAPIRO: It is up to you. I am going to go to three in a minute. It is there something -- a comment on two or one?

DR. DUMAS: I wanted to comment -- I wanted to go back to a comment on the preceding statement because I still think it is missing something. "A National Panel should be established within the Department of Health and Human Services to ensure that ES and EG cells are derived according to certain standards or to ensure the adequacy and justification for using EG and ES cells." There is something that still is missing there. They are going to review and monitor but that is a mechanism.

DR. SHAPIRO: Okay. You want --

DR. GREIDER: To ensure.

DR. DUMAS: I want something there. I want to say what we are trying to achieve by this to ensure --

DR. SHAPIRO: I understand what you are saying.

DR. DUMAS: -- that ES and EG cells are derived according to certain ethical standards described or upheld by this commission or something like that.

DR. SHAPIRO: Okay. So that is just to expand the introductory sentence and maybe a couple of

sentences by the time we are through --

DR. DUMAS: Right.

DR. SHAPIRO: -- to give a -- sort of -- a better sort of sense of what is coming below.

DR. DUMAS: Yes.

DR. MURRAY: Right. We have a statement -- I think Rhetaugh is right. We have statements of the function but not of the purpose.

DR. DUMAS: The purpose.

DR. MURRAY: So a phrase or a brief sentence.

DR. DUMAS: We say that they want -- we want them to ensure the adequacy and justification of using these cell lines. Now is that enough? That may be enough to just repeat up there. To ensure the adequacy and justification of -- to ensure that -- well --

DR. SHAPIRO: Let's think about that and let's not try to form it right here but I agree with you that this -- we need to do some work on that.

DR. DUMAS: Right. Insert it there. Right. Okay.

DR. SHAPIRO: I agree with that point.

MS. KRAMER: And it did not capture your suggestion -- your earlier suggestion about the parsimonious use of the tissue or the embryos.

DR. DUMAS: Yes. Yes.

DR. HOLTZMAN: I think there is two different things. Parsimonious use is going to come in, in three.

DR. SHAPIRO: Right.

DR. HOLTZMAN: Okay. Where it is providing guidance to the agencies. I think Rhetaugh's point about the purpose is very appropriate. And also we do not actually say in here with respect to the review and monitoring what you are reviewing and monitoring for not only is in terms of purposes to accord with the recommendations in the report.

DR. SHAPIRO: Right.

DR. HOLTZMAN: So I think what we need --

PROF. CAPRON: I thought she had a --

DR. HOLTZMAN: Right. The preamble has to capture both of those.

DR. SHAPIRO: Arturo?

PROF. CAPRON: Can we make it sort of an active sentence and just say the department should establish a panel to carry out the recommendations or to ensure compliance with the recommendations?

DR. DUMAS: Yes. Yes.

DR. BRITO: I know that we are going to work on this in the wording and all but within that purpose maybe -- this is just me but on page 24 of this chapter, lines 18 through 27 where the purpose is discussed for

this registry or this panel, one thing that I find that is missing or not emphasized enough is that -- isn't one of the purposes of this registry or panel so that individuals can make an individual choice or just have some knowledge about the derivation of certain cells or is this not the place for it or is it?

DR. CASSELL: Yes.

DR. BRITO: So should that be emphasized in the beginning also?

DR. SHAPIRO: Well, you have to -- that is something we should consider. We have to -- we do not want the first preamble to include absolutely everything in this recommendation but we can perhaps -- that should be. I mean, we can try to work on it. We ought to think about --

(Simultaneous discussion.)

DR. BRITO: I think it is important not to at least put emphasis there.

DR. SHAPIRO: Okay.

DR. DUMAS: Public record.

DR. SHAPIRO: Okay. Well, we will have to revise this first sentence in a number of ways that have been suggested here and try to incorporate as much of this as possible.

PROF. CAPRON: Mr. Chairman?

DR. SHAPIRO: Yes.

PROF. CAPRON: Just to respond to Arturo, I think that just as Rhetaugh has suggested that we give kind of the ethical groundwork for the overall recommendation in that sentence as she was revising it, we could also when it gets to talking about the registry -- I mean, Bernie has in effect said we ought to separate the recommendation one, which focuses on the approval process.

And recommendation two, the registry, in order to provide a public record that the ethical standards are being complied with, the panel shall establish a registry for two -- for containing two parts and we could have a sentence about the purpose there that this record will allow easy access to information about the origin of the cell lines for any member of the public as well. And the commentary can talk about the point you are making but make it specific there rather than trying to lay it on to the opening preamble.

DR. SHAPIRO: In this case the sort of information on the origin of the cell line is very useful for a whole number of purposes, one of which is this one but also for scientific purposes it is quite critical so it is a very good point to include.

All right. Let's look at point three here,

which is also an important issue. It reads as follows currently: "The panel should provide on a regular basis guidance to the sponsoring agencies on the nonscientific, social and ethical issues and should be considered in the review of protocols proposing to use ES and EG cells."

PROF. CAPRON: We are going to need to decide and then align recommendation eight in this because recommendation eight used the words "any requirements" and here the word is "guidance."

DR. SHAPIRO: Right. That is a critical issue here and Steve also raised that in reducing this. How do people feel about that? It is an important difference.

DR. CASSELL: Say it again.

PROF. CAPRON: Between a requirement -- the sorts of things that I understand the ad hoc panel is providing guidance to Dr. Varmus on are really requirements. In order to do X, Y, Z, you are going to need to have gotten consent in the following fashion," and not just guidance. There may be other points which are -- are just guidance and maybe we want to use both words. Any requirements or guidance.

DR. SHAPIRO: That is really my preference to do that because we are going to find ourselves, I think -- and we will have to find examples of both and use them.

And my thought -- let me just -- going back to eight, which talks about, if I remember now, requirements -- I tried to think in my own mind about how we would handle a difference between requirements and guidance and I have sort of an idealization in mind, I do not know if it is very workable, and that is requirements are requirements. And guidance, however, is guidance.

(Laughter.)

DR. SHAPIRO: That is my sense.

PROF. CAPRON: Gertrude Stein, where are you when we need you?

(Laughter.)

DR. SHAPIRO: But the issue is the -- I would be quite satisfied with a lot of guidance if I knew from IRB's when they diverted from the guidance. Some guidance is really quite important and the amount of things you would like to make requirements depend a lot on whether you know whether your guidance is being followed or not. That is not to say it is determinative in any case but if you are studying this over time you might convert guidance into requirements or vice versa depending on what you find out over time.

And it is -- I have not got the language for this obviously but it is -- I would be quite satisfied to use guidance and recommendations in this particular spot

here but then I would like to understand where -- how does that process work out.

Steve?

DR. HOLTZMAN: I think the requirements we are talking -- I think we should be talking about requirements here. I think that we are saying that there is a reason for this panel to say this protocol does or does not conform with what we expect in protocols for derivation that have received --

DR. SHAPIRO: Develop those requirements over time if they wish to.

DR. HOLTZMAN: Right. I might change "regular basis" to periodic basis. It is a minor thing. But that is the notion and I think it will resurge with -- we are recognizing the science is changing, societal attitudes are changing, we want a body to be looking at those things, and them having a public discourse about them and issuing requirements and guidance as it changes.

DR. SHAPIRO: Do people like the word "requirements" there because that would certainly make it simpler?

DR. SCOTT-JONES: Yes, I think it is important.

DR. SHAPIRO: Okay. Anything else on three

for the moment?

Diane, yes, you had your hand up before. I apologize.

DR. SCOTT-JONES: Okay. I have a comment about the phrase "on the nonscientific, social and ethical issues." I think it is sufficient to say simply social and ethical issues because inserting nonscientific suggests an opposition of the scientific and social and ethical.

PROF. CAPRON: Our own points to consider actually have a few things under the science heading.

DR. SHAPIRO: All right. Let me read item four here. "The panel should receive from all sponsoring agencies and the private sector on a voluntary basis and publish on an annual basis a description of protocols using certified cell lines and, where available, the outcomes of these experiments or those experiments. The protocols will be entered into the registry to enable..." and I know that this is where Eric wants to use somewhat different language. Let me just read what is here. "...enable the correlation of the protocols outcomes with the cell lines used."

I believe it is true -- Eric, I hope I am not misquoting you -- that you would prefer -- correlation refers to kind of the statistical, at least it seems to

refer to kind of a statistical study. I think what Eric was concerned about is the ability, if someone wishes to or some organization wishes to, to trace what the actual outcomes and uses of a particular cell line might be. I think it is based on justice considerations that if someone wanted to investigate those things they could.

That is my understanding of your position. But how would you change the words again?

DR. CASSELL: I would change it -- I mean, I actually -- what, Alex, I am making clear is that these have to be changed in a way that makes it absolutely clear what they are all doing.

I would change it to "The registry will make possible a record of the history and ultimate outcome of any protocol deriving or using human ES or EG." And then either period or "and" or "any register line of human ES or EG stem cells." So not only in the protocol but any registered line.

DR. SHAPIRO: Bernie?

DR. LO: Can we require the recipients of funding for derivation to report back on the outcomes to this panel as opposed to --

DR. CASSELL: No. No, that is what happens, you see. The -- suppose they got -- they used cell line 252, right. They have done that protocol but something

comes out of that. They result of that. We -- our registry has the result of the outcome of their protocol. Somebody else picks up on their work. It is still attached to cell line 200 and whatever it was. And so that you can still follow that -- what that cell line is leading to.

DR. HOLTZMAN: Bernie, to your specific -- in the introduction on four we said, "They will receive," "they should receive from the sponsoring agencies." So if you want to make it stronger than "should receive" but that agencies should be required to provide to it and then Eric has got a second point about not only the protocol but the outcomes of the research as well.

DR. SHAPIRO: The outcomes is in the first sentence. All right.

DR. HOLTZMAN: It is.

DR. LO: Okay. So I guess I am -- can someone explain to me how you will get the outcome of projects that are use projects as opposed to derivation projects that you are not funding?

DR. HOLTZMAN: It could be voluntarily.

DR. LO: This is all voluntary?

DR. HOLTZMAN: No. The agency -- you are talking about the agency funding in terms of --

PROF. CAPRON: You mean not funding. You are

not funding, he said.

DR. LO: So we are saying that if it is federally funded you have to -- whether it is use or derivation you have to report the outcomes to the agency which then has to forward it to this panel.

DR. CASSELL: Right.

DR. LO: And we are just saying every -- for the private sector it is all voluntary.

DR. HOLTZMAN: Right.

DR. LO: So then if it is voluntary I think we have to not be too strong on what this registry is going to be able to do, which is going to be a lot of things that may be missing data, and so it is only as good as the --

DR. SHAPIRO: That is right.

DR. LO: -- completeness of the outcomes of the nonfederally research.

DR. SHAPIRO: Carol?

DR. GREIDER: Just one point about that. For federally supported research you usually have to report every year what the results are anyway. And so there would be a mechanism by which that could be put into the registry if we wanted to suggest that.

DR. CASSELL: It is the linking of it that is allowed, you see, so they are not -- as, though, each

thing was a new -- did not have a history and does not go anywhere.

DR. SHAPIRO: Alex?

PROF. CAPRON: I just want to try to understand practically what we are thinking of under the phrase "outcome of the experiment." When you think of a registry you think of something with columns and sort of, you know, fairly discrete data points that are fairly common among these things. I mean, the columns phrase may have been an over statement but I mean sort of categories that you enter into.

I assume that people report the "outcomes of their research" in all sorts of different ways and I am trying to imagine what we think this registry will have. This is a genuine question. It is not a rhetorical or, you know, skeptical question. I mean, I am just not clear what we think.

DR. CASSELL: Well, Alex --

PROF. CAPRON: This would be something in which somebody will have a line or two, other people will have pages, some people will describe how this is making them think of the next step of the research they want to do, their outcome is to raise the following questions, which they now intend to pursue through additional research. Is that what was in mind of the people who

suggested this?

DR. COX: I have two simpleminded answers to that. The first is I do not want to get, okay, the registry of cell lines mixed up with the registry of results. So the registry of cell lines is really straight forward. It is cell line one through 899 and you figure out where it came from and that is a primary focus. The other is not a registry. It is a data base. It is a data base of information and primarily what I would look for from my perspective, both as a scientist and as a -- you know, just like Joe Blow -- is so what was done. An abstract. I do not want to see like a paper. That is what the scientific literature is for. An abstract of what was done and what, if anything, was found. And Carol is absolutely right, every time you write a grant, every year you do a progress report on that, max two pages. That is what it is supposed to be and there can be an abstract about that.

Now the whole NIH is coming up with databases for this kind of stuff to make that kind of information more publicly available, not massive amounts of information because you do not want to read through massive amounts but you want an abstract.

DR. SHAPIRO: It seems to me it is -- at least the concept I have, I think, is reflected here and

let me just see if -- I do not -- the word "registry" does, you know, invoke certain images and if you like -- I mean, the cell line data is pretty straight forward. I think we all understand what that is. You give it a number and then you just certify it or not.

And then on the outcomes if one wants to maintain the word "registry," I mean what is really going to happen -- what really is going to happen here is you are going to have outcomes which will have a file number and you will type in your computer file number 678 and you are going to get enough information so you can pursue this matter if you wish to and generally what the outcome is and so on.

So while it is not numbers -- I agree with that -- I think that it -- if I understand the objective, which seems sensible and thoughtful to me, is that we want to be able to determine at some time just who provided this material and who benefitted from it, and that is what this is aimed at.

DR. COX: Exactly. And there could be a registry and then there could be a database. I mean, you do not want to --

DR. SHAPIRO: I do not know what name to --

(Simultaneous discussion.)

DR. SHAPIRO: -- give all this. Right.

DR. GREIDER: I want to specifically add --

DR. SHAPIRO: Yes.

DR. GREIDER: -- and "published papers," which are going to be more useful than an abstract that somebody has but to specifically state in there that this cell line was used and this was the paper that came out of it. That would be very useful.

DR. SHAPIRO: Diane, and then Steve?

DR. SCOTT-JONES: I want to agree with what David said and what Carol just said. I think one of the issues that we have considered throughout this is the promise of this research, and I think having that kind of database will allow a fairly easy way to assess in a real way the promise of this research and the steps that are being made towards the realization of that promise.

DR. SHAPIRO: Steve?

DR. HOLTZMAN: Yes. I think we know what we want. I think the key is in the recommendation language to keep it crisp and then in the explication to give guidance that they should do it in a way that allows access to the following kinds of information, whether that is established in the database, whether it is having a simple relational database that gets hyperlinked to DHHS or NIH kinds of things, which may come in the future. I do not think we want to get into that.

DR. SHAPIRO: I think that is right. We do not want to get into too much detail. However, I do want to get into the recommendation with the appropriate language. I do not have any particular language right now. The point that Eric was making, namely that we ought -- someone -- one of the things someone ought to be able to do is to see who supplied and who benefitted at the end, you know, or at some point in time, and we need sufficient evidence to do that or at least try to get evidence to do it, and that idea is an ethical concern and should find its way into the language of the recommendation itself.

DR. CASSELL: And it is public -- it is part of a public record.

DR. SHAPIRO: Yes, Alex?

PROF. CAPRON: Yes, I agree. I also agree with David's caution that we be clear about the use of the word "registry." I mean, the registry will have a list of certified cell lines. Are we saying, in fact, that the registry will have a third category, which is outcomes of uses of the cell lines?

DR. SHAPIRO: Yes.

PROF. CAPRON: Then we should -- when we first describe the registry we should put that down as a separate -- I mean --

DR. HOLTZMAN: That is a good suggestion.

PROF. CAPRON: -- and that -- a database of the outcomes.

DR. COX: In that sense that linking is extremely useful because if you get different results if you can go back and you have this whole list of stuff that is sort of based on that cell line, just from a scientific point of view that will be extremely useful.

PROF. CAPRON: Yes.

DR. COX: And I think for the other reasons we have mentioned it is useful for social and ethical reasons, too.

DR. SHAPIRO: Okay. Thank you very much.

Let's go on to the -- I guess we are on number five now.

"The panel should provide an annual report to the Secretary DHHS which will include an assessment of the current state of the science for both derivation and use of ES and EG cells as well as a summary of any emerging ethical or social concerns associated with this research."

PROF. CAPRON: Is this the recommendation which is intended to indicate the role of the panel we talked about in revisiting the issue of different sources such as embryos created through IVF for research

purposes, embryos created through somatic cell nuclear transfer, and so forth? Is this the point at which --

DR. SHAPIRO: I cannot speak for the authors but, I mean, that is what I hoped it was because we do need that in here.

PROF. CAPRON: Because to me maybe it is all there but an assessment of the current state of the science as well as a summary of any emerging ethical or social concerns is really -- that does not -- that does not to me convey that thought which is sort of a -- it is a correlation of an ethical assessment with the progress of science. I mean, if we get to the point where in animal models and, indeed, with noncloned stem cells, that is I mean the ones that do not have somatic cell nuclear transfer.

If we have gotten to the point where you can show that you can get cell differentiation, you can, in effect, grow arteries or livers or something, and the question is now is there justification for using somatic cell nuclear transfer from the potential patient recipient, that is the kind of thing they should be able to do and that is a correlation not just of assessment of the scientific current state of the science for derivation of use, et cetera. You see what I am saying? I think we need to be more specific.

DR. SHAPIRO: Steve, then Bernie.

DR. HOLTZMAN: Yes, I was inclined to just have it to economize on the language as it is but we could always change the whole thing, was assessment of the current state of the science, summary of emerging ethical issues, right, and then something to the effect of "and review the adequacy and appropriateness of the recommendations provided in this report." I think that is what we are after. A way of summarizing what you are getting at.

PROF. CAPRON: Yes, I guess -- I mean, it seems to me that our own report anticipates that there could be justification so it is not as though, oops, the commission was inadequate.

DR. HOLTZMAN: Right.

PROF. CAPRON: It is not even the adequate but sort of the state of the art, the state of scientific and therapeutic progress.

DR. SHAPIRO: And I think that is very useful. Bernie?

DR. LO: Yes. I think that is useful as well and I think, also, we have to make clear in five that one, two, three and four really pertain to human ES and EG research and in five we are saying take a look much more broadly at the sort of -- the whole field, including

animal research and with a particular view to seeing whether the guidelines that we recommend, the -- our recommendations can be modified in light of existing science -- in light of new scientific development. So it is really a whole different set of tasks in five and I think we should really be clear it is a different set of --

PROF. CAPRON: To the extent that that is the case, do we want to think of that as a separate recommendation? In other words, that what is provided before is more the process of approval and then the establishment of the registry and the getting in of the results, and then it is almost the reassessment function really could be highlighted as a second recommendation. It might allow us to be a little more explicit there.

DR. SHAPIRO: Laurie has a -- and then we will come back to that issue. Laurie?

MS. FLYNN: I have a question that sort of bears on that. Should I be assuming or are we safe in assuming that this panel with which we are going to charge some significant duties is going to have nonscientist members, potentially public members? I mean, are we going to -- because of the focus as Alex is pointing out on taking a step back and looking at social and ethical issues and returning to some of the earlier

controversies, we do not state anywhere, and one could assume that it might be the scientific community looking at its scientific progress.

DR. SHAPIRO: I think that is a very good point. As a matter of fact, one version of chapter six, now five, we did talk about that and I think it is a very good point and I am very glad you brought it up. My own view on the matter is that while we need not say anything in detail about just how many members of this, that and the other, there ought to be broad membership here. I think we should have a recommendation on that side, including not just scientists but list -- make some kind of list. I think we do need a recommendation on that. That is my view.

Bernie?

DR. CHILDRESS: We have some -- oh, I am sorry.

DR. SHAPIRO: Bernie, and then Jim.

DR. LO: Following up on Laurie's thought, I mean the kind of panel you would want for one, two, three, four, I think is primarily scientists.

MS. FLYNN: That is right.

DR. LO: There may be a public representative or two but I mean I would not want to sit on that panel.

MS. FLYNN: Right.

DR. LO: But the panel in five should be a panel more like this with scientist represented but not sort of the same panel that is doing one, two, three and four. So I would think about splitting not just the recommendation but sort of who is doing recommendation 9 and 9(a). It is a different --

DR. SHAPIRO: So you would -- I just want to understand that last comment, Bernie. You would suggest that, for example, that this panel might convene periodically some group composed in such a fashion to do five as a possible? It is a possible way to do it. I understand. I just do not want to convene -- I do not want to convene too many panels here. That is what I am sort of struggling with.

DR. LO: Didn't the RAC serve both functions?

PROF. CAPRON: Yes. By suggesting a separate recommendation I would --

DR. LO: I was addressing his --

PROF. CAPRON: No, I know, but to the extent that Bernie --

DR. LO: Tell me what the composition of the RAC was.

PROF. CAPRON: The RAC was like this group, scientists and nonscientists, a larger number of scientists than this commission has, proportionate to the

number.

DR. LO: 50/50 roughly? I mean, I am trying to --

(Simultaneous discussion.)

DR. SHAPIRO: Like 70/30 or something like that.

PROF. CAPRON: But from the viewpoint of the scientists it was very multidisciplinary because some were physician/clinician, some were molecular biologists, some were microbiologists, and on and on, epidemiologist.

DR. LO: Again help me understand what the RAC did. I mean, were the nonscientific people on that committee interested enough to come to the meetings which were tasked one, two, three, four, you are saying, you know, for stem cell line 834 we want to review the following --

PROF. CAPRON: Yes, they were.

DR. LO: They were.

PROF. CAPRON: And it turned out, even had something to useful to say.

DR. SHAPIRO: Jim?

DR. CHILDRESS: Just following up on that. Yes, and there were public members, totally public members, some of whom were not heavily involved in the scientific or ethical discussions, who actually made over

time some very important contributions too.

DR. LO: Then I would be happy with one panel provided we somehow describe it as disciplinary with strong non -- you know, representation by public members and not -- and nonscientists.

(Simultaneous discussion.)

DR. CHILDRESS: And in terms of being concerned about multiplying organizations here -- because yet in recommendation ten yet another body to determine whether the bodies that were already set up are worth continuing over a period of time. So I do think we have to worry about multiple organizational structure, and if there is a way we could accomplish this end, perhaps with suitable ad hoc consultants being brought in, as RAC did as well, to help in this kind of assessment, that might be a way to proceed.

DR. LO: Help in which assessment, though? Assessment of number five?

DR. CHILDRESS: Five.

DR. LO: Well, see, but you bring in a consultant that is --

DR. CHILDRESS: The consultant is to help the panel form its -- because just as we bring in consultants here.

DR. SHAPIRO: Well, let's assume for the

moment that we do have to say something about membership, it is a very good point, and we need to formulate something on that, something specific about that, and let's assume that however we describe this that we will keep one panel entrusted to do this and entrusted also to call people it needs to call.

I mean, it will do what we do when we are short of ideas or short of -- we need some help. We call people to help us and they will presumably do the same thing.

Okay. Well, what we will try -- we have to see and stop -- at least pause for a moment in a minute to -- for public comments. But we will -- I will tag a couple of people to try and work on some of these alterations in nine today.

Tom, you had your hand up before. I apologize.

DR. MURRAY: To make the same point that was made.

DR. SHAPIRO: Okay. I apologize. I am sorry. To -- because there was quite a few changes recommended here in nine.

I think we should take a look at them again later on today so we will come back to nine and at the lunch break we will get together with two or three people

to work on that sometime early this afternoon.

Okay. Thank you very much. That has been a very, very helpful discussion.

PUBLIC DISCUSSION

DR. SHAPIRO: We do not have anybody signed up for public comment today, which was scheduled at 11:30. However, let me just check to see if there is anyone in the audience today who has anything they would like to address the commission on.

(No response.)

DISCUSSION CONTINUES OF DRAFT REPORT

DR. SHAPIRO: If not, then we will go ahead with our own scheduled business.

My recommendation right now is that we go back to look -- we will come through the recommendations now -- excuse me. Let's go to -- I was going to say let's go to one and start working through that. I think, however, it might be somewhat more helpful, at least we will get some kind of lay of the land here, if we consider a recommendation. I do not know who to ascribe the authorship to. Some combination of Rhetaugh, Bernie and David, in some order. I have a recommendation which has no number on it but it has been passed out to you on a sheet that looks like this one. It just says "recommendation" on it. And let me just read the

recommendation as you all are.

"NBAC urges all the recommendations made this report be voluntarily accepted and applied in the private sector." And then there is the following statement after that: "In some cases, particularly those that are morally contested it may be in the public interest for the private sector to operate under different constraints and/or rules that apply to the federally funded research. However, in the case of human stem cell research, NBAC believes that the public interest is best served by the common set of ethical standards and research practices that will be followed by both the public and private sectors."

But let me now turn to any one of the authors of this to see if they have anything further they want to add or do you just want us to go directly to the discussion?

Bernie, I have just read out this recommendation that the three of you worked on.

DR. COX: So I have a comment. The -- but Rhetaugh and Bernie will correct me when I get it wrong, and that is the goal here was to as crisply and clearly as possible lay out a position that, in fact, the three of us support.

In laying it out, though, okay, it is a very

clear line that is drawn and what we did in terms of doing it was to, I think, it can now be used as a straw recommendation in a way to say what would be the implications if we accepted this. And I think there is a clear implication in this all the recommendations would mean that in the private sector if those were accepted that there would be no embryos created for research because that is what we are saying. We are not creating new embryos for research. That is going to be some of our recommendations. That is some of our recommendations.

What that precludes by definition then is any use of somatic cell nuclear transplant -- transfer techniques, okay, because that is required to create new embryos in the private sector.

Now do we want to say that? Do we want to see that? What it does, though, is it makes the choice crystal clear because we either do or we do not.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I am not totally void of ambivalence on this one but I am -- I have some concern that we are consistent in what we are saying that we believe should be done. We have said very clearly that we do not recommend research that would create human beings, cloned human beings. If we support research that

creates embryos, is that inconsistent with our belief about the creation of human beings?

DR. SHAPIRO: Yes, I understand the question.

PROF. CAPRON: Yes, it is. The human beings that we said we did not want to have created were born human beings.

DR. DUMAS: Born human beings.

PROF. CAPRON: Born.

DR. DUMAS: But not their basic --

PROF. CAPRON: What we call colloquially "baby making."

DR. DUMAS: Babies. But consider the position that to create a human embryo is the first step in creating a baby.

DR. GREIDER: But this gets at an issue that we go throughout in the whole report, which is the issue of this contention of, you know, when is a human being a human being, and I think we have stated pretty clearly in the report that that is not something that we could resolve in this report, that we have to lay out that that is an issue that is, you know, polarized in our society and that we are trying to find some more middle ground. That was my --

DR. DUMAS: And not even clear in our own minds. Not even clear in my mind.

DR. SHAPIRO: Let me suggest that the commission divides into two those people who asked to be put on a list and those people who just talk.

DR. DUMAS: Okay.

DR. SHAPIRO: So just to be fair to everybody let's wait for the list.

Jim, you are next and then Carol.

DR. CHILDRESS: I am going to hold off --

DR. SHAPIRO: Alex, and then Diane.

DR. CHILDRESS: I will --

DR. SHAPIRO: Okay.

DR. CHILDRESS: -- later.

DR. SHAPIRO: Alex?

PROF. CAPRON: I wanted to respond to David crisply stating the issue, which is -- could be restated as follows: If our recommendations are followed, we would be saying vis-a-vis the federal government that there would be a minor lifting of the present restrictions on the use of embryos vis-a-vis the public sector, we would be doing something equivalent to our recommendation in the cloning report only it would actually go beyond what we have said there.

We would actually be recommending a restriction. The only way it seems to me that restriction would come about unless it were adopted

voluntarily entirely would be if there were some statement of how the federal interest is violated by an activity going on.

I think it would be very hard to make that claim vis-a-vis the creation of embryos. In part, because any number of the people who have spoken on the floor of Congress or the reports of the congressional committees about the restrictions on the use of embryos have stated that they are willing to restrict federal funding precisely because they know that valuable work will go forward without federal funds.

It would be ironic if we were, therefore, suggesting this work vis-a-vis stem cells, which we are stating is very important crucial research and a new avenue of great importance should stop, whereas other people are creating embryos for research in -- for probably mediocre research, in fact, in some of the fertility centers and so forth where they are not really doing very good research but they are creating embryos for research purposes.

I would find that a hard recommendation to support. For that reason I find the explanation given in the second paragraph here somewhat troubling because what it says is in some cases, particularly those that are morally contests, which we know has meant embryo

research, it may be in the public interest for the private sector to go forward with different constraints. That is the very view, as I said, that is stated by the people who voted for restricting federal funding.

However, in the case of human cell research we think it is best -- and let's not say served by a common set of ethical standards but by a common set of ethical restrictions and legal restrictions in effect, so I have a hard time supporting this for that reason or at least as explained here.

DR. SHAPIRO: Thank you. Other comments about this? I think it is, as David pointed out -- Diane, you had a comment?

DR. SCOTT-JONES: I think the issues that Rhetaugh raised are ones that we will need to think about. In reading our chapter one I really struggled with the way that we described the zygote, the embryo and the fetus. We call that an entity as if it could be a nonliving thing. We do not even say organism.

And I think that all of us should probably think about how we want to present our view of the development of a person at this point in time before birth. It is more than entity but I do not know how we should do it. It is something that I struggled with myself. And in my own teaching I use the word

"organism." I try not to refer to zygotes, embryos and fetuses as entities.

I think we should think more about it.

DR. SHAPIRO: David?

DR. COX: So what I am hearing and I actually completely agree with is that NBAC does not urge all of the recommendations that we make in our report to be voluntarily accepted and applied in the private sector because one of the recommendations we make, which is not the creation of new embryos, is not -- we are not recommending that be followed.

What other recommendations that NBAC is making do we not recommend to be followed? Because the path that I am trying to go down is that -- then let's say the ones that are not going to be or we do not, you know, expect to be followed but then we can make it clear which ones we do expect to be voluntarily followed.

The reason for making it so absolute in the beginning is it just helps have those things pop right to the top.

DR. SHAPIRO: Yes.

DR. HOLTZMAN: If I could follow up David's statement, I think that would be really important, that if we are going to say as a conscious decision that we think it is appropriate for the private sector to create

embryos for research either through in vitro fertilization techniques or through somatic cell nuclear transfer.

David sort of said are there any other recommendations that we think should be lifted in the case of privately funded research.

I would want to raise the other side of the equation. Since we did not think about those types of research for federally funded, what sort of conditions ought to be imposed on the creation of embryos for research in the federally funded sector -- under federal funding. Do we want to say something about what we would expect ethically or what we would hope for ethically if private organizations are going to create embryos for research?

I think there are a lot of things about informed consent, lack of coercion, things like that, which we really did not touch on because kind of we were not going to do it in the private -- in the federally funded sector.

I think it would be very important to try and lay it out so that -- again it is not so much -- if we -- if, as I hear the sense of it, that we are going to say some things are already in the private sector that are not eligible for federal funding, what do we want to say

about the conditions under which that privately funded research ought to be done as an ethical matter? We are not talking about legislation. I do not think. We are not talking about sort of voluntarily, at least holding something up.

And I must say personally I think that the evidence we have based on the Chiron ethics board does not give me a lot of --

DR. _____: Geron.

DR. HOLTZMAN: Geron, sorry. God, I am sorry.

It does not give me a lot of confidence that the private sector will do it right without some guidance.

DR. SHAPIRO: Diane? Steve, you had your hand up or you are just -- Diane, and then --

DR. SCOTT-JONES: I am wondering whether there is some middle ground where we could strongly, strongly urge that the private sector follow our recommendations and be aware that some in the private sector will not without our just openly encouraging freewheeling and widespread private sector goings on that would not follow our research.

I am not formulating this very well but I think there is a middle ground in the same way that we

allow divorce in our society but we do not tell married people get ready to get a divorce within the first couple of years of your marriage, 50 percent of you are going to end up divorcing one another. We allow it but we do not actively promote it or encourage it.

It seems to me that there is some middle ground where there are a lot of restrictions on the private sector but there is enough to let this go forward. Maybe it is related to the discussion of not having extravagant use or some very limited use. I think there is some middle ground possible here.

DR. SHAPIRO: Steve and David both want to speak. I want to say something here.

DR. DUMAS: And me.

DR. SHAPIRO: And then Rhetaugh. Okay.

Rhetaugh, you had your hand up first so I will go to you next. I apologize. I forgot.

I think we have to be very careful here taking on objectives we really cannot get to in the time we have available and I am imagining giving a set of instructions based on certain types of thinking we might bring forward to the private sector is not an unattractive idea but it is an extremely complicated issue and I do not think we can get there from here in the time that we have.

The very beginning of this report says that the focus of the report is going to be on federally funded activities. And if we can solve that problem and say what we can, and I think we do say some things about the private sector, for example, in what we do in recommendation nine, I think that is a step forward and we should not lose that step nor, however, do I think we should bog ourselves down and take on the reverse image of that, namely how do we wish the privates sector to behave. That is a very interesting subject and a very appropriate subject for us to think about but I really despair in getting there in the time that we have available.

But, Rhetaugh, you are next and then Steve.

DR. DUMAS: Well, some time ago we talked about encouraging private sector research enterprises to utilize the oversight mechanist.

DR. SHAPIRO: That is in recommendation nine now.

DR. DUMAS: It is in there now.

DR. SHAPIRO: Yes.

DR. DUMAS: Okay. That is -- that helps a little bit.

DR. SHAPIRO: I think it makes some sense, I agree.

David?

DR. COX: Actually I prefer to hear Steve's middle ground before I say it because I think Steve has not spoken yet and I think this is -- his comments will be very --

DR. HOLTZMAN: I want to make sort of three distinctions and endorse what you have said. The first is coming back with respect to the intent of this is just again to make the point that there are things which are not illegal but we make the decision for other kinds of grounds that the feds should not fund it and I think that has been a basis of this report throughout. So the decision that the fed ought not fund is consistent with being agnostic with respect to whether it is done in the private sector. That is one point.

The second point is we made a decision early on in this commission, maybe pragmatically, to tackle the fed funding question only. We had in front of us, whether as with fetuses we could go -- and organs could go broader and talk about federal legislation conducting -- that would -- under which they would be available and made for use. We chose not to do that and I think it would have been a tough thing to tackle.

The third thing is even if you do not tackle the question of which of our recommendations do we think

the private sector ought embrace, I do think we do have to ask ourselves with respect to the future which ones of our recommendations seem to be more enduring than others. I think in the last draft this started to be tackled a bit.

For example, recommendations about noncoercion. It is hard for me to imagine exactly how the moral climate could change such that it would be okay to coerce. On the other hand if we are contemplating changes in the science and in the moral climate in which SCNT embryos are -- therefore, research embryos are okay, certain features of our recommendations such as nonsimultaneous consent to donate with the decision to create. By definition it goes away. All right. Issues of directed donation, which is the paradigm case.

Again this was mentioned in the report and I think it just -- at least for me -- occasions us to think about if we want to say anything about enduring recommendations versus ones which are more or less subject to change, that -- I think that is what is partly being gotten at in this last set of comments.

DR. SHAPIRO: David?

DR. COX: Yes, so I will comment on this. I think that the -- I, too, am quite concerned about getting bogged down about making prescriptions for the

private sector and I would not endorse that in any way. Also, it is clear that not all of our recommendations -- as I said before -- do we agree that we want to encourage the private sector to endorse.

On the other hand if we do not believe in our recommendations enough to encourage the private sector to endorse them when it is creating embryos or doing whatever it is doing then what good are our recommendations at all?

So I think the enduring part of it, Steve, falls under the category of eight and nine where we reevaluate all the time but our recommendations are what they are right now and that -- I will state my position now as directly as I can and that is that I think that the big difference between the public and the private sector right now is that we are not recommending the creation of new research embryos and that is happening in the private sector. We should state that it is happening and we are not suggesting that that be different.

On the other hand is that what we are recommending the ethical principles to be used with already existing embryos in the federally funded thing, I personally believe should be the same ethical criteria that are used for the created embryos, too. I do not see the difference so that is a personal view.

DR. SHAPIRO: A number of people want to speak. Carol?

DR. GREIDER: I just wanted to make one quick comment in reference to something Steve said and that is the issue about -- and it comes to -- it is a new thing that is coming up in the recommendations that somatic cell nuclear transfer embryos would require changing regulations about directed donation. I do not see that logic because what is donated are oocytes and you donate oocytes just for general research and then the transplantable autologous nature comes in when you take a particular nucleus and put it in there. That is my opinion about that and so maybe we can discuss that when it comes up in the recommendation.

The other thing I wanted to make clear, putting together what David and Harold had said about recommendation number nine vis-a-vis created embryos, just to get this straight, what we are saying is that in recommendation number nine we are saying that voluntarily private organizations can submit to this registry for certification their cell lines.

Do I understand then that anything that is created from a research embryo cannot be certified by this panel? So maybe -- that should just be clear that that is what we are -- that is what we are saying.

DR. SHAPIRO: I think we are saying that. I understood that. You cannot get certification from this group.

Okay. Trish?

PROF. BACKLAR: Yes. And then how will that affect if we want to talk about the private sector coming into line with us? It seems to me that it makes it very complicated if they -- if they cannot register.

DR. SHAPIRO: They can register providing they meet the requirements, i.e. that these are derived in certain ways from certain sources.

DR. GREIDER: Some of them will be.

DR. SHAPIRO: And I think there is some incentive for at least some in the private sector to get registration or certification, whatever we are going to call this.

PROF. BACKLAR: But if they are going to create embryos for research --

DR. SHAPIRO: They cannot get it.

PROF. BACKLAR: -- and then one wants to make sure, though, that there are other issues that they follow like not coercing people and getting oocytes and not paying for them. We really are in something of a bind here.

DR. SHAPIRO: But we do not cover that here.

PROF. BACKLAR: The one other thing that I wanted to point out that I said to you last night because I think it is important for us to be thinking about, and when Steve talked about we want to look at that which will be enduring and looking forward, is that I think we also have to face the fact that we have a lot of emphasis on fetal tissue and I suspect with the advent of medical abortion that there is not going to be very much fetal tissue and that we need to at least address this from the beginning of this report apart from the fact from what I understand from the scientists that one is not certain whether the material from the fetal tissue is going to be useful anyway but that is another issue that we cannot forget in these recommendations because it may be very significant in terms of having to go to these embryos.

And, also, that I do not know why -- I am not certain why we are against using somatic cell nuclear transfer. I am sorry if I am bringing this up very --

DR. SHAPIRO: Well, that we can get back to later as we -- the last item we can get back to later as we go through the recommendations where that comes up.

I would note that there is in the text, I do not remember exactly where it is now, a note that the fetal tissue source of EG cells is -- really cannot be relied on and what you are suggesting is that we sort of

make that a little more specific in that area.

PROF. BACKLAR: Yes.

DR. SHAPIRO: Okay. Bernie?

DR. LO: I think this is a very important discussion. I would like to go back again to the question of privately funded research that involves the derivation of stem cell lines.

I totally agree with the idea that we cannot -- I mean, we are stretched as it is trying to get this report out under a tight deadline and trying to solve that problem is insurmountable given our resources. I do think, however, it is important to kind of at least highlight the need for somebody to really pay a lot of attention to the ethical issues that have come up when you are going to start creating -- when you are creating research embryos by whatever process.

And I have been trying to find some middle ground between trying to do that task ourselves and saying that it is an important task that needs to be done and it needs to be done with some independence and integrity.

DR. SHAPIRO: Well, perhaps -- I mean, I understand the point you are making. There might be a natural place to put that in the report. Again I cannot always remember what chapter it is in but there is a spot

in the report which says very early on that these things are not only perfectly legal but they go on without any kind of direct oversight, et cetera, et cetera, if they do not -- if they are not federally funded, if they are not allowed by the state and if they do not come under FDA jurisdiction, and we could at that point say something about the fact that we, however, feel that there are ethical issues here which need to be addressed at sometime. I mean, I do not know quite how -- the way to do it but that might be one point.

DR. LO: Well, I guess I would suggest that we urge the private sector to take these ethical issues seriously in the creation of embryos and, I mean, I do not know what the language has to be but I think if it is not one of our recommendations its absence will be conspicuous.

DR. SHAPIRO: Well, let's go back. I have my list now. Alex, Arturo, and then Steve.

PROF. CAPRON: I do not support and was not the origin, as you know, of the recommendation that was before us a moment ago but I wanted to comment on one aspect of it where it was suggested that it was sort of a little late in the day for us to take up this issue. We have discussed this issue and, indeed, I wish we had the transcript of the last meeting because we spent time

discussing it and I thought we came to a consensus and I want to restate what I thought that consensus was, which was that the commission encourages private sponsors as an exercise of their responsibility voluntarily to apply the recommended safeguards to all research in which ES/EG cells are derived, including the consent process, the informed and voluntary nature of that process, the separation of research from reproductive decisions, meaning either the decision to create embryos or to abort, parsimony in using the cells, and record keeping, and that I do not consider that new.

I do not know that it has to be a black letter recommendation but I do believe it should be reflected in the commentary at the point at which we have set forward -- set forth those basic concepts as being important and that at that point as David has said and I think Bernie has suggested what we would do is note that these should apply even to research which could not be federally funded but may legitimately and legally be carried out by private sponsors, and that these are, in effect, ethical safeguards that are equally applicable and perhaps even more necessary in those circumstances.

I thought we had agreement, and I wish -- because we spent time talking about it that as I recall it was something along the lines of encouraging this as

an exercise of their social responsibility or an indication that they were socially responsible.

DR. SHAPIRO: I think that does accurately reflect the sentiments we had discussed last time. The distinction I was drawing in my mind here when I made my own comments was that the -- at least the way I was thinking about it during that discussion -- it did not cover issues such as the creation of research embryos.

PROF. CAPRON: And I totally agree.

DR. SHAPIRO: It only goes to a part of our recommendation, not all of our recommendation.

PROF. CAPRON: I was trying to state those positively rather than saying all except something or rather state positively what we thought that was by way of consent, et cetera.

DR. SHAPIRO: I think that is really quite legitimate in that part of our recommendations that deal with the kinds of activities that we say are authorized for federal funds or should be authorized that are not currently authorized. I think we should find some way to say that -- I mean, I agree with that -- in those part of our recommendations.

Steve?

DR. BRITO: Excuse me.

DR. SHAPIRO: I am sorry. Arturo was first.

DR. BRITO: Basically what Alex just said, I mean this is -- I am in agreement with that and that is what I heard at the last meeting and I think that -- I do not agree that we should try to make the private sector or recommend that the private sector follow every recommendation that we make for federal funding -- exactly to agree with every single recommendation. But I guess it is more the general concept of making sure there is scrutiny and ethical considerations, et cetera, and there is a lot of thoughtful consideration.

The only thing that makes me uneasy, something that Carol said, is this -- it is ironic that based on the arguments that we use to say that somatic cell nuclear transfer is not as ethically justified -- the things that came out of Dr. Fletcher's paper basically -- it is ironic that this would be the one area that there would be no requirement for a registry to be made for somatic cell nuclear transfer or stem cell somatic cell nuclear transfer based on the way we wrote this.

So I do not know if we need to think about -- well, recommending to the private sector that they need to be ethical and have some sort of a registry themselves or what have you that may be apart from this, the one that we considered most unethical to make stem cells from

that I do not necessarily agree with but as a group would be the one that would be least -- would have the least amount of oversight and I am having some uneasiness with this and I do not know if there is a way to fit this in here somewhere.

DR. HOLTZMAN: We should come back and address that and think about that.

DR. SHAPIRO: We will when we get to that part of --

DR. HOLTZMAN: Right.

DR. SHAPIRO: There is a number of these we are going to have to address as we go through these recommendations.

DR. HOLTZMAN: When I made misstatements about the public sector -- private sector, I was thinking specifically about our decision not to say there should be legislation that controls the private sector as well. I was not present at the last meeting.

I would say -- now putting on my private sector hat, if you will, the notion of saying to the private sector here are ethical considerations you ought to take into account and you ought to abide by and that you ought to think about establishing professional standards for your societies, et cetera, et cetera, to implement these things I think is something that could be

embraced. All right. And I would certainly go for that. I think it is a good idea. All right. Because I think there are good and bad practices in different pieces of the private sector.

Again it just needs very careful handling because I could not endorse a recommendation that says do not make research purpose embryos.

And when you cited the consent, Alex, whether intentional or not, again you had cited as part of the consent the separation of the decision to contribute to research from the decision to make the embryo. Okay. Which is not possible in a research --

PROF. CAPRON: No, what I said was from reproductive decisions. That is not a reproductive decision.

DR. HOLTZMAN: Okay. We will just have to be very clear about that. And if you think about it in those terms we are doing little more in suggesting the extension of the Common Rule to private sector human subjects research, which is I think what we believe we want to do anyway.

DR. SHAPIRO: Bernie?

DR. LO: I just want to follow up on Steve's comments which I find very helpful. Would you, Steve, have that include both research that could have been

eligible for funding and research that is outside our recommendations of federal funding?

So what I heard Alex saying was that to the extent we are making recommendations for federally funded research, if in the private sector you do the exact same kind of research, we would like you voluntarily adopt the same guidelines. I am concerned with the --

DR. HOLTZMAN: Yes. And I am saying with respect to -- but that which would fall outside is specifically involving research purpose embryos.

DR. LO: Right.

DR. HOLTZMAN: And what I am saying is --

DR. LO: Okay. So you are --

DR. HOLTZMAN: -- I have been saying the same thing over and over again. I mean, it was all of those parts like nonmonetization, noncommoditization, noncoercion. It is clearly all in play. It really comes out as a matter of fact you are interacting with a woman who is the subject of human research, I think, under the Common Rule where the Common Rule -- applicable to that activity. It is only --

DR. LO: I would like to somehow make that into a formal recommendation we put at the end here and I guess my suggestion is that I think it is important enough there ought to be a recommendation and not just

commentary. I like the way, Steve, you are phrasing it in terms of just as we would like to see the Common Rule applied in a whole lot of other areas, we would like it to apply here. And I think, you know, we have talked about the issues of consent and nonmonetization of things, which are least the issues they need to grapple with.

PROF. CAPRON: Could we be clear, though? As I understand it, our recommendation vis-a-vis the Common Rule would be a stronger one. As I understand it, we were moving to say such research should be subject to the Common Rule. Here we are saying they ought voluntarily as an exercise of their responsibility to apply the safeguards to the full range of research, including research which could not be carried out under our recommendations by federal sponsors.

One way of thinking about this is that when privately sponsored research is published in journals that the authors could state and would, we hope, be expected to state that they have complied with the standards even though they were not bound to do so.

So there are all sorts of mechanisms that do not require the force of law that will as a social practice, as a professional standard, lead to the same sorts of results.

I wanted to comment if I could on one thing that Carol said about the donated oocytes.

Carol, I think you still could get to that issue of directed donation. Obviously in the case of creating autologous transplant material the whole purpose is directed donation but there still is a choice. The woman giving up the oocyte at that point would have to be told this is to be used in an attempt to create a treatment for the individual whose somatic nuclear material will be placed into the enucleated oocyte. It seems to me that most -- I do not know why a person would not be comfortable if they were allowing their embryo to be used in research to allow that to happen but it seems to me that there needs to be a statement.

DR. HOLTZMAN: But the point with the -- I am sorry. I am out of order.

PROF. CAPRON: Well, I mean, it is just -- I mean, and the only issue then is the consideration behind the rule on directed donation for tissue transplantation is that you do not want people creating a fetus for the purpose of treating a relative or friend or something else, right? Here the question is do you object to a person undergoing superovulation and then having oocytes removed for the purpose of helping a particular individual.

DR. GREIDER: It does not have to be a particular individual. That is the point. The person doing the donation does not have to know anything about the individual.

PROF. CAPRON: No, no, I agree. They do not have to know. You are just -- you are just pushing aside the alternative scenario, which we have to address. I am not stating an issue on it, in which a woman knowing that her brother, father, you know, somebody else, herself, is in need of a new liver, is told, "Well, the way we think we will do this now is to get an oocyte," and she says, "I have oocytes." "And we will give you a drug and we will take them out and then we will, in fact, put the nucleus in from the patient who is your father, brother, sister, self, and use that the way of treating." That is all I am saying.

That is an alternative to what you were imaging, which is college student sees the ad, comes in and donates oocytes, and I think that the person in that situation has to be told, "Am I donating oocytes for someone to have a baby or am I donating oocytes for an embryo to be created through artificial --"

PROF. BACKLAR: It is like giving a kidney.

PROF. CAPRON: You know, right. I mean, so all of these are simply possibilities and if we believe

that the latter, the one in which there is, in effect, a donation with the thought in mind of a particular patient, is that more legitimate and less problematic than the person creating, becoming pregnant in order to abort a fetus.

DR. SHAPIRO: Carol, and then we are going to wind up --

DR. GREIDER: I do not disagree with what you just said. I was just taking issue with the fact that currently in the report it states that if SCNT were to occur for autologous transplants at all it would necessitate that we change the issues about directed donation.

But as you just pointed out there are two different cases. You could say that you cannot do directed donation but you could still do SCNT from the anonymously donated embryos.

DR. SHAPIRO: Yes.

DR. GREIDER: So it does not preclude autologous --

PROF. CAPRON: It raises an issue about it.

DR. GREIDER: It does not preclude it. It does raise an issue and we have to deal with that issue but I just did not want to say that it necessarily precludes it.

PROF. CAPRON: I see what --

DR. HOLTZMAN: For what it is worth the necessitate tracks back to a conversation, I think, I had with Eric, which basically said the paradigm case would, indeed, be the mother donating the oocyte so that their child could get it or because the child suffers from AML and we all -- you can talk to anyone. That is going to be the first case that is going to come up.

So does it logically necessitate? No.

Is it going to play out that way? Yes.

DR. SHAPIRO: We will come back to that issue.

I suggest that we break now for lunch.

DR. COX: Is it possible for us to -- with this discussion on this recommendation -- to phrase this in a way that it is acceptable?

DR. SHAPIRO: We are certainly going to work on it.

We are going to put some -- I am during the lunch hour put together two or three people to work on this issue and on the revisions of nine which we had rather extensive discussion and then we will come back after lunch and start dealing with one and go through them and then come back to these revisions that we have all talked about.

Eric, is there any -- what are the arrangements -- or, Pat, what do we do about lunch?

There are three tables reserved for this group in the restaurant. You can find your seat there. And we should reassemble at 1:15.

(Whereupon, a luncheon break was taken at 12:15 p.m.)

* * *

1

2

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

DR. SHAPIRO: Colleagues, I would like to call our meeting to order.

Colleagues, I would recommend proceeding in a particular fashion this afternoon. We have, of course, some new recommendations that one or two people have been working on. We have those revisions that have been worked on. Some are being handed around right now, which is recommendation eight or recommendation X and XX, excuse me, which are new recommendations which are the focus of our discussion towards the end of this morning's session. We will get to that somewhat later on this afternoon.

There is also, of course, being worked on as we speak revisions of what was recommendation nine that was the cause of a great deal of discussion earlier this morning. We will come to that later this afternoon also.

What I would like to do now is go back to begin on recommendation one and start working through those particular recommendations and see -- some of these we have dealt with before but I just want revisit them. Some will take us presumably just a very few moments. Some may involve more extended discussions.

In any case, I would like to go through them one by one just to revisit them where necessary and to

make proposed changes in other cases if members of the commission wish to propose that.

The first recommendation, which currently appears -- recommendation one, which currently appears on page seven of chapter five, currently reads, "Research involving derivation and use of embryonic germ cells from cadaveric fetal tissue should continue to be eligible for federal funding." That is the way it currently reads.

I would like to propose that we add to that a sentence, and I think this has been handed out or is being circulated now, which says the following: "In addition, existing statutory and regulatory provisions should be amended to ensure their application to improve embryonic germ cells."

The idea here of the additional sentence needs to be discussed here since it is my own sense of the existing legislation that this is not crystal clear in that legislation but others could speak to that. If it is crystal clear that these are already covered then the second sentence would not be necessary.

And so I ask what people's judgment on that issue is.

Alex?

PROF. CAPRON: I agree with you that it is not clear because the relevant statutory provisions are

for fetal tissue transplantation. I do not think that your second sentence quite conveys what you mean in part because it is not embryonic germ cells and their derivatives that are at issue, it is really the derivation of embryonic germ cells from this source.

DR. SHAPIRO: "And their derivatives" should be taken out anyway. I do not know why I put that in there but that should be out.

I guess the first question we have is whether we should add a sentence, an appropriate sentence here, just to make sure that that act is clarified so that these -- this type of derivation of EG cells would be covered under the provisions of the --

PROF. CAPRON: If I could remark, although I tried in chapter three -- I am sorry, I do not have the exact page here at this second but I will find it -- not to include actual recommendations but really to frame the issues. I did note that there was an argument certainly in favor of applying in a blanket fashion all the rules that have been established for fetal tissue transplantation even if arguably some of them might seem sort of over kill or superfluous.

The notion of directed donation is really not an issue with this kind of research as it is with transplantation but just for ease of application and to

anticipate the day when you might have a transitional step -- in other words, you would be harvesting the cells from the fetus, culturing them and then transplanting the stem cells out of them instead of transplanting the whole tissue, it would be then odd if you set up separate rules for EG cells than for direct transplantation.

So just for both of those reasons.

And there is a passage in here, I think, on page seven of chapter three at the top, lines one through eight, which talks about the desirability of amending the laws to make them consistent.

DR. SHAPIRO: Jim?

DR. CHILDRESS: Since in the fetal tissue transplantation area the main concerns really focus on the consent questions and separate the decision and so forth, I would note that we already have in recommendation five some version of that and so it seems to me we need to connect what we are doing with the revised recommendation one with the old recommendation five on page 13 of this chapter.

DR. SHAPIRO: I think we are going to revise five in a substantial way really to focus on ES cells and -- but I agree.

DR. CHILDRESS: It would -- well, there are several ways to do it. But if we are going to consent

issues that would cut across the two then rather than getting rid of them there we need to include the other as we need to include what Diane has provided in recommendation five.

So if we preferred it that would be a good reason for going ahead and putting these -- what you now have as part two of the revised recommendation -- up under number one but that will just mean redoing them.

PROF. CAPRON: That pretty much frees up the space taken by recommendation five for something else, doesn't it?

DR. CHILDRESS: It does but then we restructure the chapter so that the consent issues would --

PROF. CAPRON: Yes.

DR. CHILDRESS: -- which is fine but I would just note that we cannot just do it in isolation from what else appears in the text.

DR. SHAPIRO: I agree. I certainly agree with that.

So you were suggesting, Alex, that we modify the second sentence in here to be -- to parallel a more useful way the material you had in the chapter. Is that --

PROF. CAPRON: Well, yes. What I was saying

was that material is certainly in the commentary category. It is not intended for the recommendation itself.

DR. SHAPIRO: Right.

PROF. CAPRON: But, yes, the recommendation ought to reflect the idea of making fully consistent and applicable to EG cell derivation research the rules that apply now to fetal tissue transplantation.

DR. SHAPIRO: Comments or --

DR. HOLTZMAN: I just have a quick fix on the language if you want it.

DR. SHAPIRO: Yes.

DR. HOLTZMAN: "In addition, existing statutory and regulatory provisions should be amended to ensure their application includes the derivation of embryonic germ cells for research purposes as well as transplantation."

PROF. CAPRON: I think that does it.

DR. SHAPIRO: Okay. Any further comment? We will add that on.

That was very helpful, Steve. Thank you.

Okay. Let me just say a word about the text. Of course, the text that appears in various -- we are eager and anxious to have all kinds of suggestions regarding the text themselves, particularly if people are

willing to help with the writing, but I do not want to focus on that right now. I want to take each of the recommendations and to the extent we have time left we can go back for the other considerations.

PROF. CAPRON: Could I ask just one question?

DR. SHAPIRO: Sure.

PROF. CAPRON: I thought that -- I had started to try to revise the introductory language of chapter five because I did think it continued unnecessarily to focus on polarization and I thought at the last meeting we said we ought to focus on the consensus and note that there are views beyond that. It also -- so if people are nodding their head, I will turn in -- maybe tomorrow we can look at it.

DR. SHAPIRO: Well, that would be very helpful. Just that we did not get to really look again at that part of this chapter since it is --

PROF. CAPRON: It is not a complaint.

DR. SHAPIRO: Yes.

PROF. CAPRON: It is just I did not want to bother to do it if people --

DR. SHAPIRO: Yes.

PROF. CAPRON: But it also seemed to me that the second paragraph that is now at the beginning of

chapter four really belongs at chapter -- the beginning of chapter five. That is a paragraph which basically says how we have framed our recommendations and since chapter four is really addressing the ethical issues more broadly this language is just perfect for the introduction to chapter -- one of the first paragraphs of chapter five.

DR. SHAPIRO: What is the paragraph again?

PROF. CAPRON: The second -- the paragraph on page one of chapter four beginning at line 13.

DR. SHAPIRO: That is the number of that paragraph.

PROF. CAPRON: Yes.

DR. CHILDRESS: That paragraph you are proposing goes in the beginning of chapter five.

PROF. CAPRON: "We aim to formulate a set of recommendations that on balance would bring our society to an even better state." I mean, it really is about recommendations and then if you go to the next paragraph here it is really more about how the report and it makes more sense not to repeat it here but it is nice language and I would just move it wholesale basically.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I think Alex is certainly right. It could go there. I guess that particular

paragraph was, in part, intending to reflect some of the struggle the commission had and we would need, I think, to have some alternative briefer formulation of that in chapter four. That was something Arturo, in particular, had underlined and I think it was an important point.

PROF. CAPRON: Well, I thought a little bit of that already came through in the lines before that and really are elaborated. I do not -- anyway --

DR. SHAPIRO: That is a useful suggestion. We will try to -- it is a helpful notion, especially the last part of that.

Okay. Let's go on now to recommendation two, which one we spent a good deal of time discussing the last time we were here. Let me just read it out so that we are all focused on it.

"Research involving the derivation and use of ES cells from embryos remaining after infertility treatments should be eligible for federal funding given an appropriate framework for public oversight and review, and this requires the Congress rescind, in part, its ban on federal funding..." The latter, I guess, is a comment part of the recommendation strictly but that is -- "Congress rescind, in part, its ban on federal funding for embryo research."

Now we had an extensive discussion on this

last time and Tom raised the issue again this morning so let's see what issues you still want to discuss on this one.

DR. DUMAS: I had just a little wordsmithing.

DR. SHAPIRO: With respect to the recommendation itself?

DR. DUMAS: Yes.

DR. SHAPIRO: Okay.

DR. DUMAS: "Research involving the derivation and use of ES cells from embryos remaining after infertility treatments should be eligible for federal funding and an appropriate framework for public oversight and review should be established."

DR. SHAPIRO: I understand the change. Does anyone have objection to that, like it, dislike it?

I will take the lack of any protestation to mean you like it.

DR. DUMAS: Yes.

DR. SHAPIRO: Okay. Do you want to say that again just to make sure I have got it.

DR. DUMAS: Okay. "Research involving the derivation and use of ES cells from embryos remaining after infertility treatments should be eligible for federal funding and an appropriate framework for public oversight and review should be established." And then

that last part of it can go down in the explanation if necessary.

DR. SHAPIRO: Congress.

DR. DUMAS: What the Congress needs to do.

DR. BRITO: Should we reference the recommendation here, nine, or I guess --

DR. SHAPIRO: Yes. There are -- we will in the -- let me mention -- I am glad you mentioned that Arturo. We will as we go through these recommendations to get the final form, a lot of them require to be referenced to other recommendations so we draw people's attention to where these things are set up including this one exactly where you pointed out and so that will be done. I just left that out until we get all the numbers straightened and so on.

DR. MURRAY: I seem to be the one belaboring this point but I am going to belabor it because I think it is important that we make our arguments as clear as possible here and that if we are going to recommend federal funding for derivation as well as for use that the case be a very strong one, indeed, as strong as we can possibly make it. I do not think the current draft does that yet and several of the commissioners have been in conversation at various points of the day today to try to explore other arguments for derivation.

I mean, I will stand by the principle I articulated before, which is that if you cannot make a good argument for why there ought to be federal funding of derivation because -- and that, in fact, you could not get effectively the same benefits by allowing derivation to go on in the private sector then we would simply -- we would lack a moral foundation to recommend funding for derivation as well.

So we have some arguments and I am actually going to act a little bit of a ringmaster here and I am going to ask Carol Greider to describe a couple of the reasons that she offered us because we learned something this morning, I did and a few others of us, from conversation with Carol about the more intimate connection of the conditions of derivation and the scientific usefulness of the cells.

DR. SHAPIRO: Carol?

DR. GREIDER: I just had a couple of things that spoke specifically to the scientific issues about the nature of ES cells and we talked a little bit about this at the last meeting but perhaps I was not clear enough about it. There has been some discussion that the idea -- that you have ES cells, for instance, that -- currently existing ES cell lines from Jaime Thompson's lab -- that those would be enough to just work with for a

long time and you could grow them up in the lab and give them out to other people.

However, one major scientific point that that idea misses is that these cells do change through time. When you take cells in culture, take cells from an organism and put them in culture, very rapidly they accumulate changes. There are chromosomal changes. Changes in gene expression, some pretty dramatic changes. Therefore, those cells which have been passed through several different laboratories might be a very different scientific entity than the cells that were initially derived.

So that is one, I think, major scientific point and I am happy to write that up into a section and give some references from mouse embryonic stem cell work where -- what you look at for mouse embryonic stem cells as sort of the gold standard for a cell that really has all of the components is that it can contribute to the germ line. If you take those cells and put it back into another mouse it will go on and contribute to the germ line of the mouse, and that is something that is clearly lost in many people's hands when they grow a mouse embryonic stem cell.

So that would be a concrete example where I can put some scientific references in and something that

can go into chapter two. So that is one argument. I have another one unless you have a comment on that.

PROF. BACKLAR: I just wanted to add that Bridget Hogan told us many, many months ago exactly this problem and laid it out, and it would be very interesting to reference some of her remarks as well.

DR. GREIDER: I will go and look at her papers and her remarks, and she has published on this.

DR. SHAPIRO: Is this on this particular point, Steve?

DR. HOLTZMAN: Yes. And that is it is absolutely true that ES cells made in different people's hands are better and worse in terms of their contributions to various cell lineages. I am not sure that addresses Tom's issue because it is not the case that the person who wants to use it is the master of making the ES cell lines, number one. Number two -- so, therefore, the person getting federal funding for use has to get the federal funding to make them.

And, number two, the masters of those cell lines in terms of making them could be in the private sector and could be available. So, for example, even though it is true that not all ES cells are created alike, everyone in the field goes to Alan Bradley's for his, right, in terms of the mouse. Everyone -- you know

what I mean. So that there are canonical cell lines out there in Bradley's hands and Deutschman's hands, et cetera, et cetera, where you know those are the good ones. So I am not sure it really addresses Tom's point directly. It creates a circumstantial case that the best producers may be people who could only do it with federal funding. It is not the connection of the use.

DR. GREIDER: That is one issue but I think that the whole concept that just because a cell line exists, people have said that there are two cell lines out there, why don't we just use those. That really maybe has not gotten across.

DR. HOLTZMAN: Well, that one is crazy.

DR. GREIDER: All cell lines are not created equal. But -- you may think it is crazy but, I mean, I keep hearing these arguments come back at me again and so clearly if I am hearing them come back at me again we must not have made them very clearly in the report and we need to do that.

DR. MURRAY: The conversation you and Steve just had was at a level of scientific sophistication that would be in excess of many of us, including me, our immediate understanding and probably for most of the readers of the report so can I just ask you a couple of questions to see if I understood correctly what you told

me before?

One is that there are always decisions made in the creation of embryonic stem cell lines that may have some consequence for the kinds of uses to which those cell lines might later be put. Is that correct?

DR. GREIDER: I am not sure. Could you restate that? Could you just say that --

DR. MURRAY: If I am stating it poorly please say again.

DR. HOLTZMAN: There are decisions made in the making of the cell lines that affect how good those cell lines are where good equals the ability to contribute to multiple cell lineages. Paradogmatically in the mouse you are seeking a cell line, which when put back into a blastocyst will contribute to the germ line of the resulting chimeric mouse so that when bred to the next generation you get a fully transgenic mouse.

DR. MURRAY: That is good. That is not the question I was asking actually because what I understood Carol to say earlier, not in the context of the full commission, was that you might make some other choices in the creation of cell lines that would make them particularly useful for certain kinds of purposes but not particularly useful for other kinds of purposes.

DR. GREIDER: And perhaps choices is not

necessarily the word to use here. You might be -- two people might be following a very similar protocol and they end up with something which can have certain properties versus someone else using the same protocol will end up using some other properties. I do not think that the science is that well understood that you could say that that would necessarily be a choice but two different people deriving ES cells can come up with cells with somewhat different properties.

Although what Steve was saying is there is one particular person, Alan Bradley, who makes very good ES cells that have these particular properties, I disagree that everyone necessarily gets his cells. I know people that derive them themselves because they want to have control over what the outcome of those cell lines are.

DR. MURRAY: You had a second point. Why don't you go ahead with the second point?

DR. GREIDER: All right. So the second point is that during the derivation of cells or working with cells that have been derived is one thing. However, deriving cells is also a scientific process and so in the course of deriving the cells if you have a number of scientists who are interested in the processes that go into the creation of the ES cells you can learn -- there

is a lot of rich science from which you can learn in the process of the derivation about specific factors that will contribute to the cells having certain potentials.

My argument has been that if you have federal funding then you have a larger number of people that are interested in those basic processes as opposed to a specific end outcome and that one of the things that you might give up in not having federal funding is having curiosity driven researchers doing this and making those basic discoveries that just come out of doing the hands on research yourself.

PROF. CAPRON: So that is synergy and adventitious interactions between derivation work and --

DR. GREIDER: During the derivation work you can make discoveries that you would never be able to make if you were not deriving them yourself if you were -- and you cannot predict.

PROF. CAPRON: Okay.

DR. GREIDER: If you have people that are paying attention and are interested in what is going on in their cell culture they can make those observations.

PROF. CAPRON: And that is adventitious and if you excluded an entire category of researchers like everybody working you would undermine their ability to take advantage --

DR. GREIDER: To make those.

DR. HOLTZMAN: That is right.

DR. GREIDER: Yes.

DR. MURRAY: Crudely -- this is very crude but there are two models of how you derive stem cells. This is off the top of my head so forgive me if it is not entirely coherent.

One is a sort of fairly technical model. All right. There is a procedure, you follow it, you can hand it to your, you know, low level lab tech, they pull this embryo apart, they culture the stem cells, and all stem cells are the same. That is the crude model.

DR. SHAPIRO: I do not think the crude model is even possible.

DR. MURRAY: Well, in fact, the crude model is wrong although I think it probably matched fairly closely to the conception a lot of people may have had about how stem cells are --

DR. SHAPIRO: That is possible.

PROF. CAPRON: And it might be worth stating to debunk it.

DR. MURRAY: It may be but what Carol was educating us about today was really -- is a much different sort of model for what is going on in derivation. Derivation is -- it is not merely the

creation of a tool for research. It is, in fact, a form of research in and of itself, number one.

Number two, you get many different kinds of results even using what may seem to be the same sorts of procedures. There is a third element which has not come up in -- around the table right now, and that is stem -- it is very difficult to keep these cells having the same properties over time. The stem cells, like all human cells, change continuously. Okay. And so cells that have gone through a couple of passages say in a commercial lab, you get them after they have done three or four divisions and they may simply not be the same cells and not be nearly as useful for science.

So to highlight the second model --

DR. CASSELL: They are two different sentences, though. They may not be the same cells and they may not be useful. The fact that they are not the same cell is not the critical fact.

DR. MURRAY: I agree the latter issue was the important one.

DR. GREIDER: They may not have the same characteristics. I mean, clearly they are not the same cells.

DR. MURRAY: Yes.

DR. GREIDER: They may not have the same

characteristics and --

DR. MURRAY: This is an ontological point that I --

DR. GREIDER: Yes.

DR. MURRAY: Okay.

PROF. CAPRON: And, Mr. Ringmaster, wasn't the point that Carol --

(Laughter.)

PROF. CAPRON: -- a moment ago was not on your list as you went through it, which is because it is a research process it has unpredictable synergistic relationship with the research that utilizes these cells. Let's just say you will be able to do things if you are involved in that process and can go back and forth between the two that you could not do if they were discrete processes. Is that a correct statement?

DR. SHAPIRO: I want to say something about exactly this point. As I have talked to scientists about this that is the point that everybody goes to first, whether I talk to scientists who are in the private sector or in the public, it does not matter. That is the point they first go to.

DR. MURRAY: That point being?

DR. SHAPIRO: That point that this is a process going on which is interactive learning and

development which has an integral and organic relationship to research both on derivation and on use that these cannot so easily be separated and the point they make in addition to that, which I refer to Carol and others who know a lot more than I do, is that as they review the work done on nonhuman animals that it is quite -- this is just very clear. This is not something that is just sort of inventing and believing but something that the work on nonhuman animals really underlines and they have every reason to expect, therefore --

(Simultaneous discussion.)

DR. SHAPIRO: -- but that is what I am told. It is not firsthand information.

DR. COX: It actually is firsthand because we discussed it extensively last meeting.

DR. SHAPIRO: Well, I -- I am -- but I learned from David and Carol and others who I speak to, not from my own experience is all I meant by saying that.

Bette, and then Steve.

MS. KRAMER: Well, I just -- I was part of that conversation this morning and Carol used an expression at that time that just cast it differently for me and that was that she said that this is an art. Whereas, I had been hearing -- what I had been hearing over the past months of the discussions was it sounded

very, very technical and I think that --

DR. GREIDER: It is both.

MS. KRAMER: Pardon?

DR. SHAPIRO: A good rule is everything --

DR. GREIDER: It is both.

DR. SHAPIRO: -- is an art.

MS. KRAMER: Right. But she said -- she explained -- and she did and she explained that there is a real art to the process of deriving these cells and, therefore, in the hands of each artist it is going to be -- look -- it could look quite different.

DR. MURRAY: Cooking is an art Arturo just said --

DR. SHAPIRO: If it tastes any good.

(Laughter.)

DR. SHAPIRO: Let's see. There are a couple of people who want to say things and then I want to get back to this because we have to get to --

DR. DUMAS: There is another implication that should not be lost and that is for the continuing advancement of the science it is important to have the opportunity to have federal funds available for people to work on that and that is one of the things that I heard Carol saying in addition to all the other things that have been brought up.

DR. SHAPIRO: David?

DR. COX: Yes. Just to exemplify that in two ways. First, it is like a menu, like a smorgasbord, the more scientists that are doing it the more things that you have on the menu and the more you see how to make a dish. It is very much like the art of cooking but once somebody makes a good recipe then other people can replicate that recipe so this is at the first stage. Someone is making it, right. And the goal of science in many ways is to make it so that it is reproducible and the more people that do it the more you know it is reproducible. That is one point.

The second point is this relationship again which we talked about extensively last time between the public sector and the private sector. The private sector is very good at taking things from the menu and saying these are the things that can basically get translated into products for the public good. The private sector, although they have very talented people, is generally not the place that populates the menu.

The place that populates the menu is the public sector so that if you want to have very few things on your menu have making these stem cells just in the private sector. I mean, it is not to the public good and that is a point that I tried to make, perhaps not very

clearly, last meeting but, I think, for me that is of major importance from a scientific and public policy point of view.

DR. SHAPIRO: Jim, and then Bernie.

DR. CHILDRESS: Since Tom is raising this particularly in relation to the question as to whether one could draw a distinction between providing federal funds for use in contrast to derivation, and asking us to consider what kinds of arguments might be appropriate to strengthen this given the direction the commission is taking, in looking back over some of the transcripts as we were reworking the ethics section I was struck particularly by the discussion among those spokespersons coming out of or relating to religious traditions about the importance of being as truthful, honest and straightforward as possible in whatever policies we recommend, and in whatever rationale we give for those policies.

And that for me actually helped a lot in thinking about these matters becasue for many of those persons there is -- from their standpoint it was -- to talk about providing federal funding for use and being able to sharply separate that from differentiation for them just made no sense. It seemed to be a dishonest deceptive strategy.

And as I thought more about this, this seems to be one way -- in some of the -- for example, Gilbert Meilander related that we would probably come out with a very different position than he would but he hoped that if we did we would be just straight forward about it and say why we had got that direction rather than trying to work with distinctions between derivation and use.

I guess I am persuaded by that and more inclined to view that as an ethical argument relating to public process that would go along with some of the scientific ones.

DR. SHAPIRO: Thank you. Bernie, and then Arturo and Steve?

DR. LO: I just want to say I thought this discussion was very useful and I would like to see some of this fed back into chapter four. On page 33 and 34 we sort of say that we think federal funding would increase the number of top rate scientists carrying out this research. I mean, I think the discussion we just had, if there is documentation of that, if there is some references we can make, and how also that would improve the research. That is what you said, Harold, and Carol said. And just to add on -- in the next page of chapter four we talk about federal funding for derivation would improve sharing of materials.

And again I guess I first want to ask a question. Since my understanding is most universities -- if a researcher derived a cell line using federal funds the university would own a patent and try and license it. Is it clear that any cell lines derived from federal funding would be more widely available to other researchers than cell lines that the universities when they do have a licensing -- patenting licensing process have fewer restrictions and make it -- so if it that is true and we can document that, that would be really useful.

DR. SHAPIRO: Steve -- oh, excuse me. Arturo is next and then Steve.

DR. BRITO: One key word with David's comments that he had made to me privately outside was the use of the word "partnership" when we are talking about federal and public research to look at it in terms of a partnership that is developing there.

I was going to bring it back full circle, Tom, and ask you just to make sure I understood you correctly this morning, is that the overall point here is that we need to be more straight forward, as Jim said, in what -- in what we are actually recommending in terms of federal funding, the reasons for that, and I just want to make sure -- I see this as an ethical argument and I

agree that it should go in chapter four based on the current science.

Are you in agreement with that? Is this more of an ethical argument and that is where it should go and that is where we should be very --

DR. MURRAY: What is the "it," Arturo?

DR. BRITO: I am sorry.

DR. MURRAY: What is the "it" that is the ethical argument here?

DR. BRITO: Not the argument, the ethical reasoning.

DR. MURRAY: Yes. I have --

DR. BRITO: Or an ethical reason --

DR. MURRAY: I apologize if I have not made myself clear before now but I have said from the beginning -- and I actually do disagree, I think, a bit with Jim. Not -- I am in favor of -- absolutely in favor of candor, of truthfulness. I do not disagree with any of that.

It seems to me that there is -- one can quite consistently be in favor of federal funding of use and not in favor of federal funding of derivation. Not because you pretend that derivation did not happen but because you do this as a matter -- a means of respecting people who may be unhappy with the fact that you fund

even the downstream use but would be really morally offended if you funded derivation. That is at the heart of my worry here.

But all along I have said I am certainly willing to consider supporting federal funding for derivation but the argument had not been made strongly enough as to why you have to provide federal funding for derivation and what you might be giving up. I think we have begun to make significant strides towards pulling that argument in now.

DR. SHAPIRO: Thank you. Steve?

DR. HOLTZMAN: A small point in answer to Bernie's question, the university can and can choose not to make it available. There is, however, new guidance from the NIH which has come out in the last couple of months in terms of better accessibility for research tools so if you want to go down that path and encourage people follow those guidelines, that would be a positive.

To the ringmaster question, I think we have assembled a series of arguments here having to do with the utility of these things, arguments along the lines that Jim has raised. But what some commentators or people reading this report will -- cannot help but strike you is that we rely on a separation between derivation and use in the case of the fetus and then we say in the

case of the embryo we do not think there should be such a split.

And, therefore, I think we do have to take on why we think the cases are different, you know, I at least took a crack at that in my e-mail. Okay. And I am not saying the argument is right but I think if one does not do that I think one is going to be hard pressed to address Tom's fundamental issue.

DR. SHAPIRO: Eric?

DR. CASSELL: It is just a slightly different question and so I will just say it quickly. Jim, in point of fact about the truth that goes into this of being absolutely straight, there is an opposite side to it, too. In Nicholas Wades' articles last week or the week before in which he talks about the destruction of the embryo in order that cells be derived from it implies that if it were not the -- if they did not do that then the embryo would not be destroyed, and so that is on the first part of it.

The second part of it is somehow to make it clear to people who read it -- not the scientists, they know -- that we are talking about the typical pencil or pen, you know, so we are not talking -- we are talking about something that they have to visualize as going to degenerate anyway and being that size so that it is not

the implication that this procedure destroys embryos that otherwise would be okay.

DR. SHAPIRO: Alex?

PROF. CAPRON: I have three points. The first is in response to Eric's last point. I think it is not size but developmental status that is important.

DR. CASSELL: Either way so that --

PROF. CAPRON: The people -- the people whom we are addressing are people from whom the issue is potentiality and we all know that all organisms begin with a single cell and so it is a point where simply emphasizing that it is very small simply means that it is just that much more vulnerable. The point that at that stage the kinds of considerations that most people would regard as germane do not yet apply.

DR. CASSELL: I accept that.

PROF. CAPRON: Okay.

DR. CASSELL: I accept that. So that it is clear what people are looking at in their mind's eye.

PROF. CAPRON: I think -- yes, we should throughout. The second is in response to some of the comments about where this belongs, I think a certain amount of this really belongs in the science chapter by way of explanation of what the process is, in part, because it can be presented there in a less tendentious

way.

It is descriptive of the process and I think a reader coming on it then will see it as more descriptive that researchers working in this field are not doing something equivalent to buying reagents from a chemical company if they -- for -- in use. They are engaged in a research process in which the derivation and use research is very closely connected both for reasons of tailoring what you do and learning from what you do.

The third point is something which comes out in chapter three but which we have not discussed yet. We, in other ways, have tried to emphasize that the most important distinction is between embryos remaining from IVF treatment and embryos created for research. And at this point that is where we think a strong line should be drawn.

If the NIH policy is followed it is very hard for NIH or anyone else in that position to exercise any force on that line because as to the statutory line both the creation of embryos and their destruction are equally prohibited from federal funding.

And if what they are saying is but we are not engaged in any of that, we are just funding use then they are -- and we can do that because these are two morally and practically totally separate activities and what we

do over on the use side has nothing to do with the derivation then how can you say that it is wrong to use cells that were created through a process by privately funded process that involved the creation of an embryo for its destruction for this purpose.

And it cuts the legs out under -- out from under what I think -- well, I will -- I think that most people and the people who matter on all this are those people in Congress who are going to have to pass judgment on this. We will be more bothered by the notion of the creation of embryos for research purposes. We know the president is more bothered by that than the use of existing embryos.

DR. BRITO: And most people.

PROF. CAPRON: And I think most people and I think we ought to underline the ways in which ironically separating and saying use is discrete from and can be funded without getting into any involvement removes the ability to be involved on the positive side with saying we care about that distinction between remaining IVF embryos.

DR. MURRAY: It does not follow at all, Alex. It does not follow. You can say -- I mean, I think I agree that the -- probably the largest policy issue is going to be between creation of embryos for research and

the use of spare embryos. We agree perfectly well on that.

It does not in any way follow that you, therefore -- that introducing a further distinction somehow obliterates or removes the force of the private sector.

PROF. CAPRON: I think it does.

DR. MURRAY: Well, we disagree.

DR. SHAPIRO: One rejoinder and then we have others who want to speak.

PROF. CAPRON: Try to reason it through. If you are saying that the two are discrete and then you are faced with someone who says, "Well, I have a cell line here that came from embryos that were created by the Jones' company for the purpose of deriving cells and they derive cells," you say, "Well, we will not allow those to be used in federally funded research," and you say, "Well, what is your basis for not allowing them?" "Well, they are less licit." "Well, in what sense are they less licit?"

The only statement on licitness that we have is the ban on either making or destroying them and you have said that your use of cells that came from a destruction is not implicated in that destruction. How can your use of cells be implicated in the way in which

they were created through IVF embryos made for research purposes? You are no more implicated. Therefore, you have no moral ground for saying that you would -- you can practically say anything you want.

Of course, you can say we will not fund cells derived from the State of Arkansas. I mean, you can say whatever you want but on what ground would you distinguish those that come from Arkansas from Massachusetts. You cannot.

If the Congress has declared that what is wrong is federal funding of research that destroys embryos or that creates embryos for research purposes, and you have said we are not touching that, we are coming no where near that, we are only using the products. There is no -- you have no moral stance for differentiating at that point because you have disassociated yourself.

DR. MURRAY: I have lots to say but I think it would belabor a point and I actually think we would be better served by moving to the question of let's get the strong arguments in favor of derivation, funding derivation. I think you may find agreement here. We can still disagree about this --

(Simultaneous discussion.)

DR. MURRAY: -- should not play a primary

point in our report, though.

DR. SHAPIRO: All right. Carol?

DR. GREIDER: I just wanted to go back to the second point that Alex made, which I agree in terms of where we should put some of these arguments that I initially laid out. There is a section that can be written for the science chapter and I volunteered to write a section in there about the changes in cells over time as you culture them and their derivation, the different properties can come from different people doing the derivation.

But I also think that in chapter four on page 30 where we lay out the arguments in favor of federal funding for certain types of stem cell research that a few comments should also go in there and Eric pointed out to me some places that -- I guess on page 33 where some of those issues come out but I am also happy to draft a section on some of the scientific reasons.

We lay out under different headings some of the reasons for federal funding. Just put in a whole subheading on some of the scientific issues and refer back to the issues in chapter two.

DR. SHAPIRO: Bernie? Excuse me. Bette was first. Bernie?

DR. LO: Go ahead.

MS. KRAMER: That is all right.

DR. LO: I want to raise a question of kind of whether our recommendations really capture all that we are intending to recommend. I mean, what we have done in this last discussion is that we have to be very clear about where we are drawing lines and Alex's point was that we are drawing a line between IVF "spare embryos" versus creating research embryos that we are funding derivation and use federally for the IVF spares, and we are drawing a line.

As I look through the recommendations we actually, I do not think, explicitly comment in the recommendations what we are saying about federal funding for the use of stem cells that were derived from research embryos created specifically for the purpose of research. As I read through the recommendations that is not really covered here. I am wondering if we really need to get in the spirit of what Jim was saying, be explicit and clear and say what we mean to say.

DR. SHAPIRO: Is that part of the certification process?

DR. DUMAS: Yes.

PROF. CAPRON: I agree with you it is not clear but we intended that you could only use ones which were certified and only the certified ones could be ones

which were created in an approved protocol and the only protocol that could be approved is one which has fetal tissue or remaining embryos.

DR. SHAPIRO: I want to thank -- Bette, did you want to have anything to add?

MS. KRAMER: No, not now.

DR. SHAPIRO: I now want to return to recommendation two. We will, of course, need to incorporate a lot of the issues that came up in the text and so on. I think the recommendation, however, we ought to keep coherent and straight forward. We will get the commentary and reasoning in and improve it as has been suggested here but the recommendation currently says, "Research involving the derivation and use of ES cells from embryos remaining after infertility treatment should be eligible for federal funding."

And then using Rhetaugh's amendment, "and an appropriate framework for public oversight and review should be established." And then the references to the appropriate place.

Now last time that we voted on the substance on this, I am not talking about the specific language but the substance of this arrangement, this recommendation, excuse me, we were not completely unanimous on that but we had a very large majority of the commission in favor.

So I just want to revisit this now for -- on a substantive level here for the last time and just ask how many commissioners continue to favor recommendation two.

(A show of hands was seen.)

DR. SHAPIRO: This is that we would add federal funding eligible for derivation and use.

DR. MURRAY: I think depending on how the text appears and how strong the arguments are I could --

DR. SHAPIRO: You could abstain.

DR. MURRAY: I am abstaining at the moment.

DR. SHAPIRO: Steve?

PROF. BACKLAR: Excuse me. I am sorry. Could you -- would you mind making clear exactly what you are asking us again?

DR. SHAPIRO: Recommendation two, I will read it again. "Research involving derivation and use of ES cells from embryos remaining after infertility treatment should be eligible for federal funding and an appropriate framework for public oversight and review should be established." Now this reads very similar although the wording has changed from the last time.

All those in favor, please just raise your hands.

(A show of hands was seen.)

DR. SHAPIRO: Okay.

DR. MURRAY: I am abstaining.

DR. SHAPIRO: Okay. Tom wants to abstain pending how -- which I understand perfectly well -- pending if the arguments --

PROF. CAPRON: With adequate argumentation.

DR. MURRAY: With adequate argumentation I would vote for it.

DR. SHAPIRO: No, I understand that. I understand that.

PROF. CAPRON: Unanimous with an asterisk.

DR. SHAPIRO: Unanimous asterisk. Excuse me but now a few people want to say things right away. Diane?

DR. SCOTT-JONES: So would we omit that second sentence about Congress rescinding the ban on federal funding?

DR. SHAPIRO: I think that has to go in but I do not think it is the recommendation.

PROF. CAPRON: Could I offer just a quick way of doing the whole thing? An exception should be made to the present statutory ban on federal funding of embryo research to allow federal agencies to fund research involving the derivation and use of ES cells from embryos remaining after infertility treatments under appropriate regulations that include public oversight and review.

One thought, one sentence.

DR. SHAPIRO: It sounds fine. We have quite a few people who want to speak.

Steve?

DR. HOLTZMAN: I think we should acknowledge that this recommendation is going to raise a lot of issues. All right. And that it would not be unlikely, given past history, for part of it to be accepted and part of it to be rejected.

I cannot help but wonder whether we should not, therefore, split it into two separate recommendations, either part -- there is a reason why I say that so that people can be clear on when they say I do not like this part, I am throwing out, they do not throw the baby out with the bath water. Okay.

And the second point is that -- the second point is that in terms of this language about the change under existing statute, it is far from clear to me that the change -- that there is any change necessary for the use as opposed to the derivation and so, therefore, I think you have to be very -- first we need to decide that issue, whether -- with what we believe and if we believe that change is only necessary for derivation, not use, it should only be used to modify that part having to do with derivation.

DR. SHAPIRO: I think -- okay. I understand. I guess, I understand the points here. And we could do it in either one or two for various reasons. I really want to -- and if anybody has alternative suggestions, breaking this up into one or two, write them out and put them down because I want to -- I do want to get on and look at some of the other recommendations which we really have to face up to.

And so we -- we can devote any amount of time tomorrow morning to this despite the fact that we have other issues on the agenda. This really preempts everything. So things that you want to feel separated to respond to the spirit of this, what you think is an improvement, and that could easily be the case, let's write them down and let's look at them and see if we agree.

Carol, and then Arturo.

DR. GREIDER: My comment was just going to be on the specific language that Alex just recommended but if you want me to wait and write them down I can write it down.

DR. SHAPIRO: That is what I would like to do so we can get on to some of the other if you do not mind.

DR. GREIDER: Okay.

DR. SHAPIRO: Arturo, then Rhetaugh, and then

we are going on.

DR. BRITO: I had a comment on it but I will pass on it right now because I think recommendation three will help us with the --

DR. SHAPIRO: Okay.

DR. DUMAS: Mine is a little bit of urging for the people who are going to rewrite this, that we should not make a recommendation to the Congress. I think we are making these recommendations to the President and the President will need to consider what approaches he might need to take in order to correct or rescind or whatever existing legislation. So, please, that that in consideration when you start to rewrite this.

PROF. CAPRON: That is why I left the word "Congress" out.

DR. DUMAS: Yes. Well, we do not want to rescind -- I would suggest that you not talk about rescinding anything.

PROF. CAPRON: No.

DR. SHAPIRO: Okay. Let's go on -- I am sorry. I may have asked -- told someone else I was going to turn on them.

Bernie, did I say I was going to turn to you?

DR. LO: No. I want to get into

recommendation three.

DR. SHAPIRO: All right.

(Simultaneous discussion.)

DR. DUMAS: Recommendation three, moving right along.

DR. SHAPIRO: We will not revisit the spirit of recommendation two although we may revisit the --

DR. MURRAY: It can revisit us in our nightmares.

DR. SHAPIRO: Yes. That is right. It may visit us but we -- let's go on to recommendation three.

It currently reads as follows: I am trying to look in my various comments I have here. Let me try to read it from the material that was distributed to everyone yesterday. There is a slight change. There is not a major change. It currently reads in the draft that was sent around to everyone in the briefing book, "At this time there are no persuasive reasons to provide..." et cetera.

What I will read in fuller is the one change that was made to that or at least one proposed change. Namely it says, "At this time rather than saying there are no persuasive reasons..." it says, "At this time there is not on balance a set of persuasive reasons to provide federal funds for the purpose of making embryos

via IVF solely for the generation of ES cells." The second sentence, "More research should be done on stem cells derived from aborted fetuses and embryos remaining after infertility treatments to determine the extent of the need for this additional source of cells for research." That is what recommendation three currently says. Let's see how people feel about three.

Bernie, and then Rhetaugh?

DR. LO: I am fine with the recommendations, the amendments to recommendation three. I also suggest -- I suggest that we also have a 3(b) or something that says, "At this time there is not on balance..." blah, blah, blah, "...reasons to provide federal funding for research using embryos derived from -- stem cell research using lines derived from embryos created by IVF solely for the generation of ES cells."

So I would like to see us address it explicitly in a recommendation and not in recommendation nine our position on funding for use.

DR. SHAPIRO: Let's make sure I understand it. I think I agree with what you have said but I want to make sure I understand it, that is you want something of the nature of recommendation three to cover not only the derivation but use. That is certainly consistent with what we have talked about.

Alex?

PROF. CAPRON: This is just a suggestion as to how we put it. What if we said, "At this time the reasons to provide federal funds for the purpose of..." blah, blah, blah "...are not on balance persuasive."

DR. LO: That is better.

DR. DUMAS: That is an observation. That is not a recommendation.

PROF. CAPRON: That is equally true of the present statement.

DR. DUMAS: So what is the recommendation? The recommendation is that federal funds not be provided to make the embryos via IVF solely for the generation of ES cells.

PROF. CAPRON: Because the reasons for doing so are not on balance --

DR. DUMAS: And I would add the because.

PROF. CAPRON: I think you are absolutely right.

DR. SHAPIRO: I think that is right.

But let's talk. We know what the -- excuse me, Arturo.

DR. BRITO: The second sentence makes me a little bit uncomfortable but I do not know I walked out for a second so I hope I did not miss this but the second

sentence I do not feel comfortable with. It sounds like we are encouraging the research on stem cells from aborted fetuses and embryos remaining after IVF treatments. I think what we are trying -- I think -- I do not understand why we just do not say we are not -- at this point we are not recommending research on IVF -- embryos by IVF solely for the generation of ES cells, blah, blah, blah. But why do we need that second sentence in there? I do not understand.

PROF. CAPRON: Certainly not as part of the recommendation.

DR. SHAPIRO: I agree with that as a matter of fact.

DR. CASSELL: I agree with that, too.

DR. SHAPIRO: I do not think we need it and I think the way Rhetaugh has suggested rewriting the first sentence is a very good idea and I think Bernie's suggestion that we have to incorporate both derivation and use are essential. I mean, I think both those are. So as we think about three, let's think about it now if we can in our heads as incorporating both Bernie's suggestion and Rhetaugh's suggestion and dropping the second sentence, which is gratuitous at this point.

Steve?

DR. HOLTZMAN: I made the observation of what

I wrote that you have the same issues at stake in four as well though there is two different pieces and you could handle it with subparts.

DR. SHAPIRO: So pending those -- excuse me. Are there other comments that people --

DR. MURRAY: Do you want to direct people to your e-mail text because you have the text right there?

DR. HOLTZMAN: Well, I mean, I gave two different alternatives of how to do it and handle -- how to handle recommendations three and four in harmony.

DR. SHAPIRO: I think what we need to do is actually produce a new three, okay, which incorporates both some of the observations Steve made but the principles we are after here, the ones enunciated by -- also enunciated by Bernie and Rhetaugh, and dropping of the gratuitous.

Okay. Thank you very much. Let's go on to recommendation four, which we should also discuss and which Steve, those of you who have gotten to his e-mail, also focuses on and it may be that Carol will have a -- others will have comments here.

Let me just repeat recommendation four as it currently stands. "At this time the use of SCNT into an oocyte to create ES stem cells should not be eligible for federal funding." Again a comment: "More research

should be done on how to differentiate cells into specific tissue types..." et cetera, et cetera. That is really more by way of a comment and probably should be out of the recommendations just as we have talked before but let's talk about comments really on the first sentence of what is currently four.

Eric, and then David.

DR. CASSELL: Just following on our discussion before that the real recommendation is the use of SCNT, et cetera, should not be funded, period.

DR. SHAPIRO: Right.

DR. CASSELL: And then the discussion can rewrite it.

DR. SHAPIRO: You want to write it in the active voice here.

DR. CASSELL: He makes another hopeless plea to get rid of abbreviations.

DR. SHAPIRO: By definition this is hopeless or just by prediction?

David?

DR. COX: So this is a logical argument so by definition it will not carry the day.

(Simultaneous discussion.)

DR. COX: I am going to make it nevertheless but I wanted to put that preface in. The -- you cannot

do somatic cell nuclear transfer without creating a new embryo so if we have already said creating new embryos for research is not acceptable then this is redundant and it unfairly, okay, singles our somatic cell nuclear transfer as something, okay, that basically has an onus on it. So I would just like to make that logical point.

DR. SHAPIRO: I will let -- if Carol does not object, I will ask her for a comment on that since I thought this was specifically an issue that, Carol, you brought up last time and the two scientists here will have to settle this in some way. Carol?

DR. GREIDER: Well, I would not argue with you over whether an SCNT embryo is an embryo just like I would not argue with you when life begins. I think that those are arguments that one does not win or lose but I think that for the purpose of thinking about the utility of an IVF created embryo versus an SCNT embryo, they have very different downstream consequences and if we lump them into one it is much more difficult to articulate what those downstream consequences is.

So what I was trying to argue the last time is that an IVF created embryo by fertilizing a sperm and an egg creates more embryos of the type of which we have spare embryos. Whereas, SCNT creates a different kind of embryo or organism, which has different utility, i.e. the

possibilities of autologous transplant down the road.

So that is why I thought there was some utility in distinguishing those categories even if we are going to treat them the same because some future look back at this whole situation, the science may have changed in those areas.

DR. SHAPIRO: May I ask a question on this in the spirit that Tom put up before, namely not having as full an understanding of the biology here as many people sitting at this table.

When you brought this up the last time, Carol, I had the -- the thought that came that came across my mind, which may easily have been mistaken, was that we are not sure yet about the properties of the embryo or the characteristics of the embryo that are created by SCNT. That remains to be decided. We do not know, for example, whether the embryo created this way, in fact, can be implanted or otherwise brought to term but that is something we may know in the future but we do not know now and, therefore -- and that was the reason to separate this out if I understood it correctly.

If all my "if's" true, and that is what I will let someone else tell me, it seems to me there is a reason to separate it out because it could be that if SCNT creates something which is embryo-like but really

cannot be used to implant and bring to term different ethical issues might arise than would be the case for IVF.

But now I have got so many if's in there that I am not sure that I understand this whole thing but, Carol, did I get this halfway right?

DR. GREIDER: I agree with that and I think that I argued the last time that it should follow the discussion of the IVF created embryo from the standpoint that there is a certain amount of scientific evidence that suggests it may be a subset thereof but if it is a subset of a created embryo then it should come after most of the discussion about the IVF created embryo where a lot of the issues arise and just point out that there is this additional category that may, indeed, be a subset or may be a separate category and what the specific issues of that kind of an embryo are.

DR. SHAPIRO: Trish.

PROF. BACKLAR: That may be why we want to be very, very careful about the language we use so when you describe it you may not want to describe it as an embryo because you do not know, in fact, what it is and so you want to go back and use the word "organism," which may -- and then go on and describe the possibilities of which you are not sure.

DR. GREIDER: I mean, I have argued with people about this and I think that for most people to understand it, I do not have a problem with using the word "embryo" but we do have language in here which says, you know, "Is likely to be able to -- is likely to be an embryo based on animal research." As long as we have that kind of qualifying language in there and we do not just state outright this thing is an embryo because we do not know scientifically but I also do not want to be really misleading in the sense of calling it an organism when it is probably most closely -- when what it most closely resembles is an embryo.

PROF. BACKLAR: But the only reason I bring this up is that I am very concerned about people reading this who are not going to read all these qualifying words so carefully and when they see the word "embryo" they only have one thing in mind.

DR. SHAPIRO: David, how does this little conversation strike you?

DR. COX: Tortured. So if I take Carol's point, and as a scientist I would say, "So what scientific information is available about whether these are embryos or not?" Well, how about in mice if you do this? Is it an embryo in mice? You bet. It makes live mice. Right? How about if you do it in cows? Yes, it

makes live cows. How about if you do it in sheep? Yes, it makes live sheep. All right. But we have not done it in humans so we do not really know. Well, there are three organisms that we have done it with and it makes live organisms.

DR. GREIDER: A very low probability of success.

DR. COX: That is a separate point.

DR. GREIDER: Right.

DR. COX: Right. That is a quantitative issue, not a qualitative issue. What you are arguing, Carol, is a qualitative difference. I have trouble with that because the scientific evidence is in the other direction.

DR. GREIDER: Which is why I agree with keeping the word "embryo" in there but I still want to keep them as two separate recommendations because you can say different things about them although what we are saying in terms of recommendation for federal funding is the same but I like having two categories to be able to call people's attention because as Trish points out people do not always think about the details.

DR. COX: So what I would like to argue is the following: And this is my point. Not to do it in the context of making a somatic cell nuclear transfer

embryo be different from one that you make by the process of in vitro fertilization but to state, I think something that is more sort of straight forward, that there are potential benefits in terms of having embryo -- having research derived embryos that are not possible with nonresearch derived embryos and that we are precluding those benefits right now by not allowing research derived embryos.

They are happening in the private sector but we are not recommending those right now and we are precluding that because I think that this dream that is going to happen with somatic cell nuclear transfer embryos could happen by a variety of other technologies, too, that all are going to involve a common theme. A common theme. It will be research embryos created for research purposes and that is the class, okay, that I think is a more candid description of what we are doing.

And if you take this one technology right now it is sort of, I think -- well, I do not want to pass judgment on that. I just wanted to state a preferred way of dividing things up.

DR. SHAPIRO: If I could try to see where we stand here. On both three and four we have to incorporate Bernie's observation that we are talking both about use and creation as happening in both of those. We

both want -- we want to put them in the active voice and so on and take out the comments out of the recommendation and so on.

But if I understand this conversation or perhaps disagreement between David, you, and Carol, it is a question of whether we combine three and four, that is to talk about them as a class, and these are the two members of the class for now that we know about, and then in the text make any kinds of distinction we would like but no in the recommendations vis-a-vis saying let's separate these out and treat these -- they are members -- somehow they are members of a similar class, that is they are both research embryos. The other differences are unknown this time.

Carol?

DR. GREIDER: Another reason why I felt more comfortable keeping them as two separate categories is at least until we see what the rewrite is, recommendation there said at this time there are no persuasive reasons to provide federal funds for the purpose of making la, di, da, di, da. I feel differently about the IVF created embryo at this point than I do about the SCNT embryo. I would disagree with that statement and would not go along with that recommendation if it incorporated both with that language. So there is a very substantive --

DR. SHAPIRO: Let me ask the following question: We already have agreed to rewrite three so that we eliminate "there are no persuasive reasons"" because there are some persuasive reasons.

DR. GREIDER: Right. And that is not in there.

DR. SHAPIRO: Yes, that is not in there, right, and I agree that that has to be changed to say something like on balance -- Alex had some good language here -- that, you know, there are pluses and minuses but we come out against it for now.

That is -- what is the language we have now, Eric?

DR. MESLIN: For new text?

DR. SHAPIRO: For three.

DR. MESLIN: Dividing into two parts, "At this time research involving the derivation of ES cells from embryos created solely for research purposes using IVF techniques should not be eligible for federal funding." And then the same text with the word "use" rather than "derivation." "Research involving the use of ES cells from embryos created solely for research purposes using IVF techniques should not be eligible for federal funding," and then Alex's commentary would go later.

PROF. CAPRON: "At this time federal agencies should not fund research that make embryos through IVF solely to generate human ES cells or that uses such ES cells."

DR. DUMAS: "Derived from those embryos." That is exactly the way I wrote it down.

PROF. CAPRON: If we said, "Derived from such embryos because the reasons for removing the present ban on such funding are not on balance persuasive."

DR. SHAPIRO: Now that is the kind of language we are going to have in three.

PROF. CAPRON: And the same language would be in four except we would say -- in four we would say -- I have got it here somewhere. "At this time federal agencies should not fund research using SCNT with oocytes to generate human ES cells or that uses ES cells derived in this fashion because of the reason for removing..." blah, blah, blah.

DR. GREIDER: But it is the blah, blah, blah that I am contesting.

(Laughter.)

PROF. CAPRON: And not "on balance persuasive?"

DR. GREIDER: That is what I -- I disagree -- I agree with that for IVF embryos. I do not agree with

it for SCNT embryos.

PROF. CAPRON: At this time they are persuasive?

DR. GREIDER: I think that at this time they may be persuasive for the SCNT embryos and so I --

(Simultaneous discussion.)

PROF. BACKLAR: Let's be clear.

DR. SHAPIRO: I agree. Let's not worry about the particular wording right now but there is a very substantive issue here which we should decide on right now and that is whether we feel there is a persuasive reason for federal funding for creating research embryos through the SCNT procedures.

DR. COX: Now we are talking because that is the issue.

DR. SHAPIRO: Okay.

DR. COX: It is not whether they are embryos or not.

DR. SHAPIRO: All right. Let's -- okay. That is an issue so if we were to say that would -- whether it is a good idea or a bad idea, it is different from the way we have proceeded up to now. And so let's just ask that question directly and not worry about the exact language just to get -- see where the -- that is how many commissioners would feel that it is -- we should

provide or should be eligible for federal funding -- again I do not want to cut open the language here -- research embryos created through the SCNT techniques?

MS. KRAMER: Can Carol or somebody lay out for us the strong case or their best case for it? I mean, if we are going to distinguish between the two.

DR. SHAPIRO: Let's just see if any of us are interested in distinguishing.

MS. KRAMER: Oh. Interested in distinguishing. I am sorry. I did not think that was your question.

(Simultaneous discussion.)

PROF. CAPRON: We have already said no to the IVF created embryos.

MS. KRAMER: Right.

DR. SHAPIRO: The question is do we want to say no to SCNT embryos.

DR. DUMAS: This morning we said yes to SCNT embryos.

(Simultaneous discussion.)

PROF. CAPRON: No, we did not.

DR. GREIDER: No, we did not.

PROF. CAPRON: We have never said yes to them.

DR. GREIDER: We have never said.

PROF. CAPRON: We have always had that as categories three and four which we were not thinking were eligible for --

DR. COX: That is what I want to discuss. We are voting now if we would be interested?

DR. SHAPIRO: In what?

DR. COX: In creating SCNT embryos.

MS. KRAMER: SCNT embryos.

PROF. CAPRON: Making them eligible for federal funding.

(Simultaneous discussion.)

DR. GREIDER: Eligible for federal funding.

DR. COX: SCNT embryos, yes or no.

DR. SHAPIRO: Just let me state my --

DR. DUMAS: There is some inconsistent --

DR. SHAPIRO: Just a minute. I think we have steadily forever in this committee up till now said research embryos, no, at this time.

DR. GREIDER: That is what I thought.

DR. SHAPIRO: From any source.

PROF. CAPRON: Right.

DR. SHAPIRO: Now I want to know if there is anybody on the commission or a subgroup who want to go back and reconsider that position?

PROF. CAPRON: As to?

DR. SHAPIRO: As to the fact that we have said no to research embryos for federal funding.

(Simultaneous discussion.)

PROF. CAPRON: IVF research embryos.

DR. DUMAS: SCNT.

DR. GREIDER: Of any kind.

DR. SHAPIRO: Of any kind.

(Simultaneous discussion.)

DR. SHAPIRO: Creation of embryos for research purposes only.

DR. DUMAS: Okay.

DR. SHAPIRO: Up to this moment or these moments we have always said no to research -- what I will call research embryos from either of these techniques and I want to know how many members of the commission would like to reconsider that position.

PROF. CAPRON: Either. As to either.

DR. SHAPIRO: Either.

DR. DUMAS: To IVF or either?

DR. SHAPIRO: Any combination. Research embryos. I think we know what that means in our heads. Okay. So that is not --

(Simultaneous discussion.)

DR. GREIDER: I would not say that I would feel comfortable saying that there are no persuasive

reasons --

DR. SHAPIRO: We are not going to say no persuasive reasons. That is already --

PROF. CAPRON: On balance.

DR. SHAPIRO: That is right.

PROF. CAPRON: We are not persuaded on balance at this time.

DR. SHAPIRO: That is right. That is what we are saying.

(Simultaneous discussion.)

DR. LO: Do you want to fund -- federal funding for SCNT techniques to use --

PROF. CAPRON: To make ES cells that way.

DR. LO; -- ES cells created through SCNT techniques, should we have federal funding for that, yes or no, and should we fund the use of such ES cell lines.

DR. GREIDER: I think that there are many persuasive reasons even on balance for which the SCNT embryos should be funded and so I would not feel comfortable saying that there are no reasons, which is one of the --

(Simultaneous discussion.)

DR. GREIDER: -- which is one of the reasons why I would --

(Simultaneous discussion.)

DR. GREIDER: -- separate out the categories and distinguish them as different.

DR. SHAPIRO: Please let me try to get some order here.

(Laughter.)

DR. SHAPIRO: I asked a very simple question. I could not think of a simpler question to ask in which there seemed to be unanimous agreement here, namely that we did not think at this time for what -- describe it the way you like -- that it was appropriate to provide federal funds for the creation and/or use, derivation and/or use of research embryos by which we mean embryos --

DR. DUMAS: Purely for research.

DR. SHAPIRO: I beg your pardon.

DR. DUMAS: Go ahead. I am sorry.

DR. SHAPIRO: By which we mean embryos created solely for their use in research. Now we had unanimous agreement on that 30 seconds ago.

DR. DUMAS: Yes.

DR. SHAPIRO: All right. So I want to make -- now as I understand the disagreements that are floating around here, it is the following: That the arguments you might make for one case and the other case -- we are going to disregard both, not disregard, not

approve both, but the arguments you might make, the text that you might use following these will be somewhat different.

DR. COX: Yes, that is right.

DR. SHAPIRO: And, therefore, it pays to put them into separate recommendations here.

DR. DUMAS: Yes.

DR. SHAPIRO: Now are people satisfied with?

DR. DUMAS: Yes.

PROF. CAPRON: Yes.

DR. GREIDER: Yes.

DR. SHAPIRO: We make them separate. We understand what the policy is but the text that goes along with this might be different because you might propose different balancing arguments and so on and so forth.

DR. GREIDER: That is my point.

DR. SHAPIRO: Okay. So let's agree. We will make an executive decision to do that. Okay. And now the only issue is since we are going to take the commentary out of the recommendation, the commentary is going to go after the recommendation, whatever the commentary is, we are down to the issue of what commentary we want to provide for either three in the case of three and four in the case of four.

So now let's see if there are issues that would relate to the commentary that surrounds four that the commissioners would like to bring up so that the commentary can reflect the views of different people.

Arturo, Carol, and Steve, and Diane.

DR. BRITO: One issue that I have not heard that in my mind is one of the main reasons for making these two issues distinguished is that the IVF embryos already exist, they are already basically going to be destroyed. With SCNT the main reason is that you are actually creating something that you are going to end up destroying.

DR. GREIDER: No, both of these are created. They are specifically created. These are embryos that do not exist, the IVF embryos under recommendation three are embryos that do not exist yet, you take a sperm and an egg, and you create that embryo and then you make ES cells.

DR. SHAPIRO: Saying no.

DR. GREIDER: We are saying no to that.

DR. SHAPIRO: And recommendation four --

DR. BRITO: Well, I just --

DR. SHAPIRO: -- repeat that only it says SCNT procedures rather than IVF procedures, and we know what that difference is. Okay.

Steve?

DR. HOLTZMAN: Back in the text somewhere we talk about the reasons why we take the position we do and we say that the primary reason is we are not persuaded that there is not enough spare embryos. Okay. I suggested in my e-mail that there is other reasons which have to do -- let me get this right. Why one would argue for research purposes are there not enough spare embryos? The other reason is becasue there is experiments you could only do with research purpose embryos. Okay.

So if you think about these two recommendations and the distinction between the cases and the text, I think you can make the points clearly with respect to the SCNT's that there is research you could only do with those of a very special type. It is true with respect to IVF research embryos -- well, certain classes of research that require research embryos but there is something very special about these research embryos, you can make the case. And so, therefore, you -- and in both of them what you will share are other kinds of public policy considerations that can, as it were, override or trump the science.

DR. SHAPIRO: Let me go down my list here. Carol, you are next, and then Diane, and then we will go to the side table.

DR. GREIDER: This is just a minor point that I made before and you asked about the text that follows. So the text that currently follows recommendation four still has this language in there about directed tissue transplantation in a directed manner. We discussed this earlier that it does not necessarily follow that designation of a donor would have to be directed if you use this technique and I think we should revisit that issue.

DR. SHAPIRO: Next on my list is Diane.

DR. SCOTT-JONES: In thinking about recommendation four I want to express a view that is different from the view that we have agreed to and that is it seems to me on balance that it would be far better to have federal funding of SCNT for research purposes than to have that in the private sector. I think there would be a far greater likelihood that the oversight would be appropriate.

I think there would be a far greater likelihood that issues of social justice that might arise would be attended to and just trying to think ahead to what might change in the future. I cannot see that there would be great changes in our enduring moral values that we have now or great changes in what we know for sure about research that could arise or benefits that could

arise.

It seems to me that the best way is to let this go in a very deliberate way with federal funding and that is not what we have agreed to but I just want to say in thinking about it, it seems to me that that would be the best way to go at this time with very careful federal oversight.

So my minority view.

DR. SHAPIRO: Thank you. As always with any of our recommendations that we come out, people always can make their own personal statements that relate to those in any way that they think is appropriate.

Bernie?

DR. LO: Yes. I think as we think about considerations that should go into the accompanying text there is one I would like to see discussed under recommendation four and that has to do with the risk of abuse and the nature of abuse that might occur and there clearly are abuses that could occur with deriving stem cells from IVF fertilization. We talk about that elsewhere having to do with consent and coercion and those sorts of things.

I think there has got to be some concern that what we -- that the research to derive embryonic stem cells from SCNT would also be research that makes it more

feasible to create a child through SCNT, which we said in our cloning report that we did not think was ethical acceptable.

So there is, it seems to me, concerns you are having -- that if you had federal funding or for that matter private funding you are developing a technique which could be used for a purpose that we are on record and other people have said would be inappropriate to apply to the purpose of what we have called baby making. That kind of fostering a technology that could be used for purposes that people have very strong reservations about even if that technology is meant in this case to be used for other purposes is a dilemma. I think, you know, we should acknowledge that.

DR. SHAPIRO: Carol, and then Trish.

DR. GREIDER: I just want to address Bernie's comment directly and that is one of the things that I thought that we were very careful to do in the cloning report is to single out baby making from research for the express reasons that one could make autologous transplant tissues, which is what we are doing here. So I do not see -- going along with what Diane just said -- I do not see that we are in any way inconsistent with that cloning report by suggesting that this is somehow a different category.

DR. LO: I think we are being logically consistent. I think it is a matter of pragmatics. You are creating a technology that could be used in a lot of different ways and we do not have any assurance that it will be used solely for the purposes of stem cell research to reap those benefits and that someone else might use the technological developments for the other purposes which we, you know, projected. So it is not that we are inconsistent but it is the use that we cannot control that might be at odds with what would recommend.

DR. GREIDER: We were talking about federal funding here, right, in this case so it is going to go on anyway in the private sector and the question is whether one wants the federal --

DR. LANDER: Just that whole question, right. Absolutely.

DR. SHAPIRO: Trish, and then Rhetaugh.

PROF. BACKLAR: Except that what perhaps one wants to do is again just as we did in the cloning report make it very clear that we absolutely disapprove anywhere and certainly, you know, if we are not going to have control of it then nothing should come out of this that makes a baby.

DR. GREIDER: We have said that in the cloning report.

PROF. BACKLAR: Right. But we may want to say it again here.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: The most convincing argument that occurs to me is the one that has to do with the widespread moral concerns of the American public about destroying human embryos and this particular recommendation speaks only to the creation of embryos for the generation of stem cells. So the only argument that makes sense for me has to do with the widespread public concerns.

DR. SHAPIRO: Yes, Alex?

PROF. CAPRON: I think that the point that Rhetaugh just made is a useful one if we think about the commentary here and David's earlier point about logic because having stated a conclusion in recommendation three that could be seen as all encompassing, any creation of an embryo, having separated it I think we could well begin by saying that the argument against -- the principle argument against SCNT is as with IVF for research purposes that it involves creating an embryo for its destruction, a step which is deeply troubling to many, many people.

DR. DUMAS: Large numbers of people.

PROF. CAPRON: Then we should go on, it

seems to me, to say that as to SCNT there is some difference and then the point that Carol has made, the point that Diane made, can be cited as among those differences. I would say that coming to the -- in balance that we would -- or the on balance, I guess, is that we would say that at this time research in animal models is not so advanced as to make it timely to confront the issue of whether important clinical benefits will be either foregone or limited to nonfederally funded research because those clinical benefits are still hypothetical. In other words, we really need more work.

DR. SHAPIRO: Yes.

PROF. CAPRON: I mean, it is part of what the second sentence of the original recommendation four was trying to get to that we have taken out of the recommendation and put in commentary. But in other words what I am trying to do is not just state that there are arguments but try to encapsulate by saying that basically we are starting off on more or less the same footing as we were in recommendation three so we do not have to repeat all of that, then give the reasons for, and then say why on balance those reasons do not at this time persuade us.

(Applause.)

DR. COX: I am completely supportive of that because it is logical and it also --

(Simultaneous discussion.)

DR. COX: And it states why we think the somatic cell nuclear transfer embryos are different.

PROF. CAPRON: Yes.

DR. COX: It is not that we are separating them out because we are not sure what they are going to turn out to be, we are separating them out because we can think of specific scientific things that they may make better for us.

And you laid this out for us, Harold. It is the text, okay, that is important here. Not the fact that they are different.

DR. SHAPIRO: Yes.

DR. COX: And also you laid out very clearly for me by taking that vote, okay, that we have to figure out, you know, where we stand on this issue. I found that a very interesting little exercise because I think that we have people on the commission that are clearly uncomfortable about the idea of allowing, okay, creation of stem cells at all. Okay. We have -- and they prefer just the utility.

On the other hand, we have people that are not only comfortable about the creation but would like to

even push it a little bit further and maybe let these stem cell embryos take place. But overall as a commission, okay, we are at the position that I think in the middle of it -- okay, the middle of the commission is saying no research embryos but that they are not all created equal but we need to state clearly what that inequality is.

DR. SHAPIRO: Okay, Carol, then Steve, then Diane.

DR. GREIDER: We are in violent agreement. That was my original point, is the reason I wanted to separate this out even if we are going to treat them the same is that they have different downstream uses and different reasons for why you would or would not do it, and that was --

DR. COX: The only thing is say what those uses are.

DR. DUMAS: Bravo.

DR. COX: Say specifically what the uses are.

DR. SHAPIRO: Okay. Steve, Diane, Bette.

DR. HOLTZMAN: I endorse that, the downstream as I would be very careful with Alex's line of argument because there are uses which are not about transplantation that have significant potential medical and biomedical research benefits which cannot be

conducted with animal cells, can only be conducted with the human cells, all right, and if you are going to go down the path of saying it is a matter of solely medical benefit you are going to have to confront at some point why we do not allow research purpose fetuses, all right, even in the face of medical benefit that are contemplating, as per your argument, that the medical benefit could trump such -- such that there could be research purpose embryos.

I do not think this -- we do not have the time to get into that whole issue.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I just want to add to what I think David said that there are some commissioners who would like to see this go forward. I would like to add to that that there are some commissioners who are worried about what might happen as research goes forward but would have greater faith in the public or federal oversight of this than in leaving it to the private sector alone that some of our ethical concerns could be addressed better in the federal context because the work is going to proceed anyway in the private sector.

DR. SHAPIRO: Bette?

MS. KRAMER: Well, that is similar to what I wanted to say in that if we adopt -- if we think about

the arguments that Carol laid out for us earlier that for those of us who are concerned about the lack of a persuasive argument for federal funding for derivation from existing spare embryos, if we take those arguments and apply it to the questions we are now looking at, don't those arguments persuade us to a similar conclusion?

DR. SHAPIRO: Well, let me state where I think we are on all this. I am perfectly well aware that there are strong arguments and they have been all expressed here at various meetings to not distinguish between these various sources. I mean we have -- I, myself, have articulated at our very first meeting what I thought was convincing argument that really the moral distinctions here did not necessarily drive us to the distinction we have made, and I think there are people with a variety of feelings on that. Some because of the oversight.

Let's not forget that oversight could be accomplished by other methods other than federal funding. It is just a question that you need legislation and you have a much -- I mean, it is not logically true that the only way to get oversight is through federal funding. You could get it by passing legislation that required oversight in the private sector or wherever it took

place.

But that we came to the distinction we did -- to repeat a phrase that has been often mentioned in our discussions -- because of an understanding that there were people who had different feelings on this and we wanted to accord that sufficient respect in view of the cost of making this distinction. Not that we would accord that respect at any cost but because we thought the scientific agenda was at a place in the moment where the cost of making this distinction was not overwhelming and, therefore, from the point of view of public policy and society's interest, it paid to accommodate some of the concerns and interests of others. That is how we came to make the division.

It is not that I as that person or any of you perhaps were convinced that this was the law that we would draw for ourselves. It was that we were trying to -- our best to reach out in a sense, or maybe that is the wrong word but at least to reflect and to tell others that we had heard them, and that given the fact that the cost was not overwhelming at the moment to reach what you might consider an intermediate compromise of whatever position you want. And that I thought was where we had got to this distinction.

So I am not particularly anxious to go back

and revisit that now because this will --

DR. DUMAS: No.

DR. SHAPIRO: -- move faster than we can --

(Simultaneous discussion.)

DR. SHAPIRO: -- move. So that I think we ought to stick with this. I think the recommendations made under three and four are extremely useful both with respect to the commentary which needs to be changed substantially and, of course, we have talked about the changes in the recommendations themselves. So it was a very, very useful discussion.

Bette?

MS. KRAMER: I think this is a good time for me to express a concern that I have had with the entire draft and that is that this has been an enormous struggle for us as a commission and for all of us as individuals and to find a way in which we can both allow science to go forward and we can respect the deeply held views of people that have serious issues around these, and I do not think -- I do not think the degree to which we have struggled with this, the amount of concern that we have had and the respect that we have tried to show really comes through in the draft, and I think that -- I think it not only would make it a better report but I think that, you know, we are selling ourselves short in now

capturing this in the language.

DR. SHAPIRO: Thank you. That is, I think, an appropriate and useful comment. We had made very little -- also that comment was made also persuasively last time and especially in this chapter there is no account of that at all because we just did not get a chance to redraft large parts of it. We did make an attempt in some of the other chapters to reflect that but probably not as effectively. We ought to go back and see if we can do it better because I understand and accept your point.

PROF. CAPRON: One of the reasons I was recommending moving that stuff in four here is because it has a little bit of --

DR. SHAPIRO: The stuff that was at the beginning of chapter four in the second chapter, the second paragraph in chapter four.

PROF. CAPRON: Yes.

DR. SHAPIRO: All right. Let's move on now to deal with recommendation five, and then I think after we deal with recommendation five or at least after we begin dealing with recommendation five we will take a break, which is probably what we need more than anything else right now.

There is a new recommendation five, which is

somewhere in all these papers I have got and trying to shuffle around here, that was -- I had spoken to Diane earlier today as we were looking over these various recommendations. And when I looked at recommendation five what somewhat bothered me about it, and this may not be of concern that is shared by other members of the commission, is that it was expressed as trying to make the consent issue for ES cells more or less identical to what it was for federally funded research for fetal tissue transplantation; that is just take the consent process from one and apply it to the other. That is how I understood this recommendation to be; that we might be better served by looking at having the recommendation focus on whatever we want to say about consent for the use, derivation and use of ES cells. The other already has a set of consent requirements built in.

And Diane and I discussed that a little bit this morning and then Diane doing all the real work her has a revised -- do people have the revised new recommendation five before them? I know we all had a lot of papers thrown at us so it is easy to -- I, myself, have not been able to find my five so I have borrowed Eric's.

Do you have one, Jim? Okay.

Do you want to speak to this?

DR. SCOTT-JONES: Yes. As Harold said, he asked me if I would take a stab at rewriting this and I got much of the language from an appendix in the back and Carol also looked over the draft that I put together and basically what I did was just lay out the elements of informed consent and also included the point that Alex had reminded us of earlier and that is that the asking of a prospective donor should occur after the decision has already been made to discard remaining embryos. Once that decision has been made there are elements of informed consent and I will just say what they are briefly.

The researchers should disclose that the research is not -- will not benefit the donor directly. It should be made clear that refusing or consenting will not affect the care that the prospective donor would receive, that there is a general description of the research area and of the specific project if that is already known at the time, also the source of funding and the expected benefits of the research, commercial benefits, should be disclosed. It should be clarified that the embryos would not be used for baby making. It should be clarified that the research will result in the destruction of embryos.

DR. SHAPIRO: Thank you very much.

Let me just ask two questions as people respond to this. One, whether it was a correct decision or proposition that Diane and I made together, namely to really have this focus on consent surrounding ES embryos themselves.

DR. SCOTT-JONES: Yes.

DR. SHAPIRO: That is number one. Okay. All right. Okay. Then let's put that aside and now let's just see what comments there are on this particular recommendation.

Jim?

DR. CHILDRESS: Perhaps what I am going to raise is actually a question about whether we should simply ignore the consent issue surrounding the other in the context of the recommendation and this goes back to our earlier discussion.

Go back to page four. We list -- in this chapter we list four major areas that we are going to cover. The source, consent issues, which presumably apply to all the research that we are going to fund, clarification of existing laws and statutes, and then the need for oversight and review.

I guess I would feel a lot better if we made -- however much we say about the fetal tissue part, if we actually said something about that here. The consent

issues, which are very important for us, that relate to both so I think it is great we have Diane's addition of the materials that relate to donors of embryos for research but I would like to see us bring back some of the other.

But if I could go ahead and a make a few other comments about the discussion here, which I think moves us forward a great deal, that is what Diane has provided. I guess I am overall more persuaded that a donation model is the one that works better here than an informed consent model drawn from research for several reasons.

In the donation model which we operate with all the time when we are donating cadaveric tissue, fetal or otherwise, we do not put as much emphasis on all the elements of disclosure that are present here and some of those that evolve from the medical or research model like quality of care do not seem to me to make a lot of sense in this setting where we are talking about people who have made -- undergone treatment for infertility and now have some remaining embryos. I am not quite sure what it would mean to talk about the quality of the care not being affected.

So I guess I would prefer to see us think more in terms of consent rather than informed consent if

we are thinking of informed consent as drawn from the research model or the therapy model. And in consent which we have all the time a variety of ways for donation of body parts, we need to ask there how many -- what sorts of information should be disclosed but the reason we have to be very careful about that here is that part of what we are recommending, part of what is present in the fetal tissue transplantation research area, and in this area is actually a reduction of information for consent.

Not increasing it because you do not want to provide the information until the person has already made the decision to abort. You do not want to provide the information here until the person has already made the decision to discard. That is not the way we operate in the true informed consent model in the research and therapy area.

So I would just be very cautious about importing too much from the therapeutic research model when what we really have here is a decision to donate extracorporeal tissue -- tissue outside the person's body. Okay. -- for research purposes or in this case to donate the material, the embryo, for another couple.

And what I am preciping is it seems to me that if we are taking an informed consent model actually

we would want -- you ask mainly when you are thinking about what kind of information needs to be disclosed for purposes of consent and how we are going to work all this out, I think especially in terms of invasion of the body or risk, and I think the risks are a lot greater to a couple deciding to donate an embryo to another couple for implantation than for research here. So, I guess, I would raise those kinds of reservations about importing too much.

And then one part that relates to the text that I think does come in when we are talking about benefitting the donor, when the text is redone and there is an effort to again make it work especially for the use of the embryo in research, I would be very cautious here about the language that no personal benefit will accrue because as a matter of fact people donate for a variety of reasons and some of those have to do with gaining some meaning in a setting where they are not happy with what is going on, et cetera.

And I think that what we are really concerned with on the benefit side is making sure that people are not paid and that is the fundamental consideration that is at work in the fetal tissue transplantation area and in this area is making sure that people are not motivated by the financial incentives.

Well, that is a mouthful and I apologize for it but I hope it may help a little bit.

DR. SHAPIRO: Alex, then Carol, Bernie.

PROF. CAPRON: Jim, without disagreeing with your commentary about which kinds of decisions need more information, I do not follow to the same conclusion as you do as to the enumerated information here. It seems to me --

DR. CHILDRESS: I think much of it is imported here. I only raise a question about two of them.

PROF. CAPRON: Well, you raise a question about not affecting the quality of care and it seems to me that at a point when a person is ready to discard and it is at that point the fertility center knowing that someone has an interest in getting these extra oocytes, fertilized oocytes, that they are going to ask them if they will consent to research, there is still an issue. That couple may have decided that these embryos for whatever reason they have been told are not grade 1 and if they want to do it they really ought to go through the process again.

They may still be under care of that center and the suggestion, well, you know, I have raised this with you and the implicit suggestion that some people may

take that I ought to say yes is exactly the same issue that arises in a lot of other situations where you have a more powerful person and a less powerful, and you want -- it is true that you are parallelling a rule that has to do with ordinary research here because you are supposed to say that your decision will not affect the quality of care.

I do not see anything objectionable. It seems to me a good precaution. What was the other one?

DR. CHILDRESS: Well, again, it is less than Diane's statement here of benefitting the donor and more in the text I said where we talk about no personal benefit and I just think that is nonsense in the context of --

PROF. CAPRON: But no material or direct benefit.

DR. CHILDRESS: It says no personal benefit --

PROF. CAPRON: I am agreeing with you that we ought to say no material or direct benefit. The notion that you are going to get something in exchange directly. Obviously you may feel --

DR. CHILDRESS: It seems to me a major concern in the donation model rather than the other model is coercion, that is what we are really concerned here

primarily is voluntariness and going in the direction we have gone we tend to pile on the information. Again I have no objection to these things being here but I think it makes a lot of difference in how it is set up and that is the major point I am making. The sort of paradigm that we are using for talking about the transfer of the materials.

PROF. CAPRON: Just to respond again directly, I do not think that this -- I do not think Diane has stated here we are employing the paradigm of research or treatment. We are simply -- informed choice. It says informed voluntary choice. That is what we want people to engage in. It is an informed voluntary choice. The fact that we also want them to do that in therapy, we also want them to do that in more conventional forms of research in which there is an invasion of their body, fine, that is true and some of those may have greater risks. I agree, Jim. But certainly the risks that are outlined here are exactly on point and the very one that I was --

DR. CHILDRESS: I concede that.

PROF. CAPRON: -- moment ago is as to coercion.

DR. CHILDRESS: I concede that with two exceptions.

DR. SHAPIRO: Let me just --

DR. CHILDRESS: I want to challenge the wording in two of those and you have responded to one of those and I might well be convinced by that. The other one you have amplified -- you have agreed with what I was saying.

PROF. CAPRON: Which was not on her list you said.

DR. CHILDRESS: I am sorry.

PROF. CAPRON: Which was not on her list in any case.

DR. CHILDRESS: Which one?

PROF. CAPRON: The material --

DR. SCOTT-JONES: It is in the text.

DR. CHILDRESS: I said text but also it is not intended to benefit the donor directly, which again is working with a kind of medical model here but also benefit as it is explicated in the text again is, I think, much too broad so I made a comment about text as well as about the particular recommendation.

DR. SHAPIRO: Quite a number of you want to speak. I just want to -- since I am trying to keep notes here as to how we want to move ahead, I just want to make sure I have understood this last.

If I understood, Jim, your point, which I

largely accept, that it is a donation model that we are dealing with here, the -- when you go to the actual recommendation that Diane has proposed here, we might not want to use like the informed consent process. We might want to say the consent process or something of that nature. Plus there are two areas you have brought up if I remember.

One is a question of benefit to donor that you pointed out might indeed be of a benefit and, indeed, the donor might feel very good about it feeling that they are doing something useful and helpful and so on, and we should try to get that in, in some appropriate way, whether it is the same material benefit or to say in the negative no financial or something, something that reflects that, I think, could be dealt with very modest changes in the words there.

The second one had to do with quality of care in which -- if I understood the point you made is that care is over now or at least the current round of care is over and the only issue that Alex raised is there might be future care. So we could use the word "future" or something like that or something that gets to the point that Alex makes.

So I think I really accept most of the things you said. I think that this can be used as a framework,

not talking about the text now, talking about this, which is the only thing we have changed so far but I think generally your point is extremely well taken.

Steve, and then Carol.

DR. HOLTZMAN: I endorse Jim's model and way of thinking of it. I think there is an intersection with the notion of the respect and consent.

One of the questions that arises is the whole issue of designated donation where some of our statutes on organ donation allow it and in the fetal case it does not, and I believe that the fetal case expresses something beyond the issue of coercion but has to do with the notion of instrumentalization as really what is at stake because I can imagine people who are not being coerced freely choosing no money involved and yet in the face of that people on the panel said we do not want the fetus instrumentalized, we do not want fetuses that are grown in order to be able to get their islet cells and whatever.

So Jim's point about the donation versus the consent model, you have a little bit of an oddity here. If you look at the fourth point where you are disclosing who is providing the money, that is who is getting the cells presumably, effectively, you have got the moral equivalent of designation of who is going to get it.

Though I think this was probably against the backdrop of assuming there would not be designated donation so I think we need to make a decision on how we think about designating the recipient of embryonic cells, whether that is licit or not.

PROF. CAPRON: If known. Would that satisfy you?

DR. HOLTZMAN: But that does not answer the question. Right, okay, if known, should that be withheld or should that be disclosed. That is the question.

DR. SHAPIRO: I think we come to some -- under six to some specific -- under revised six to some specific --

PROF. CAPRON: It is listed here.

DR. SHAPIRO: Right. Let's see. Carol, you were on the list.

DR. GREIDER: I was persuaded by the gist of the arguments that Jim was making. I thought it was a very powerful argument that we should be using a donation model rather than the research informed consent model here and I just wanted to point out that if we are going to make the language commensurate with that kind of a model that this language also appears in the points to consider at the back of the appendix and all the things in the points to consider are again on a research model

and that one might want to do the same thing to make the language more a donation model for that document as well.

DR. SHAPIRO: Bernie, Rhetaugh?

DR. LO: I found Jim's comments to be very thoughtful and I am not sure I am completely persuaded yet that the donation model is more apt here than the consent model. Let me try and articulate some of my concerns with the donation model.

First, I think this is occurring in an IVF setting where there is a lot of potential for -- if not frank abuse -- very problematic conditions of decision making and where we are unlike in other donations -- I am thinking, Jim, more of organ donation -- where there is a separation of roles and you do not have the IVF physician, in essence, asking for the donation and you have sort of separated out now the organ donation team from sort of the transplant surgeon, I would be concerned about sort of taking of the donation model.

Another concern I have of donation model is that you very rightly point out that consent makes no sense where there is bodily invasion, serious medical risks and so forth. I would argue that consent is also important when the options are quite different qualitatively to the person making the decision so I think there is no invasiveness or physical risk if there

are other things that make one option very different to the person making the decision.

A consent model is appropriate in terms of making sure that the decider (sic) has understood those choices. And again, to go back to my first point, I can well see it happening in an IVF setting that a lot of these sort of points to consider are not explicitly brought to the attention of the woman making the decision.

I guess just to go further, I think although we have set out a very nice sort of time line where first you make the decision not to continue to store or to give these spare embryos away for implantation, only when you have made a decision to discard do you then face the decision to thaw versus donate them for research. I think in practice it is all going to be jumbled up and I think they are not going to have that clean separation and I think to the decision is going to be there is a bunch of options and you can either continue to store them, give them to another couple, let them thaw, or donate them for research.

There is so much in the context here that is going to make it less likely that people will appreciate factors that if they were really known might color their decision. So I think the fact that, you know, the embryo

will destroyed, will not be transferred and result in a baby, that there could be some financial gain for the people. Any one of those if really brought to the attention of a woman or a couple, they might say, "Oh, gee, if that is what is involved with donating for research even though I would like to help in this kind of research, now that you have pointed that out I cannot do that."

So, I guess, I am arguing, Jim, for the continued emphasis on sort of providing more information rather than less.

With regard to your specific comments, the first bullet, the benefit to them, I absolutely agree that people donate for all kinds of altruistic feelings of importance. While we say no clinical benefit, they are likely to have in the IVF setting that somehow this is going to help us get you a baby the next cycle, and I think that is just a really unfortunate misconception that is kind of perpetrated.

And then, secondly, I would agree with Alex's point about the future care and that I think that it is very likely there will be situations where it is just this cycle or this batch of embryos is completed and yet the decision to do another cycle -- I think that is actually where I think the most coercion will take place.

It is sort of persuading the doctor to, yes, give me another chance even though it might make your statistics look worse. It might be very hard to kind of say no to an IVF doctor who also happens to be asking you to donate the "spare embryos" for research purposes.

DR. SHAPIRO: Rhetaugh?

DR. DUMAS: I am getting confused about references to these models of donation and what have you. It seems to me that what we have been saying is that we would only support the use of embryos that have been discarded.

DR. SHAPIRO: The remaining is what we said.

DR. DUMAS: Oh, remaining. So the concern that I have is whether or not we should address our recommendation and focus it around prospective donors and focus it on the methods that are used to procure the embryos. It seems to me that -- it seems to me that we are somewhat extending our boundaries when we talk about the whole process of consent to use the embryos in research.

We have a certification process that we have recommended and one of the aspects of that certification is to ensure that the cells were derived from embryos in a way that conforms to the recommendations that we are making. So if we say that -- these things here, it seems

to me, would be an elaboration of what we expect the -- expect in the process of certifying the cells. I am getting -- I am drifting now because I am getting confused about this.

DR. SHAPIRO: I think maybe I can be helpful, Rhetaugh, I hope I do not confuse -- we do not drift off together --

DR. DUMAS: I thought I was --

(Simultaneous discussion.)

DR. SHAPIRO: I think that what we are trying to construct here is that we believe that it is essential to obtain consent for the use of embryos for research purposes, that is even though they remain after IVF treatment if they are going to be used for research purposes we believe that there ought to be consent. And what we are doing in this recommendation is trying to say what does this consent mean? That is we do not leave it to the IVF clinic to decide that this should be discarded or this should be stored or this should be used for research, that the -- those who provided the gametes here really must give their consent for its use in research.

And I think the discussion here has been, well, as you think about how this consent process should be structured, is the donation model or the informed consent model the right model to use? As I listen to the

discussion what I believe is that one does not have to make that decision. There is a set of issues which need to be brought up and articulated such as the ones Diane has here and has suggested modification, which reflect both of these. It reflects some insights gained from the donation model and some insights gained from the informed consent model. And just the critical thing is to lay them out in these kinds of bullets, whether these or some modified ones.

Does that help?

DR. DUMAS: It helps some. And I think maybe one of the areas where I get confused is that we had a discussion about the advisability of people being able to donate what -- cells or whatever.

DR. GREIDER: Oocytes.

DR. DUMAS: Donate what?

DR. GREIDER: Oocytes.

DR. DUMAS: Oocytes, yes. But they are able to donate embryos. So it seems -- that seems a little bit inconsistent.

DR. _____: Actually they are able to sell oocytes.

DR. SHAPIRO: They could donate them also. We have got a lot of people who want to speak so let's go first of all to Carol and then Diane and then Tom.

DR. GREIDER: I am trying to understand some of the -- what are the differences between Jim's donation model and the informed consent for research model. Bernie made an assertion a minute ago that there is a pretty big difference between the donating of embryos and the donating of organs, and you said something about how the physician doing the -- in the IVF clinic -- is somehow different.

And I do not understand the distinction about why that physician in the IVF clinic is any different than the physician in the emergency room or wherever, or somebody comes in and ends up donating an organ because they have filled out an organ donor card or whatever.

I do not understand why you think that the IVF physician is going to be the one doing the research on the embryos.

DR. LO: Well, that is --

DR. GREIDER: Well, they might be and they might not be. I mean, it could be that the way things currently go, you know, if I, as a researcher, want to do research on a human liver then I would go through some process of obtaining that. It has nothing to do with me being the person taking it. So I am just curious as to why you are assuming that it is going to be the same person.

DR. LO: Well, I think my general point was that in the organ donation model it is acknowledged that there are problems with the assent or consent to donate or to use the organ for transplantation and one of the ways that is dealt -- there are several ways one could deal with it. One is to try to provide more information to the person making the decision and for a lot of reasons that is problematic in a setting where someone is either brain dead or about to be declared brain dead.

Another way of sort of protecting that decision is to be aware of potential conflicts of interest and to separate roles where they may be in conflict. Certainly one potential conflict is if the IVF doctor is both the clinician caring for the patient and perhaps providing future care, is the person requesting consent, and a person who may have a stake in the research for a number of reasons, one of which --

DR. GREIDER: Then we should state that.

DR. LO: Okay.

DR. GREIDER: We should state that as an issue then.

DR. LO: Right. And given that -- I mean, given that we are not talking -- I mean, one could hypothesize that someone other than the IVF clinician asks consent for donation for research. I am just saying

that if we take away -- if we think seriously about the different models and sort of help us think through the issues, we have to sort of be aware that there are other aspects of the donation model that attempt to address some of the ethical dilemmas in ways that are different than the consent model does.

And we should just be very clear about what we are giving up or taking from each of the different models and whether it will serve the purpose of making sure that people's decisions are not ones which they later regret and having to say, "Well, gee, they did not tell me that was what was going to happen. And had I known that I would never have made that decision that I made at that time."

DR. GREIDER: It is not necessarily that the IVF clinician is going to be the one using it. I mean, I can imagine in the organ donation it could be the person's personal physician asking the family for the organs because they want to get it off to an organ bank or something like that. And so I see these as a more parallel situation just logically than a nonparallel situation.

DR. SHAPIRO: Okay. We have quite a few people who want to speak and then we are going to take a break. I am going to turn to Diane, then Tom, Alex, Jim

and Trish, and then we are going to take a break.

Diane?

DR. SCOTT-JONES: I wanted to respond to a couple of the comments. Rhetaugh had a question about the role of the panel and I suppose the point was why would we need this if we have the panel and I wanted to point out that this is more the individual or the couple level and so it does not -- neither one negates the need for the other. You would still need the panel and you would still need to have quite a bit done at the individual or couple level.

Jim's comments about the donation model were really important ones and ones that I had not thought about when I was trying to put this together earlier today. I think that sometimes the ways the prospect of participating in research can be presented to a person or the prospect of in this case not directly participating but giving the embryo for research, there can be very subtle coercion. And I think even the word "donation" itself because donating is a social good, a great social good in our society, I think that in itself can be a subtle coercion and that needs to be balanced by presenting carefully these other issues that might cause some individuals or couples to be reluctant to donate to the research process.

So I think it is important to take into account Jim's points but also to balance with other information that might cause a person to be reluctant to participate.

DR. DUMAS: May I ask her one question?

DR. SHAPIRO: Ask one question. I think Jim agrees with this.

DR. DUMAS: One. Diane, do you see need to make a distinction between donating the embryo and consenting to have a discarded embryo used in research?

DR. SCOTT-JONES: Okay. The way that this is set up is that the person or couple would have already made the decision that they would discard the embryos and it is at that point that they would be asked to donate so that there is not a pressure before they have thought through these other options to contribute to research. So the way this is set up, the time line that is envisioned, there --

DR. DUMAS: That is part of my confusion.

DR. SHAPIRO: I do not know if it will help. If you read the congressional debate that surrounded this issue as it affected fetal -- aborted fetuses, there was obviously in some people's minds an enormous difference between discarding and using for research. That does not mean to say that I or anyone here would

agree with that but they made this -- this in the congressional debate got to be an enormous issue.

And so I do think that we have to sustain this distinction. We may want to treat it in the same way and just allow individuals to decide where they stand on this. People feel emotionally, I think, quite differently about the prospects for the embryo or in the previous congressional debate fetal tissue as to what it is -- how it is being used and it seems to me they do have some interests that are at stake here and we ought to allow them to decide.

So I think that is --

PROF. BACKLAR: It is no different than the John Moore case in that sense.

DR. SHAPIRO: Tom?

DR. MURRAY: Rhetaugh had mentioned or asked if there was a difference between donating an embryo and donating oocytes, and the answer is there is a big difference at least given the way that is currently structured. Not in the -- not necessarily inhering in the entity, whether it be the oocyte or the embryo, but in what is being asked of the donor. I mean, we have got some frozen embryos banked somewhere for two years. That is -- the question is do I have permission to take them out of the bank, thaw them and use them.

If the question is oocytes then you are talking about a regimen of hormonal hyperstimulation and various procedures, ultimately aspiration of the oocyte, which is actually quite burdensome on women and may even have some long-term risks. So a great deal more is being asked in that case.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I think there is a lot of overlap obviously in the models and even in the very language that we often use "consent" and "donation." Consent is necessary when you do not have donation. The only question that I was trying to emphasize was, you know, how much do we want to focus on the disclosure of information versus other possible ways to protect the voluntariness of choice and whether we might be overdoing it in certain directions and so forth.

The question I would have that I think we need to talk about is to whom this is directed. It is presumably directed towards those in the IVF clinics but how are we going to go about in our own way of -- if it is going to be another part of the certification process and not simply the source now but the way in which the donors of the source material were approached. Is this what we are going -- is this going to be our way into it?

DR. HOLTZMAN: It is what --

DR. CHILDRESS: I am sorry.

DR. HOLTZMAN: It is what is going to define the cell line as having been certifiable.

DR. CHILDRESS: That is right. Is that the direction we are going? It is a question of clarification if that is part of our overall view of what certification means. Not simply the source but also how.

And then lastly I would just mention that it would be possible here, I think, also to refer to the points to consider in which you have further amplification of the kind of information that might be needed and Diane drew, in part, she said, on that right but also others -- some of the other issues relating to consent. So we probably want to at least cross reference that in what we are putting in the text.

DR. SHAPIRO: Thank you.

Trish, did you have anything further you wanted --

PROF. BACKLAR: What I have to say does not make any difference.

PROF. CAPRON: You had me on the list.

DR. SHAPIRO: I am sorry, Alex. Steve is on it also.

PROF. CAPRON: I wanted to suggest, Jim, that before -- at first I had hoped to convince you without

confronting your models but since your models have been so frequently invoked I want to challenge them.

I do not think there is the so-called donation model separate from the informed consent model. The basic notion of donation is a gift originated by the donor. The donors usually prescribe the uses and the purposes, and they are taken if they make such a step to know what choices they can make and there is no consent process because they are not otherwise being constrained.

In situations in which people seek gifts it is usually required that the person seeking the gift use the gift for the purposes which were explained in the first place and there is huge amounts of litigation on gifts and trusts where people have tried to do otherwise.

When we get to organ donation, I got out my organ donor card that is 20 some odd years old and looked at it, and I realized that in the context here I was given a lot of choices so I checked off certain boxes. At the point at which my organs would be taken even more information would be given to my family about what was in prospect and what would be done, and I think one of the things people have learned is it is necessary to give that information to get permission because people worry. Will the body be disfigured? Can we still have an open coffin funeral and so forth?

There are all these -- in the context here, it seems to me, absolutely appropriate to realize that we are concerned both about the absence of coercion, that it be voluntary, that there be no undue inducements or threats, and that the person have a choice, and I think even beyond the donation of organs the notion that an embryo, which is a full -- it is in the minds of some people a full entity not yet deceased that will be used for certain purposes and in certain fashions. It will be unconscionable to imagine our endorsing a process that did not provide that information.

So I know of no donative model that says that information of that sort and restrictions on purposes are not part of and parcel of the gift. I would find as problematic here only the absence again of an active verb and so forth.

And I would suggest that the second sentence be modified in something along the following way: "Prior to raising the potential research use of the embryos the prospective donor should have been presented with the relevant options, i.e. storing the remaining embryos, donating them to another couple or discarding them. If the prospective donor then goes on and chooses to discard, the option of donating to research may be presented during which the person seeking the donation

should:" and we get rid of that language that seems to exercise you so much, the informed consent process, and just be direct that the person seeking consent should do the following things.

DR. DUMAS: That is what it is.

PROF. CAPRON: Is that more satisfactory to you? I mean, we do not have to battle out whether there are two models. I just do not know where you got the notion that there is a donation model. Obviously in 1969 or '68 when the Uniform Anatomical Gift Act was created we were not quite as sensitive to the full range of information because the purposes were being described.

DR. CHILDRESS: I got the donation model from looking at social practices and there are elements that one can draw from each of these. I have suggested a way in which they overlap but there is clearly a difference in emphasis in what one does in the different models. It is not that they do not overlap. There is clearly a difference in emphasis.

PROF. CAPRON: Can we agree on a practical --

DR. CHILDRESS: I agreed at the very beginning.

DR. SHAPIRO: Yes.

(Laughter.)

DR. SHAPIRO: I agree with that.

Steve?

DR. HOLTZMAN: So whether it is a consent or a donation model we are agreeing to, given what we are agreeing to I want us to focus for a moment on two elements we seem or potentially are agreeing to. The one is the separation of the mandated separation between the decision to abandon the embryo and the decision to use them in research and the second is the designated -- whether or not designated donation is allowed.

With respect to the first, all right, by definition that separation cannot exist in the case of research purpose embryos so that if we are going to say that we are mandating that separation, that firewall, now here are we contemplating that that firewall will not be necessary in the future, by definition we are if we are contemplating the possibility of research embryos. And, if so, we have to say why that condition is one we see as waivable in the future whereas others are not. I would make that first point.

And the second point, I think, is the same point as with respect -- if we decide no designated donation, while not mandatory and not necessary, that designated donation in the case of SCNT highly likely and, therefore, I would again have to say that we need to make clear whether in mandating this we are saying it is

waivable in the future.

Not all things, I believe, again are waivable that we are going to recommend here and simply saying the medical benefit will outweigh is just not true because we are going to say certain things the medical benefit ain't -- not going to outweigh under any circumstance so I think we need to be clear about the principles under which we are going to say some are waivable and some are not.

DR. SHAPIRO: Just so I understand, Steve --

DR. HOLTZMAN: I have written that. I gave that to you last Thursday.

DR. SHAPIRO: Just a minute. This issue deals with whether we ought to in this report anticipate the conditions that will change if, in fact, research embryos --

DR. HOLTZMAN: Well, my point, Harold, is I think we can sit here today and say here are things with no change.

DR. SHAPIRO: We have not done that but I understand we could do that. Right. There are some things that do not change and that I would be cautious about anything that is forever myself. I mean, so I think everything is changeable.

DR. HOLTZMAN: Permissible coercion.

DR. SHAPIRO: Who knows? I do not have an example to give. But it seems to me the issue that you are raising is whether or not in this report we should point out, whether in the text or somewhere else, that if you have, so to speak, recruited embryos, whether you recruit them through SCNT or recruited through IVF, that you cannot separate these decisions. I think that is pretty obvious.

And in the SCNT case it is probably, as you point out, it is donation by definition in some sense donating to yourself or to a twin or something else like that. But the issue in my mind is whether or not we really have to flag those issues in this report although I accept the point that you are making.

How do people feel about that?

Bernie?

DR. LO: I think we have used this wonderful phrase over and over of "at this time." And I think that Steve is absolutely right from a logical point of view that given the possibility that we may be changing some of the categories of permissive -- permissible uses, we ought to be aware of contradictions.

But, I guess, I would adhere to sort of the concern of the position that you settle the case at hand and do not go looking for issues in the future that you

cannot predict but you know very well that you could end up falling in some traps down the road. I think that right now we have enough to do trying to settle what we are recommending now to try and predict into the future. It will be awfully tough to do on our time frame.

DR. SHAPIRO: Let me just say trying to just make sure that we make this decision appropriately this is not perhaps so far in the future if you are talking about the private sector here, right, that is the point. And the question is we are going to get back to recommendations but hoping the private sector deals with the spirit of this report and so on and so forth, whatever -- we will take a look at what that new recommendation says.

And so really if we were to say these things they might speak immediately to projects going on in the private sector while they are just speculative you might say for what goes on in the federally funded sector if our recommendations are followed.

PROF. CAPRON: Recommendation five is only about the remaining embryos. Steve's comment about SCNT --

DR. SHAPIRO: That is right.

DR. HOLTZMAN: Alex, my point is that we are making these as important principles in the case of

leftover embryos, correct.

DR. SHAPIRO: This is not only SCNT here. This is --

DR. HOLTZMAN: These are left over after fertility. That is absolutely correct. You are about to erect an ethical framework for their --

PROF. CAPRON: The opening line is "embryos remaining after fertility treatment."

DR. HOLTZMAN: Yes. You are about to put up an ethical framework --

PROF. CAPRON: This is only SCNT.

DR. HOLTZMAN: -- for their use. All right. And I am asking if there is going to be things for other kinds of embryos. You probably are going to say which of these principles apply? And you are probably going to say why do they apply or why do they not apply and why am I going to waive some and not waive some.

PROF. CAPRON: The review panel is going to say that because we have --

DR. HOLTZMAN: Okay. So we do not --

PROF. CAPRON: -- we say --

DR. HOLTZMAN: -- to the review panel. Then I think we should put in a statement that we will observe that these questions will arise and that we give no guidance to the review panel, all right, on these issues.

That is fine.

DR. SHAPIRO: Bette?

MS. KRAMER: I think what this question really comes back to is the fact that we have got to deal with a situation that we have got today in that we want to construct a set of recommendations that is going to allow this research to go forward and we have got to do it within the existing moral controversy that exists and let those questions be taken care of down the road when the scientific developments reopen the -- when as a result of scientific developments the question is reopened and possibly different guidelines will be written.

PROF. CAPRON: Precisely.

DR. SHAPIRO: David?

DR. COX: So you made a good suggestion, Harold, once we get to this other recommendation, you know, recommendation X, about the private sector that there are things that are going to be going on today there that are not going to be covered by what we are doing.

I understand Steve's concerns precisely because he is going to have to live with this not down the road but today. But the -- maybe in the text we can put it there but to consider all these possibilities, I

think, is too confusing in the body of it and I support your view that -- and what Bette just said.

DR. SHAPIRO: Okay. Let's proceed on recommendation five. We might put some material in the text or somewhere that refers to this because I think, as Steve has, pointed out some of this will not affect the federally funded research at all until sometime in the future, some will affect the privately funded research today, that is people who care about what they are doing might want to look to us for some guidance but let's not put it in the main body of this.

Let me suggest that we have been at this now for a couple of hours, let's take a break for 15 minutes while I sort of reorganize with the staff here how we are going to get some of these recommendations rewritten. So let's a 15 minute break approximately.

(Whereupon, a break was taken.)

* * * * *

1

2

3

4

5

E V E N I N G S E S S I O N

DR. SHAPIRO: If we could reassemble. There are a limited number of objectives that I would like to achieve with the remaining moments of this afternoon's meeting.

There is one issue which I would like to have clarified at least in my own mind having to do with, I guess, what is recommendation five that we just spent a good deal of time discussing and will be rearticulated for tomorrow. I have one issue there that I would like to make sure that we understand or at least understand what it is we are saying.

Then the only other recommendations that we have not discussed explicitly are six and seven. I would like to go those and see how we feel about those. And then that should enable us to get a brand new set of recommendations available for us tomorrow morning when we get together. We can -- we will try to get those all done tonight and typed out so we can then go through the whole set of recommendations tomorrow morning. Obviously the text is going to be changed. We cannot do that quite so quickly but we can get through the recommendations at least.

Now turning back to what will be the new recommendation five, which we spent a lot of time talking

about the donation versus consent and the overlap between the two, and I think we will be able to articulate a useful recommendation here with some working -- starting off with Diane's and just trying to modify that in certain ways.

There is one issue that I wanted to raise. We seemed to go over without much comment and seemed to agree, and I think we have done this at previous meetings as well so it is consistent with what we did previously or said previously, have this idea that one had to make the distinction of the decision to discard before being presented with the notion of whether we wanted to -- whether you wanted to donate this, if that is the right word, for research.

And one way of thinking of it -- I certainly understand -- and that has been repeated quite a number of times in our last few meetings without much comment one way or another. I certainly understand the analogy to the fetal tissue case where you want to really just make the firewalls as they are and I have no -- I am not raising that issue right now.

But in the embryo case and one way of thinking it kind of says there is a preference for discarding over donating to research. At least that is one way of thinking about it. I want to make sure that

we are comfortable with that before we start rewriting recommendation five and it might be, at least I want to suggest, or see if there is anyone else who has any views on this, that it might be that we do not want to make that quite so recursive in the way that it is but perhaps I have misunderstood and I am sure that I do not understand all aspects of this.

Eric?

DR. CASSELL: Just on the consent issue itself, you are asking somebody to give consent to the use of their embryos for research and you -- and they do not even get to do that until they say, well, we want to discard it. There is something specious about that consent.

One of the options with your embryos, embryos can be used for implantation, your embryos can be donated to somebody else, your embryos can be allowed for whatever, and they can be used for research. Those are the four options you have and they should know that right from the beginning.

DR. SHAPIRO: Well, let's see what the views are on this matter.

Tom, then Alex, then Steve, and then Jim.

DR. MURRAY: If I understand correctly, this is at a point not when the couple is creating embryos but

at a point when they have decided that their, as we put it, reproductive project is over. It seems to me --

DR. CASSELL: No.

DR. MURRAY: No.

PROF. BACKLAR: That is the question.

DR. MURRAY: The question is when they --

PROF. CAPRON: When they are discussing that issue. They have not decided yet.

DR. MURRAY: When they are discussing -- why are they discussing it?

PROF. CAPRON: They may have spares.

DR. CASSELL: They are coming in --

PROF. BACKLAR: They are coming in for the procedure.

PROF. CAPRON: And then two or three times. They come back and see the doctor and the doctor says, "Well, we have tried two or three times. What can we do now?" And they say, "Well, let's see. We can try again or what else can we do, doctor?" "Well, we could hold the embryos for a while in storage while you make up your mind." Some people decide that they do not want to go forward and they give them to others. Other people decide that they are finished with the process and they discard them. That would be the conversation.

DR. MURRAY: And the --

PROF. CAPRON: They do not come in with a set mind --

(Simultaneous discussion.)

DR. MURRAY: And the other possibility is that you could donate them for research.

PROF. CAPRON: That is the question of --

DR. MURRAY: And can we raise that at a point when the couple is having -- already created the embryos and are now making the decision about what to do --

PROF. CAPRON: Yes.

DR. MURRAY: -- with one of the choices being the abandonment of the reproductive process.

MS. KRAMER: And how about at the possibility of when they are initiating the process?

PROF. BACKLAR: That is when those questions are asked.

DR. MURRAY: Initiating which process?

PROF. BACKLAR: The IVF process.

(Simultaneous discussion.)

DR. CHILDRESS: Make decisions about what will happen to disposition --

PROF. BACKLAR: Right.

(Simultaneous discussion.)

PROF. BACKLAR: They are going through what the procedure is going to be, what the possibilities are,

et cetera.

PROF. CAPRON: Well, I can tell you that as I understand it the NIH Panel is going to recommend that it not be permissible, that IRB's -- what should I say? -- ironically, IRB's which are concerned with research will need to ensure that the process of consent and choice in the creation of the embryos not raise for them the prospect of the use of these embryos in research at the time that they are created.

DR. DUMAS: For the reason of the legislation because they are not supposed to be --

PROF. CAPRON: No, it cannot be that because they are already saying that they are only concerned about use, not about the creation. What I think they are trying to say is that the process has to be one -- well, maybe you could say it is --

DR. DUMAS: This embryo would be discarded in any case and it is not just being destroyed for the purposes of research. There is a thin line but I think that is what is motivating this and that is what makes it kind of mushy to deal with because --

DR. SHAPIRO: It seems to me that dealing with this at the initiation, okay, raises problems as far as I am concerned. It raises a lot of problems because --

(Simultaneous discussion.)

DR. SHAPIRO: Just a minute. Let me finish what I have to say and then there is plenty of time for everyone else.

So I do not think we ought to consider giving the option at the initiation because then we are into -- myself, I think we are into research embryos, and if not that you have up in the air why you are creating so many embryos. There is a lot of issues that come up if you do it at initiation.

I am -- and we have been very careful to talk about so far embryos that remain after the project -- this reproductive project has been completed for whatever set of reasons. Okay.

And so my question really was at that stage, which is all that we have been talking about all along, at that stage what options do you give the couple, the donors of the gametes?

Alex?

PROF. CAPRON: I wanted to disagree with the suggestion that Eric made. Hello, Eric. Hello, David.

DR. SHAPIRO: Colleagues, we are talking to you.

(Laughter.)

DR. SHAPIRO: I am talking to you, the two of

you.

PROF. CAPRON: I want to disagree with your suggestion. I think logically what we contemplate is that it becomes a fourth choice but I think that there are strong reasons for not raising it then. Principally they are two.

One, we want to really draw on the analogy to the fetal transplantation situation, not fetal transplantation, the use of fetal tissue. The analogy is that this is something which is already at the point where it is about to be discarded. In the case of the fetus it is an aborted fetus, here it is an embryo. The difference being one is still alive but it is as close to being dead as it can be because it is about to be discarded.

The second point would be to separate quite clearly the role of the person seeking consent. In the one person, the clinician is having a discussion about clinical uses. One of those choices is to end the clinical process and discard these embryos.

After that has been reached it would seem to me preferable -- and Bernie and I were talking about this at the break -- to have at that point someone from the research team with no implication that this is any longer of interest to the IVF clinic which way you go, someone

from the research team who is interested in the donative use to say, "We have been told that you are planning to discard. There is an alternative. We are doing research of X or Y sort. Would you be willing instead of discarding to donate? If you do, here is what is going to happen: We are going to take the embryo, we are going to take out some cells, and it will die in that process or it will be destroyed in that process." Whatever phrase you want to use.

And that helps to separate the two roles in a way that is a further inundation or elaboration but it emphasizes, I think, the advantage of not getting to research in the same conversation as you get to storage, donation to another couple or discard.

DR. CASSELL: I can see that. I can see that. And that is like the transplant situation where the --

PROF. CAPRON: Yes. The surgeon who does the transplant cannot get the consent for it.

DR. SHAPIRO: Bette?

MS. KRAMER: Okay. But, you know, there are two issues. It is not just what you say but it is also when you say it. So suppose you have got someone who has got a personality like mine. They are going into the IVF clinic and they say, "Okay. Describe to me what

happens." And they say, "Okay. We are going to stimulate the production of eggs and we are hopefully going to capture multiple eggs, we are going to fertilize them, and we will implant some and we will freeze some."

And then I say, "Okay. And then if the procedure works then what happens to the ones that you have frozen?" "Well --" "Will you tell me?" "We will discuss it later. I cannot tell you now." I mean, but I say, "But I want to know what happens to them. What are you going to do with them?"

DR. SHAPIRO: Steve?

DR. HOLTZMAN: I wonder if someone on staff knows the answer to the following question: I seem to recall a few years back Great Britain faced the issue of a whole bunch of left over embryos with no instructions left in the deep freeze and they just summarily destroyed them all but in connection with that so that they would not face this problem in the future they instituted certain regulations about getting various kinds of consent. Does anyone know what they put in?

DR. SHAPIRO: I do not know the answer to that.

DR. HOLTZMAN: It seems a relevant data point. It is not necessarily --

PROF. CAPRON: The Society of Reproductive

Medicine also has recommendations and my suspicion is the recommendations are closer to Eric's viewpoint but we should check those because beyond the British situation there have been a number of situations in which people have died or they have divorced or they have simply walked away and they are saying get consent up front of what will happen with these. The interest that the clinics have had is not ES research but their own fertility research.

DR. HOLTZMAN: Or less pejoratively they have an interest in having some sort of disposition.

PROF. CAPRON: Yes.

DR. HOLTZMAN: And then if we say that the only disposition that we think is reasonable at that point in terms of prespecification, that is donation to another couple or discarding, it does raise the question of why we are eliminating that other option, and I would refer us to the argument we make on page 19, chapter four, from lines 9 to 12, in this regard.

DR. SHAPIRO: A couple of people want to speak and I want to get back to Bette's question also but let's go to Trish.

PROF. BACKLAR: Everybody is addressing exactly the problem that I wanted to address.

DR. SHAPIRO: Bernie?

DR. LO: This is a very important and very difficult discussion. It often helps me to go back and think through what the problem is that we are trying to address and one of the ethical concerns about using the model that you ordinarily use, which is up front at the beginning give people as much information as they want about all the options, it seems to me that the concerns that are raised here have to do with anything that might be interpreted as an inducement to produce more embryos than you really need for reproductive care in order to in a sense create embryos either subconsciously or explicitly.

I think there are also concerns about conflicts of interest, coercion, and they go back to the dual role that at that point of entry into the system your IVF doctor whom you are talking to you are extremely dependent upon and that if there is any suggestion that there is a research program at that institution or of that individual physician or they have a link with an active research program elsewhere could be interpreted to be an unfair inducement.

So I think that the principle is to try and not allow those kinds of forces to come into play as much as possible. You are absolutely right. There seems to me a couple of ways you can do that. One is a temporal

separation, which, as you pointed out, does not make a lot of sense if you think about all these situations.

It seems to me the other option is to separate the people in different roles. I mean, elsewhere in our report we have talked about having someone -- an independent person obtain the consent and rather than the suggestion that a research at that point, of course someone I -- you know, I would be very happy to have someone like the organ donation team, who is sort of independent and does not have a stake in the research but is specially trained to talk about these issues come into play at any time so that I am less concerned with people being informed up front at the onset of their IVF care of the option of donating embryos later if it does not work out but that discussion, it seems to me, might be better handled by someone independent and specially trained to handle all the sort of nuances of the discussion.

I just think that when you start having the IVF doctor having those conversations up front it is a very, very complicated sort of discussion and fraught with ethical problems.

DR. SHAPIRO: Jim, and then Eric.

DR. CHILDRESS: Building on that Alex point earlier about the donation, a possible parallel between what we said -- what is present in the fetal tissue

transplantation area and what we are talking about here in terms of consent or donation, it seems to me that suggests again why we ought to have something spelled out here about that and not simply say repeat those regulations that we already have.

So I would like to see us actually say something in the text if not recommendations in this section about the similarities and differences between what we are thinking about in terms of consent in the two areas. There are some similarities. There are some differences and so forth. And some of those we try to get at a bit in the ethics chapter where we have added some things, as Steve mentioned, on page 19, around that area.

Second, in relation to Bette's concern, much of the discussion in the fetal tissue transplantation area focused on not raising the issue of possibly donating fetal tissue as different from being willing to answer questions that people raise about it. So that is something that opens the door.

And it seems to me then if we are thinking in terms of consent and the provision of information there does seem to be something very restrictive of choice to say, "Well, we are not even going to answer your questions about it." So we have to think through that

part of it.

And, last, I would certainly support the kind of direction Bernie is proposing about something that is developed in the organ transplantation area -- even though we talked about organ donation, keep in mind that most of the donation is actually tissue donation and much of it is for research and other purposes.

So donation covers a lot of practices but the focus now is on routine referral in which a cadaveric donor, a potential cadaveric donor becomes available, there is a referral to a team well-trained in dealing with issues of consent, disclosure of information and the like, and something like that might be appropriate here.

For the -- as Bernie pointed out in conversation, for basically the relatively small number of situations where we would be talking about this particular kind of consent for this particular kind of research.

DR. SHAPIRO: Eric?

DR. CASSELL: You know, we get into a situation of if they do not ask we do not tell and that has already got overtones that are not too pleasant in this country but in the context of breast cancer what was done was the State of New York required every woman with a diagnosed breast cancer to get a pamphlet that told

them all their options and make it separate from -- because it is hard to say, "We are going to get a special person in there to do that." Otherwise this will be the commission that created 20 new jobs in the economy, the ones who get consent, the ones who --

(Laughter.)

DR. CASSELL: But there are ways of sharing information that are independent of the people who do it and publications are one of the ways. But I think it has to be independent of the IVF people who have that self-interest. On the other hand, they should get the information up front.

PROF. BACKLAR: Then the problem, of course, is maybe the intention of making these for research.

DR. SHAPIRO: Bette, and then David?

MS. KRAMER: Just two quick points. Another model is -- that could be useful is in clinics where women go to have an amnio procedure, and that consent process and the information is done and handled by genetic counsellor as opposed to anyone else in the clinic.

But, you know, something else is that if, in fact, this becomes a reality the use of these remainder embryos for research then that is going to -- that knowledge is going to become a part of the generalized

knowledge in the community and it is not going to be -- you know, people are going to know about it going in no matter what.

DR. SHAPIRO: That is right.

David, and then Alex.

DR. COX: So this is probably over simplifying the situation: Let's step back. We are talking -- this is talking about creating stem cells and we are not talking about donating embryos for research. That is a very much broader sort of issue. So what we are doing is we are talking about a subset of embryos that are donated for research. In fact, we are already putting restrictions on them. You know, they cannot have been sort of in vitro fertilization embryos created for research. We have said that. Okay.

And so we are not really saying -- we are not limiting people's informed consent by saying we are only going to look at that subset of embryos that people have already said they are going to discard. We are making that as a conscious decision, not as a scientific or an ethical decision but in some ways as a political decision that those are the subset of embryos that we are going to look at because they have right now the least apparent as well as potential real conflict of interest associated with them.

So then when you have those embryos then what do you do with them? So I must say that I think that is the cleanest and the easiest way of doing this because otherwise you get in -- just as we had done from the beginning. Because otherwise you get into this problem of creating research embryos as we have said and I think that it gets to the bigger issue of talking about embryos for -- embryo donation overall.

So I do not think this is being cute or not being honest. What we are doing is we are saying that for this process of making stem cells, which is all we are talking about, is that it is only these embryos that are being considered, period.

DR. SHAPIRO: We still have to worry about what we are going to say about obtaining consent.

DR. COX: I quite agree but see it is different. These issues in terms of talking about obtaining consent and whether it has to be up front or not up front, if you make the decision first there is going to be this subset where people have already made the decision they are going to discard them then these discussions about whether, you know, you have been honest with them or not are mute, it strikes me.

DR. SHAPIRO: Steve? Excuse me, Alex first and then Steve.

PROF. CAPRON: I liked Bernie's suggestion that we try to keep in mind the purpose for which prior rules have been developed and ask their applicability here and I certainly like Bette's very sensible view that we have got to look at the world the way it is going to be both in the conversation and in the information people bring into the room.

It strikes me that there is no limitation that can be put that will keep someone who is for some reason bound and determined to come in and go through a process of creating embryos to do it because the couple wants to create embryos only for research purposes and give them away to researchers. It would be an odd motivation. Perhaps a scientist and his wife or a scientist and her husband would want to take on that role but we are not going to prevent that through any consent process or anything else so we can put that aside.

If we talk about people who come in who are going to a fertility clinic in the context of trying to achieve pregnancy, the question would be is it enough to take the suggestion that Bette, I think, and Jim said, which is any questions that are raised should be honestly responded to, is that enough. If the only concern is not providing (a) an inducement to create extra embryos or (b) an incentive to discard embryos that you would

otherwise keep then I think that probably is enough because -- and we can -- we can say what we were going to say about still dividing the process and have it make sense for the reasons that we have given before.

After all, the choice to discard, I think, in most people's mind is a less morally burdened complicated choice than the choice to have an abortion because the organism is much more developed in the case of an abortion. So it is at that point that people who are very worried about and opposed to abortion are concerned that the incentive that is provided by doing good for society would lead some women to do this and the chapter four discusses that very elegantly now, I think, and I do not have the sense that people feel that the choice about discarding is quite as equally burdened but there still is enough of a sense that it ought not to be induced in some fashion, that it makes sense to separate them and I think we solve our problem.

I want to endorse Jim's and Bette's suggestion that we acknowledge the reality that people may ask questions and they should honestly answer that besides discarding at that point we could discuss research with you but that is all hypothetical now.

DR. SHAPIRO: I understand. And I think we ought to go on to six and seven now and attempt to get

through somewhat on time. We want to maintain that with the provisos that have been mentioned that, of course, we ought to answer any questions honestly and straight forwardly that anybody brings up that relates to their treatment and what they are doing.

All right. Let's go on now and see if we cannot deal with -- at least begin to deal with six and seven. The recommendation six that came along in your briefing book said, "Recipient specific donation of fetal or embryonic material should be prohibited."

I think -- and then there is a revised suggestion to replace recommendation six, which is currently written in two and, of course, it could be rewritten as a single recommendation but it is currently written as follows: "Recipient specified donation of cadaveric fetal tissue should be prohibited." So that just says what it says so I think that is pretty clear.

The second one says, "Recipient specified donation for research purposes of embryos remaining after infertility treatments should be prohibited."

The second one talks about recipient specified donatio for research purposes, okay, because at least when I went over this I wanted to be leave open the possibility that a couple might want to donate the embryo to someone else to carry to term or those purposes so

that was a simple motivation here. It was not anything more complicated than that but let me just see -- not worrying for the moment whether it is 6.1 -- what is specified here as 6.1 and 6.2 should be combined into a single one. That is not --

PROF. CAPRON: By recipient do we mean someone in the patient role as opposed to someone in the researcher role or the institutional role?

DR. SHAPIRO: In which case?

PROF. CAPRON: In either case. I mean, what I am wondering is do we mean donation which specifies an individual (other than a researcher or research institution). Is that what we mean?

DR. SHAPIRO: What I meant, I want to tell you, I do not know what we want to mean here.

PROF. CAPRON: Right.

DR. SHAPIRO: But what I meant in these cases was that in the case of embryos that you could not -- they would be donated for research. You simply could not specify.

PROF. CAPRON: What research?

DR. CASSELL: When the beneficiary --

(Simultaneous discussion.)

DR. DUMAS: Who is it going to?

PROF. CAPRON: Well, I mean, I think what we

were talking about before in recommendation five where all this contemplates a description of the general research and of the specific research protocol of known disclosure of the source of funding and so forth, and the description of how the process will go on.

It may very well be that at the point that we have gotten to the discard point, the couple is now sitting down with someone who is a -- runs an operation where embryos are taken to be used for research, and they say, "We have several research protocols right now. One is from the Jones Company, blah, blah, blah; one is from Dr. Thompson at the University of Wisconsin, and here is what their objectives are. Are you interested in donating to either of them for either?"

Now that to me does not run the same issues as lay behind the transplant, the fetal tissue transplant thing. Maybe I am wrong about that.

DR. SHAPIRO: No. That is exactly what I want to discuss.

PROF. CAPRON: Okay. So I would opt for limiting the phrase to donation to an individual other than a researcher or research organization is prohibited. Is that -- you look puzzled.

DR. SHAPIRO: No, I do not --

PROF. CAPRON: I said donation of cadaveric -

-

(Simultaneous discussion.)

PROF. CAPRON: It explains that recipient --

DR. COX: Who is the recipient.

PROF. CAPRON: Yes. Instead of saying recipient specified as an adjective here, say donation of cadaveric tissue to an individual (other than a researcher or research institution) should be prohibited so I cannot give it to my mother.

DR. SHAPIRO: I understand. Yes.

PROF. CAPRON: Right.

DR. SHAPIRO: Now what is -- but I thought you were really referring to the embryo one and what --

PROF. CAPRON: The same thing there.

DR. SHAPIRO: Okay.

PROF. CAPRON: Yes, I was referring. I mean, the example I was using was the embryo so I was referring to both.

DR. SHAPIRO: Carol, and then Steve.

DR. GREIDER: We get into these problems a lot when we start talking about who is going to be the one that is asking for the embryos for the research as Bernie had brought up in the last case and as you are bringing up here, who is the person that you are specifying it to or the research organization. What if

we thought of some sort of a model of a banking model where you -- there would be a bank of these donated embryos and you could -- research protocols could be submitted saying we would like research protocols for this -- research embryos for this purpose and then the people that give -- the IVF clinics that get into it just give it to the bank so that there is no -- you know, more like a blood bank. You do not specify -- well, I will not go into that.

PROF. CAPRON: But when we are dealing with human biological materials, which is in some ways less sensitive we set out a whole list of options people ought to be given and I might say, "Well, if you are going to use human embryonic stem cells -- I mean, if you are going to use embryos for this kind of research, fine. But if you are going to use it to develop an aborted fasciant; no." So I will donate --

DR. GREIDER: But those are uses, not who. You could give to a bank in that method or not give to a bank in that method.

PROF. CAPRON: Or to a commercial versus noncommercial.

DR. GREIDER: Okay.

PROF. CAPRON: Versus someone in my own state versus -- I mean, at some point I think those are not

your relevant considerations and they do not have the bite of I am making a baby to give its brain to grandpa. Sorry for it to be so --

(Simultaneous discussion.)

PROF. CAPRON: But that is what excited the Congress.

DR. SHAPIRO: Steve?

DR. HOLTZMAN: To follow on that, so we are really dealing with four cases. It is not whether the use is an individual or an organization. The issue is the use of fetal tissue for transplantation that is of medical use or for research use of embryonic tissue for research but also could be for transplantation a little bit down the road. All right.

The motivation behind the prohibition on the donation in the case of fetal tissue with respect to transplant -- and, note, we have already observed I think earlier in these recommendations that we want it to be clear that that -- those provisions apply to research as well so interalia we have just said research with fetal material should be handled the same way as transplant.

You are now making the argument that research with the embryo should be treated differently than research use of the fetal material. Okay. And now we then should take on next, and be very quickly, of

embryonic transplant, tissue transplant, whether or not we want to handle it like the fetus or not.

I am not making any recommendations other than let's get the four cases in front of us and decide.

DR. SHAPIRO: Eric?

DR. CASSELL: I am not clear why embryo stem cells cannot be directed towards somebody.

DR. GREIDER: Why not?

DR. CASSELL: I mean, we have already satisfied the conditions and it was not created to do that. Why not?

DR. SHAPIRO: In the case of embryos we have decided that because of the way we have got the consent worked out. Is that right? Is that what you were thinking about?

DR. CASSELL: Yes. Now with the stem cells, if I was going to derive stem cells, bone marrow stem cells, my so and so has leukemia, why can't it go to them?

DR. SHAPIRO: Arturo?

DR. BRITO: It is late in the day but I thought that the main reason for this was to make clear the conflict of interest that might exist between the donor and recipient. Therefore, there is not any implicit or obvious motivation to create embryos.

DR. CASSELL: To create an embryo, right. In this instance the -- we get over that because this has to be -- to qualify in the first place it has to be a spare embryo.

DR. HOLTZMAN: But in the fetus case you have to have the separation of the decision to abort and even in the face of that they have said there could be no designated donation.

PROF. CAPRON: Right. And certainly it is an easier thing to create an embryo than it is a fetus. I mean, technically it may be more difficult but it is an easier thing morally, I think, for someone to say, "Well, create it in the petri dish, take the cells out," and as Steve says --

DR. CASSELL: Yes, but do not call Harry.

PROF. CAPRON: -- yes, you simply do not call Harry. The language from the fetal tissue statute is for the purpose of transplantation of such tissue into another person so that the recipient there is clearly a patient recipient. It is not -- you cannot say, "Well, Johns Hopkins can use it."

DR. BRITO: Under 6.2 or 6.2 now the recipient specifies for research for purposes. Well, if you are doing something for research purposes you really -- it should not be an issue if you are donating

something to an individual. That is really referring to therapeutic purposes unless -- unless you do a therapeutic trial. But is that what we are referring to here?

PROF. CAPRON: Research on a cellular transplant in the future is what Steve is talking about.

DR. HOLTZMAN: No. I am talking about four cases.

DR. SHAPIRO: Four cases. That is one of Steve's four cases where it is for clinical purposes.

PROF. CAPRON: It is still research. It is not --

DR. SHAPIRO: He is looking ahead.

DR. HOLTZMAN: In the simplest sense there is research which is not actually involving a patient and stuff which involves a patient, call it research or therapy, I do not care. When they said transplant in the fetal transplant they were talking about not just -- they could have been in a clinical trial, that would have counted as well.

It would not have been a clinical trial as it turns out but basically if it involves a patient you could not specify the patient because what they were saying is they did not want people to decide to have -- get pregnant, have fetuses in order to have

transplantable tissue to another child of their's who needed it. That was the animus. Okay.

Again we have to look at what we have already recommended about extending those thoughts to research uses of EG cells, that is of fetal tissue, because we brought in all of this apparatus for nonpatient involving research. All right.

PROF. CAPRON: Harold's reason for putting "for research purposes" was to distinguish it from fertility purposes.

DR. SHAPIRO: Well, I wanted to distinguish it from donation for a patient as well -- to a patient.

DR. HOLTZMAN: Right.

PROF. CAPRON: To a patient of the embryo for birth --

DR. SHAPIRO: Correct. That is what I had in mind. That is for implantation to -- that is what I had in mind when I said that. That is right.

Well, let's just think about this for the moment as research use. I understand these other cases. I am not denying that but let's just think about this for a moment and see if we can straighten out what we believe. If what you are doing is donating either -- well, let's say embryos in the embryo case, if you are donating for research purposes, that is people are going

to derive whatever, stem cells or other things from them, Alex's suggestion was that we do not allow recipient specific donation to individuals. Is that --

DR. BRITO: That does not make any sense. That is what -- no, I -- I am sorry. I did not mean to raise -- no, I agree with what Alex said initially. What I am saying is it makes -- why -- maybe Carol or Dave or somebody can help me with this here. Can you give a specific scenario where someone would give a specific donation of embryo to an individual for a research purpose?

DR. GREIDER: Well, I mean, I think part of what was in number five, and that is what Alex was referring to, recommendation five is that it said that one of the informed consent criteria is that if known you will talk about the specific research protocol.

DR. BRITO: That is not to an individual, right?

DR. GREIDER: Right. I am understanding Alex then saying if there is a specific research protocol there is an individual that is the head of that research protocol.

DR. BRITO: That should be okay.

DR. GREIDER: That is what I am hearing but that should be --

PROF. CAPRON: That should be -- that is the exciting --

DR. BRITO: I agree.

PROF. CAPRON: -- other than --

DR. BRITO: I agree with that but I --

PROF. CAPRON: But the one to the individual in the way you are using it is a patient in -- when you -- sometime in the not too distant future when someone wants to do a stem cell transplant to an individual, which they are going to come out of the embryo and go into a patient-subject, it will still be research but it will be therapeutically oriented research as opposed to laboratory research, and we would still say nix to that. In other words, you cannot --

DR. BRITO: I am in agreement with that.

PROF. CAPRON: Just the same way as with the fetus even though we think it is unlikely that the embryo would have been created for that purpose although we cannot rule that out that someone would not have done it and as Steve said the same is true with the fetus, the fetal stuff. They said you have got to separate abortion and research or -- excuse me, abortion and transplantation but they are recognized they could not perfectly do it so they said take away the incentive to have an abortion and give it to a friend or relative.

DR. HOLTZMAN: So are we going to endorse that for embryos here as well?

PROF. CAPRON: I would.

DR. HOLTZMAN: I would not.

DR. GREIDER: Well, we still have the two cases. There is the research case and then there is the clinical case, let's call it. There is the nonclinical and the clinical. Is there a patient involved, a patient recipient involved?

PROF. CAPRON: Other than the potential infertile woman getting the whole embryo for --

DR. GREIDER: Yes. Again in that case.

PROF. CAPRON: She is not a patient.

DR. GREIDER: She has already decided that she is not going to donate to another couple. That is already in the --

PROF. CAPRON: Right.

DR. GREIDER: She is not going to donate to another couple so that has already been decided. She is going to donate for research and it is just going to be research. Those cells are never going to go into another person. So you would say there is no recipient in this case?

PROF. CAPRON: Well, yeah, there is no recipient in that case.

DR. GREIDER: There is no recipient.

PROF. CAPRON: So you do not need the restriction.

DR. CASSELL: If it is not federally funded then Uncle Harry can have it.

DR. GREIDER: What?

DR. CASSELL: If it is not federally funded Uncle Harry can have it.

PROF. CAPRON: Yes. We do not reach nonfederally funded stuff.

DR. CASSELL: That is easy. Uncle Harry will have to pay for it.

PROF. CAPRON: So if we said donation outside the context of fertility treatment -- let me just -- as opposed to saying -- is there a problem with saying -- of embryos remaining -- not be made to an individual other than a research institution? I mean, just we are covering that future case in which there would be a clinical research.

DR. SHAPIRO: Steve?

DR. HOLTZMAN: This is not about federal funding by the way. This is a too poor, all in, everyone in the United States we are recommending this is the way this ought to be done in the same way in which the fetal transplant and the organs, it was not about funding, all

right. Just we are saying as a social practice it is -- the following is beyond the pale and is unacceptable. That is what this is saying.

PROF. CAPRON: You are saying morally responsible companies will behave this way. That is what you are saying.

PROF. BACKLAR: So --

DR. HOLTZMAN: I am saying that we are making a recommendation that is not about federal funding but goes to the heart of --

(Simultaneous discussion.)

PROF. BACKLAR: So then you also have the problem if you make this a social practice there may be cases where somebody wants to donate to themselves.

DR. GREIDER: Right.

PROF. BACKLAR: So this is --

DR. SHAPIRO: When I was thinking about this -- to be honest about it, when I was thinking about 6.2 -- I mean, 6.1 in a sense -- I do not know if we have to say anything about it now that I think about it. I do not know whether 6.1 is even required for us to -- that is already pretty heavily covered in existing legislation. I do not know what we gain by making any recommendation in this area. That is my own feeling.

DR. CASSELL: That is the best recommendation

of all.

(Laughter.)

DR. SHAPIRO: Take one away, right. It is always good to have one of those. Now maybe I am wrong about that but that is my sense of what it is. And in the 6.2 I had -- when I wrote this down I really had the federal funding in mind to be honest.

PROF. CAPRON: That should be prohibited though and it should not be funded.

DR. SHAPIRO: That is right. That is what I had in mind. Now you may want to do something else.

PROF. CAPRON: Steve's point is independently later on we are saying what is sauce for the goose ought to be sauce for the voluntary gander and so --

(Simultaneous discussion.)

DR. HOLTZMAN: I read six as going with seven because if we turn to seven again we are not talking about federal funding. We are talking about what social practices we as a commission believe constitute the good of society.

DR. SHAPIRO: Okay. I did not read that but I understand that. I understand that.

DR. MURRAY: Less is more in a lot of cases but I think I would not be favor of taking out the recommendation concerning donation of cadaveric fetal

tissue because the casual reader might think that we have sort of stepped back from the fetal transplantation -- fetal tissue transplantation research position.

Now either we can say in the text that we do not need to make a recommendation because we agree wholeheartedly with current policy. That would be fine but I think we need to make some affirmative statement.

PROF. CAPRON: Don't we say in revised recommendation one that the policies now applicable to fetal tissue for transplantation should become applicable to fetal tissue from ES or EG research and if we do we have already said that and we should emphasize at that point that one of those limitations is on patient specific donation even though it is much less relevant at the moment.

DR. SHAPIRO: We say recommendation one has to do only with EG cells and it asks for the expansion or amendment of the existing regulatory, et cetera, language so that research on EG cells --

PROF. CAPRON: And that is what --

(Simultaneous discussion.)

PROF. CAPRON: That is 6.1

DR. SHAPIRO: That is correct.

PROF. CAPRON: I am saying we have already said 6.1 so it is not that we are ignoring it, we have

already said it, and in the commentary we should emphasize --

DR. MURRAY: And say it clearly. I mean, I understand your point.

PROF. CAPRON: It does not say a lot.

DR. MURRAY: A very careful reader will make the two or three logical steps but I think we should say it.

DR. SHAPIRO: We can at the very least note --

PROF. CAPRON: We can really cross reference back and say we have already addressed -- having already addressed the issue of the fetal tissue we come here to the issue of the embryonic.

DR. SHAPIRO: Now the question we have in front of us, what do we want to say about that? About the question of whether we can -- anyone can designate -- if they have decided to donate, can they designate and, if so, in what way?

PROF. CAPRON: Which is really the question of do we object to the creation of oocytes for -- I mean, the creation of embryos for this purpose because that is the thing that you would be afraid of that someone would come in the door and say I want fertility treatment

DR. DUMAS: We have already said we do. We

are against that.

DR. COX: We have been there.

DR. DUMAS: We have said many times that --

DR. SHAPIRO: That was exactly my --

PROF. CAPRON: That is my reason for saying that we should say it is not eligible for federal funding.

DR. DUMAS: That is right.

PROF. CAPRON: Because we recognize that it is an incentive that can be disguised. If you take away the incentive --

DR. DUMAS: What would you say -- recipients that -- no. Research that utilizes or solicits recipient specified donation of so and so as not eligible for federal funding.

PROF. CAPRON: It is not a matter of soliciting it, it is just saying donatio cannot be -- cannot specify an individual recipient (other than a researcher).

DR. SHAPIRO: That really -- the way I thought about it, I just want to repeat it once again, this is a federal funding issue when it was in my head here. It was not as a case -- and, therefore, it is not parallel to the fetal tissue in that sense.

PROF. CAPRON: Fetal tissue is fine. It is

not a statutory prohibition. It is a limitation of the federal funds.

DR. SHAPIRO: I realize that.

DR. DUMAS: But I would say this is recipient specified donation is prohibited in federally funded research.

DR. SHAPIRO: We will get this -- we can get this worded properly. I do not want to --

PROF. CAPRON: Once we are agreed on it.

DR. SHAPIRO: Yes. That is right. Once we know what we are agreed on we will get it worded properly. We can take care of that. But I want to go back to what we mean in the case of research use that is donating embryos for research.

What we are going to prohibit? They cannot designate an individual. I think we have all agreed to that but the question is what else can they designate. Can they designate for a particular research project? It is a difficult thing to separate here in this case. This is one of the reasons I raise this, that is research projects are typically headed by someone and --

DR. HOLTZMAN: We have also built into the consent that there is a commercial interest, for example, on what is the funding source so you are saying who is doing it. Right?

DR. SHAPIRO: Right.

DR. DUMAS: Right.

PROF. CAPRON: That should be okay.

DR. GREIDER: By definition you are designated to a particular project.

DR. HOLTZMAN: So, therefore, we want to make sure these things are not created for this purpose and we are positing that if someone were to designate someone to receive it in a patient mode that might provide an incentive to --

PROF. CAPRON: To create the embryos.

DR. HOLTZMAN: -- to create the embryo. Whereas for good old Princeton and Dr. So and So it would not create a sufficient incentive.

DR. SHAPIRO: Individual.

DR. GREIDER: It is the patients in terms of recipient, right.

DR. SHAPIRO: Yes. Excuse me for being so dense on this. But we are talking about research embryos that are now being donated for research purposes, right, not for --

PROF. CAPRON: Yes.

DR. SHAPIRO: That is what this says.

PROF. CAPRON: We are past the point -- we are dealing with embryos created for fertility which are

not going to be continued in some fertility use.

DR. SHAPIRO: Right. And donated now for research purposes.

DR. GREIDER: What about the case where they are donated for research into transplantation into a person?

PROF. CAPRON: Yes.

DR. SHAPIRO: Yes. As part of a clinical research project.

PROF. CAPRON: Yes.

DR. GREIDER: Right. I mean, I think that there is a big difference between just research on the tissue in the lab versus putting it into a specific person.

DR. SHAPIRO: What if you did this and said I have a friend in Johns Hopkins and I want this to go to their lab, they are not doing clinical research, they are just doing research on the biology of this part of human development? What would you say?

DR. GREIDER: I do not have a problem with that.

DR. SHAPIRO: Does anybody have a problem with it?

PROF. CAPRON: The probability you would have

created an embryo for that purpose as Steve said.

DR. SHAPIRO: Okay.

(Simultaneous discussion.)

DR. HOLTZMAN: I just want to get back -- it is getting late so it is hard for all of us -- if you think through the abortion case, the fetal case, right --

DR. DUMAS: Speak a little louder.

DR. HOLTZMAN: When you think about the fetal case, they were saying that even -- the woman could say, "I am done. I want an abortion. Wink and nod. All right." And to avoid her having done that and made that independent assertion you said you cannot say where it goes. So in having said -- we are dealing with the case where the woman has already decided to discard, you run a parallel with what was the case in the fetal, even in the face of that they said we need these additional protections.

DR. SHAPIRO: Correct.

PROF. CAPRON: But there are two choice points. One is I have gotten to the point of aborting or discarding and there the fear is some inducement to do something you would not have done. What they were really dealing with is the initiation of the process and the fear that people would become pregnant, which is not something that requires a lot of technical intervention,

just show up pregnant --

(Simultaneous discussion.)

DR. HOLTZMAN: But the way they did it was by the expo facto controls.

PROF. CAPRON: Right. I agree.

DR. HOLTZMAN: So completely logical and apart.

PROF. CAPRON: I totally agree.

DR. SHAPIRO: Trish, and then Jim?

PROF. BACKLAR: So on the -- I just want to bring up something and I am not certain it is going to be appropriate. We certainly are going to let people -- if they are going to donate to research, are we going to let them refuse it to go to certain kinds of research.

PROF. CAPRON: Yes.

PROF. BACKLAR: And so, therefore, if you let them do that, in a sense you are going to by the back door perhaps have them designate where it will go. So I just want to make sure that that is not -- that we do not get confused or we do not confuse others with that.

PROF. CAPRON: Harvard, no; Princeton, no; Columbia, no; Johns Hopkins, yes.

(Laughter.)

DR. SHAPIRO: Jim?

DR. CHILDRESS: Alex, you have emphasized the

notion of preventing the creation of the fetus, that is getting pregnant and then having an abortion, but as our discussion took place in the late '80s there was also a concern with the situation of a woman already pregnant who might then have an incentive to abort having -- so both kinds of cases were present.

PROF. CAPRON: For a recipient?

DR. CHILDRESS: Yes.

DR. MURRAY: Grandpa has Parkinsons, developed Parkinsons. We really could use the --

PROF. CAPRON: You could really use that fetus you would otherwise -- you were looking forward to having a child and you will have a treatment for grandpa instead.

DR. MURRAY: That was the claim.

DR. CHILDRESS: Both were present.

(Simultaneous discussion.)

DR. SHAPIRO: Let Jim finish.

DR. CHILDRESS: Now in this area I am -- even though again we have emphasized that the goal is to avoid creating an embryo for those purposes, it seems to me in the larger society the issue is not simply that but rather how we think about those embryos that are out there and decisions to discard them. So I guess I would not want to limit our -- if we go back to Bernie's point

about what is the problem we are trying to address, I would not want to limit that from the larger societal concern to simply avoiding creation.

It is also avoiding in the case of pregnancy or in the case of embryos that have been stored, avoiding destruction, and we have made certain decisions at least in the second recommendation --

(Simultaneous discussion.)

DR. CHILDRESS: -- worried about that and I think the larger concern is that both of those present.

DR. SHAPIRO: All right. I think I am just trying to understand where we are, where the commission is on this. I understand on the fetal tissue one, and we will handle that either reemphasizing what was brought forward from recommendation one and so on and so forth, and on the question of embryos what we are concerned with is recipient specified, i.e. individual. But -- yes, that is right, patient.

PROF. CAPRON: Patient.

DR. SHAPIRO: Right. And that is what we want to avoid.

DR. HOLTZMAN: Okay. So I will step up and say that is exactly what I do not want us to -- I mean, are we talking federal funding?

DR. SHAPIRO: Yes.

DR. GREIDER: Federal funding at this time.

DR. SHAPIRO: Both.

(Simultaneous discussion.)

DR. SHAPIRO: Everything in the world is at this time.

DR. GREIDER: We have it in the language of the earlier recommendations.

DR. SHAPIRO: Okay. Let's try to -- we will try to draw that up carefully. Let's look at -- before we adjourn, which I hope will be very shortly, let's go to the recommendation seven.

PROF. CAPRON: That is on your suggested revision.

DR. SHAPIRO: That is right. It says, "Sale for research purposes of cadaveric fetal tissue following abortions and embryos remaining after infertility treatment should be prohibited." Which is just a way of expanding what was meant by fetal and embryonic material in the initial suggestion, at least that is what I had. And this again in my mind was not directly related to federal funding in my mind.

Comments, questions, concerns, et cetera?

PROF. CAPRON: This is not covered by one. This is much broader.

DR. SHAPIRO: Right. Steve?

DR. HOLTZMAN: I think we ought to put gametes in here, too.

DR. SHAPIRO: You think we ought to put gametes in here and maybe other things in addition to that which we do not think should be bought and sold in addition to those three things.

PROF. CAPRON: Is that a mischievous suggestion?

DR. HOLTZMAN: No. I mean, this is -- this is not -- this is something where you are recommending about --

DR. SHAPIRO: Correct.

DR. HOLTZMAN: Make it seriously what we are recommending as a society that we want.

DR. SHAPIRO: Right.

PROF. CAPRON: Well, I did not hear what you said.

DR. HOLTZMAN: As a society we want mainly ones in which -- those things which are necessary --

(Simultaneous discussion.)

DR. HOLTZMAN: -- reproduction is not turned into an act of commerce, all right, and I find that a little odd that we are so concerned about the sale of the -- if we are so concerned about the sale of the embryo I think we would be equally concerned about the sale of the

oocyte and the sperm for that matter. And part of the reason for that is issues of coercion, all right, isn't it equally -- what is the coercion we are dealing with? It is when the woman is endangered via the superovulatory regime that gives rise to an oocyte. All right.

DR. CASSELL: That is not equivalent.

DR. SHAPIRO: What?

DR. CASSELL: That is not equivalent.

DR. SHAPIRO: Eric, we cannot hear you.

DR. CASSELL: That is not equivalent. I mean, it is not the same thing at all.

DR. HOLTZMAN: They are different. They are very different. That is true. I am talking about the social practice and what is the goal of such a recommendation of this? Do you think that it all resides in the --

DR. CASSELL: But in this instance the goal of this is to permit research on stem cells derived from human embryos. We are trying to get that moving and that is one of our goals and we found a way we believe is ethically acceptable and we are also trying to do it in a way that does not produce obstruction to it and the goal of this is to have no question that anybody would be selling it or you would be producing embryos for sale. I mean, that is what we are doing. A very practical issue.

Even businessmen are practical sometimes.

DR. SHAPIRO: Any other comments or questions on this before we reach total exhaustion here? Okay. We will declare it --

(Simultaneous discussion.)

DR. GREIDER: So that stands as it is?

DR. SHAPIRO: That stands as it is unless someone has got another proposal to make.

(Simultaneous discussion.)

DR. SHAPIRO: Okay. We are -- to remind you what we will try to do tomorrow.

Yes?

PROF. CAPRON: When we say "sale," do we mean any payment or are we talking about the way it is defined in all the other statutes as payment in excess of the costs of obtaining? The latter or the former?

DR. SHAPIRO: It is the latter that I intended. I am sorry. "Sale" does not get it.

PROF. CAPRON: Payment beyond --

DR. SHAPIRO: That is right. I apologize for that. That is not --

(Simultaneous discussion.)

PROF. CAPRON: Because, you know, there is a severe noncommercialization and there is the nonprofit model.

DR. SHAPIRO: Okay. Let me just say a word about tomorrow and then we will -- Steve wants to say a few words perhaps about this evening after we are adjourned.

Tomorrow we will try to have available to you -- what time do we start tomorrow? We start at 8:00 o'clock tomorrow. We will try to have available a list of all the recommendations as modified by today's discussion and see if we feel that is -- that we are satisfied with those and, if not, we will spend as much time as we have tomorrow to try to get ourselves in a position where we feel we closed in on it and then we will take whatever time is left over to deal with whatever issues. Ruth Macklin will be here tomorrow. If we have time left over we will certainly get to that and I hope we will have time left over.

So our job here will be to get that list available to you so we can have it all in one place tomorrow morning and we will just hope we can get all that done.

That ends today's meeting and we will get all that done but, Steve, do you want to say a word before we all disburse?

(Whereupon, the proceedings were adjourned at 5:32 p.m.)

* * * * *