31ST MEETING
OF THE
NATIONAL BIOETHICS ADVISORY COMMISSION

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OPENING REMARKS

DR. SHAPIRO: All right. Let's call our meeting to order. I think this is working. Can people hear back there?

First of all, welcome. I thank all of the commissioners who are here for being here this morning. There are others that will join us during the morning whose planes are either arriving now or arriving shortly and will be here as soon as they can.

I want to spend the bulk of this morning, if not all of this morning, on our human biological materials report and I am hoping that this will be the last day that we discuss these recommendations as a group, although there may be an opportunity to discuss it electronically in the next few weeks because I think we are at a stage where we have to decide what we are going to recommend.

And we are going to leave some of the editorial and organizational issues to -- which are still outstanding on this report to myself and the staff, and so we can try our best to issue this report some time in
June, hopefully before our next -- before our June meeting, which occurs, fortunately, late in June so that gives us a few weeks in there. So my plan is this will be our last discussion today.

I have gone over all the recommendations in chapter five. I think there are something like 25 recommendations, 16 of which we have already agreed on, which are unchanged from the last meeting and I do not intend to discuss those today at all.

There are 9 other recommendations, some of which were agreed upon in the meeting in Virginia but I want to revisit them to make sure that we agree and are satisfied with them. There are one or two, like 24 and 25, which we have never discussed because we just never get to it in our meetings. We will have to get it to them today.

And there are some, which I think need some rewriting and what I intend to do today is when we decide that we are going to recess and rewrite bring them back and present them to the commission so that we can at least agree, at least pending small editorial changes, which we will not focus on in detail.
Once that is done, and that is subsequent to today's meeting, we will produce a draft of the entire report, charts and chapters one through five, and so on, so commissioners will have a chance to review the report in its entirety and make one final set of suggestions for changes which we can accommodate.

And, of course, as always, if there are any particular recommendations that any particular commissioner or group of commissioners might feel strongly about that is different than where the commission comes out there is, of course, every opportunity to make that a part of the report and that is an open issue for any commissioner on any of the recommendations that we come to.

So I will turn in just a few moments to just start going through the recommendations that are in chapter 5. I'm not going to deal with the text, although if there are some -- as we discuss the recommendations if there are some particular ideas about the text. As we work to reorganize and do the editorial work in putting this report together we could accommodate those suggestions that seem useful and helpful.
But before going to the Human Biologicals Material Report itself, I did want to ask commissioners who were present at our special meeting in Washington last -- I guess it was last week -- Friday to bring commissioners up-to-date on the nature of that meeting and what their overall judgment of opinions and reactions were.

I'll turn to Jim first for some remarks and then to other members of the commission who were there who may wish to add their own perceptions of those proceedings.

Jim?

DR. CHILDRESS: Those of us who were there, Larry, Eric and Arturo, found this to be an exceedingly productive meeting. It involved representatives from the Roman Catholic, Protestant, Eastern Orthodox, Jewish and Islamic faiths. And in the case of Protestant, Catholic and Jewish traditions we had three people speaking so we had a range of views within those traditions.

It was probably 1,000 times better than my expectations actually in terms of what we were able to learn and I won't go through all that was involved there.
A summary is being prepared by one of my graduate students who was present and will use the transcript, which will be available later, to modify this and it will also be circulated to the participants to make sure that they agree with the summaries offered of the positions presented.

I really want to express my appreciation to Pat Norris and Eric Meslin for putting this together on such short notice and getting -- with suggestions from several people -- some of the best people in the country to participate and we are grateful to them for participating on short notice.

What was important, I think, was to see the diversity of views even within particular traditions but also some common themes that emerged across traditions. Some of the things will not be surprising to you but let me just mention two or three and then stop and see what my colleagues might like to add.

First of all, there was a great deal of attention to the issue of social justice throughout. That was a persistent theme as an important background consideration if we are talking about research in this
particular area.

Second, there was a great deal of interest in public review and oversight even of the private sphere. There is some question there and Ed Pellegrino will be offering a further statement for us about whether, say, from a Catholic standpoint that kind of oversight could be justifiable without excessive complicity in the practices that are being regulated.

And then so much hinges on debates about the status of the embryo and about complicity that those vary a lot not only according to a particular tradition but within traditions and when you see the summary and the transcripts because they will be available, too, I think you will get some of the flavor of this very rich discussion.

But let me pause and see what my colleagues might like to add.

DR. SHAPIRO: Larry, anything?

DR. MIIKE: I think Jim countered it pretty well. The complicity issue was quite an important one. The other area which I think I asked a very specific question was that I noted we had been urged by some that
one develops a moral stance and then that stance is
impervious no matter what the situation, that was not the
stance of most of the people there. They thought it
depended on the particular circumstances in which you are
faced with and one had to adjust to the actual situation
that -- so it was quite the opposite of what I thought
that they would come to a conclusion on.

Then, of course, what was good about that
meeting was that even within the three religions that had
three representatives there is quite a diversity of
opinion.

DR. SHAPIRO: Thank you.

Eric?

DR. CASSELL: I think that I wanted to
emphasize also the diversity of opinion within the
religious groups as well as across faith. In attempting
to understand what the status of the fertilized ovum is
and then embryo, it is very important to read what they
said because the black and white view that we came into
this with is really not black and white when this thing
is looked at closely and that is very important.

But I also think it is important to realize
that they brought to this discussion an understanding
that Jim just pointed out that there are other issues
that any resolution of this issue requires attention to
the issue of social justice to the issue of oversight.
There is a larger set of issues that we have to be
concerned with. To come away and just say we -- whatever
it is we come up with -- only about the embryo would be
lacking faithfulness to their views.

DR. SHAPIRO: Thank you.

Arturo?

DR. BRITO: Not to belabor the issue but,
yes, the diversity of opinion is probably the most
striking thing. Especially I was struck with the
diversity within each group. In terms of the social
justice, specifically distributive justice, and that was,
like Jim said, heavily emphasized throughout.

When you all read the summary I think
probably the first part I would go to, and I know that --
I am sorry, I forgot her name, but I know she is going to
put this I think I counted about nine points he made at
the end where he basically summarized areas that we could
all or everyone there would be in agreement were really
necessary to include in there such as oversight and things like that. So I think that was probably one of the most important things towards the end of the meeting was Eric's summary.

DR. SHAPIRO: Which Eric was that?

DR. BRITO: Cassell.

DR. SHAPIRO: Cassell. All right. Thank you.

Bette?

MS. KRAMER: Is that summary available or do we have to wait for the --

DR. CHILDRESS: There is a draft of it that she prepared and got to Eric Meslin and me yesterday. I don't know whether it's something you want to see. We could go ahead and circulate that as long as you understand it is a draft that will be revised with the input from the four who were there and with the input from the participants.

MS. KRAMER: Not just as a matter of curiosity but I think it could be helpful in informing the discussion.

DR. SHAPIRO: I agree with that. I think we
should try to get it distributed as a draft document because we don't have a lot of time and the sooner we get at least a sense of it allowing the fact that it might be -- it is a draft and people may wish to correct what they say and certainly no one should quote from this in any way, especially the participants who may be referred to here should not be quoted until they have a chance to review it. So with that understanding, we could distribute it as a draft working document to the commissioners who were interested.

DR. CHILDRESS: So I think Eric is getting copies made of it right now.

DR. SHAPIRO: Any other comments or questions regarding that particular meeting?

Arturo?

DR. BRITO: This may be obvious to others but one of the things that is hard to get out of the transcripts is the fact that the opinions were very strong and there were very opinionated individuals in that room and that was very clear and there was a lot of flavor in that meeting.

DR. SHAPIRO: Committed people. I am not
surprised.

Alex?

PROFESSOR CAPRON: Actually I found that last comment of Arturo particularly interesting because I had the sense, as you were going around a moment ago, that maybe we were dealing with the academic branches of theological thought, people who by inclination are more analytical and less dogmatic, which is a good and suitable word for discussing religion.

Did you feel you came away with the sense that if our conclusions were permissive as to certain things we would have at least heard from people who are in that group if we recite those 11 names, people who would be recognized as taking very firm views against?

DR. SHAPIRO: Other comments or questions?

Eric?

DR. CASSELL: Well, that is really one of its advantages was that the firmness of the opinion, you know, that -- they were not fighting. There was an instance of a public testimony that was unpleasant but other than that people were not fighting. They had very strong opinions about their religious viewpoint and that
is much better than wishy-washy, aren't we all in this
together. It is much better than that.

DR. SHAPIRO: Thank you.

Further comments or questions?

Alta, do you have a question or not?

PROFESSOR CHARO: No.

DR. SHAPIRO: Okay. Well, then let me

express my gratitude to the staff and also my own

gratitude for putting this together. Eric and Pat

especially. Jim, you and others who attended the

meeting. All of us have busy schedules and I appreciate

the special effort you must have made to get there and

represent the commission so thank you very much.

THE USE OF HUMAN BIOLOGICAL MATERIALS IN RESEARCH

DISCUSSION OF DRAFT REPORT

DR. SHAPIRO: Let's now turn our attention

then directly to the recommendations of the Biological

Materials Report. As I said before, there are

approximately 25 recommendations here, most of which we

have already agreed to and, unless there is some special

reason to do so, we will not return to them. I do not

expect to return to them today.
We will start off with just going through them by starting with 1 and going through those that I think need some of our attention, even if only to say we agree, which may occur in some cases. Some, I think at least one or two, need to be -- at least a few need to be rewritten in my judgment and we will find some appropriate spot this morning and assign some of our colleagues to do that where that seems to be appropriate.

And we want to make sure this time that we finally do get to 24 and 25 and decide what we want to do with those, and if it looks like we are getting along this morning without getting to those I will just stop and go directly to them because we have left those behind in a number of meetings already.

So let's go to recommendation 1. This recommendation is different -- at least it has been rewritten since the Charlottesville meeting -- and so let's see what comments or questions there may be with respect to recommendation number one.

Bette?

MS. KRAMER: No. It is not in recommendation
number one. Just before we get started I would like to say that I thought that the beginning language of this chapter was terrific. It really was. It is very, very accessible. I think it is a straightforward statement on how we feel and I want to express my appreciation for the author or authors.

DR. CHILDRESS: Could I just add to that? I think the whole chapter is much, much improved and we really are grateful to Kathi and others for bringing this into the shape it is.

DR. SHAPIRO: Okay. Thank you very much for those comments. We appreciate it.

Recommendation 1.

Alex?

PROFESSOR CAPRON: I realize that there is a history to subsection (b) that probably explains the italics on line nine but I think that we do not need to italicize the word "is." The flavor is "is after all our discussion" and I would remove that.

The parenthetical in recommendation subpart (c) lines 13 to 15, seems a little cumbersome and I would suggest a modification of it. Shall I just read that to
you?

DR. SHAPIRO: Sure.

PROFESSOR CAPRON: On line 14, I would strike from "link" to the word "between" and just say "code that links a --" actually through the word "the" so it would read "samples taken -- i.e., samples taken from identified specimens with a code that links a particular sample to the particular specimen." It is just a simpler way of saying that.

DR. SHAPIRO: Thank you.

Any other -- yes, Larry?

DR. MIIKE: You are dealing with both coded and identified so we cannot say in the parens that it is coded. Why don't we just leave the parens. We discuss these things long enough in the body of the report.

DR. SHAPIRO: Yes, I agree with that.

You need to press the button unfortunately. We have found out that there is -- each meeting has a different version of a PA system, which requires a new set of skills and habits. This one apparently requires that we all press the button down as you speak and it is very important for the person doing the transcript to be
able to hear it all.

Larry's suggestion is, which I think is actually a good one, is we do not need to repeat yet again what these are since we go through that. We just would omit the parenthetical expression.

Am I correct, Larry?

DR. MIIKE: Yes.

DR. SHAPIRO: It seems redundant now to me, also.

Yes, Bette?

MS. KRAMER: Except for those people that do not read the material ahead and just jump to the recommendations.

DR. SHAPIRO: Well --

MS. KRAMER: Okay.

DR. SHAPIRO: -- I certainly understand that but I think -- well, I do not know how the rest of the commission feels. It still seems to me we could do without these things. They are long enough as it stands.

PROFESSOR CAPRON: Yes. We are not writing recommendations for statutory or regulatory language here in which that explanation would have to appear. It is on
the previous page.

DR. SHAPIRO: Jim?

DR. CHILDRESS: I guess that raises a question as to whether in (a) and (b) we want to have them removed from the parenthesis.

DR. SHAPIRO: Well, I can tell you what my view is that we should remove it.

David?

DR. COX: I agree with that and I think with respect to Bette's points, is that we specifically do not -- in my view, we do not want the recommendations sort of as stand alone points and the reason why we write the rest of this text is because the recommendations do not stand alone. They have to be in context. So if we have a definition there then there is no need to do it again unless we expect them to stand alone, which I do not.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: One last minor thing is that sub (d) really is not a sub (d). Sub (d) just should be pulled out. It is the same as the text on top. (a), (b) and (c) are specific interpretations of specific regs. Sub (d) is not that.
PROFESSOR CAPRON: Indeed, sub (d) really is the introductory text, isn't it?

PROFESSOR CHARO: You can easily just leave it where it is just by taking away the (d) and pulling it back to the --

PROFESSOR CAPRON: Right. Because we already have the "should" statement in the -- at the bottom of page 10. "Should be interpreted in the following particular ways." And all that says is they should do it, which is -- I agree with you.

DR. SHAPIRO: Okay. There does not need to be a sub (d). I agree.

Anything else on recommendation 1?

Thank you very much.

Let's go on to recommendation 2. I have a suggestion to alter here. It is just a suggestion of changing one word, although the substance of it, I think, is more than a simple word and so I want to mention it.

I would recommend that we consider in the -- for example, the first parenthetical expression where we say "or other review committee." I would prefer myself to use the word "procedure" rather than committee. The
same thing in the second parenthetical expression. Without trying to get tied down to the words or whether that is the most felicitous way of expressing it, I do not think we need another committee necessarily. If someone wants to designate a procedure or a person they should be able to do so. Otherwise we are going to burden the system down with too much bureaucracy here and let each IRB decide what procedure it wants to use.

PROFESSOR CAPRON: Does "process" work equally well because "procedure" appears immediately after that as the thing that the person is supposed to be doing.

DR. SHAPIRO: My first thought is yes. It works just as well. That is right because it has the procedures after. I had not noticed that. But the main thing is I want it to be possible -- just to tell you what is on my mind -- for an IRB to identify an individual who people will consult on this as a possibility.

Yes, Alta?

PROFESSOR CHARO: I agree with the sentiment. I think I would probably want to keep playing with the
language and there is substantive reason why. This is an example of how the phenomenon of exempted -- of research eligible for exemption is going to be handled and every institution negotiates differently with Washington how they are going to manage the process of granting exemptions.

It is sometimes by their IRB administrator. It is sometimes by another designated official at the institution. And I have some suggested language that might make it possible to accommodate any number of arrangements that exist already out there without any hint of our suggesting there should be a particular one that they follow.

Secondly --

DR. SHAPIRO: Would it allow -- would the language you have in mind allow for a single individual to serve in this function?

PROFESSOR CHARO: Let me try reading it although it is always difficult, I know, to do this verbally.

"Investigators proposing to use unlinked samples may request an exemption from their IRB or other
official designated by their institution..." Right?
"...but should explain the procedures that will be used
to qualify the samples for this category..." and da, da, da.

So it just recasts the sentences as the
investigator is requesting from whoever is designated by
their institution.

And then on the following -- well, for me, it
is the following page -- if the official rather than the
IRB or other committee, if the official determines that
the procedures are sufficient it may -- you know, then
the language -- it may certify the research as exempt
from IRB review requirements of the Common Rule as
opposed to not subject to since that really is about no
human subjects.

And then finally I will save for when you
want to discuss it, I had a proposal for two additional
sentences on the substance of when those exemptions
should not be granted.

DR. SHAPIRO: Let's just get to the first
part of this first and let's not -- I mean that language
just on first blush seems all right but I want to make
sure we agree with the substance here and then when
everyone sees the final language they know what the
substance is. The substance here is, as I understand it,
that the investigator has got to see someone. That
someone may be an individual to do these things. It may
be, depending on what the IRB decides, some other
process, I presume. If an IRB decided they wanted to use
a process, it could even use a committee if in their
judgment that is what they wanted. Is that right?

PROFESSOR CHARO: It is actually not up to
the IRB. It is up to people higher up in the university.

DR. SHAPIRO: Right. They will have to
decide something but that we want to allow for the fact
that it could be a single person and, therefore, a
relatively simple procedure if that is what that
institution decides to do.

Are people agreed with that issue?

Larry?

DR. MIIKE: Just to review how we got here:

Normally this would not even go to an IRB and what we
wanted to do was to make this transparent so that we know
that they were doing this. So your language actually
puts it in a more assertive way than the way it is now.

DR. SHAPIRO: And you agree, however, with the general plan here?

Jim?

DR. CHILDRESS: I agree with David Cox's comment earlier that we really need to read the recommendations in relation to the text but there is one qualifier that I think is appropriate to bring into that very first sentence. I am just now going back to the way it is formulated in the text.

It seems to me we need investigators proposing to use unlinked samples from specimens already in their possession or under their control because that is -- and the first sentence in the text on page 14 -- and we really are limiting it to that. And if one reads through the recommendation -- it is only when one gets to the text that this particular qualification comes into play and I would propose we include something like that in the first sentence.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Actually this was a point of confusion for me because some of the concern -- some
of the uses of this section would extend to unlinked samples coming from repositories. For example, just to preface what I was saying before, I had a couple of proposed sentences that basically said that the exemption should not be granted when an IRB would review the protocol--would assist the investigator in avoiding group harms or when the scientific merit of the experiment could be compromised by the use of unlinked samples in lieu of using coded samples with appropriate human subjects protections. Those are things that would apply even if the unlinked samples came from a repository. All right.

And part of this confusion in my mind, I think, comes from the history of this section. Some part of the section seemed to grow out of the concern about investigators stripping identifiers but some part of it also was a way to take advantage, and I think this is what Larry may or may not have been talking about, taking advantage of the phenomenon of exemption as a way to provide a quick very easy point of interaction between the investigator and somebody else to discuss whether there is anything special about this use of unlinked
samples that would benefit from additional oversight and assistance.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: I guess, I should use the language that Alta just used about Larry's comment. I think I agree with what Alta just said and I do not recall in our history of this -- the material that is on lines 9 and 10 on page 14, the sentence that Jim read -- was intended as the limitation on this section.

What we did is we merged together -- we started off with the idea that samples coming from outside were going to go through a process, which we said should be done by a third party, some intermediary, other than the investigator who was going to use them and it could be someone at the repository. It could be somebody else. Then we recognized that a lot of people would be using samples already in their possession and you would not have that and yet in certain circumstances they might be using a protocol, people said, that was going to be adequate and we did not have to say you cannot use those samples and you have got to send them out to somebody else. If you have some kind of a protocol that does it
that your institution has looked at and they check off, yes, you have used the standardized protocol, we said that would be okay.

So I do not believe that sentence, Jim, is appropriate and it should not be in the recommendations and it should not be in the report because I do not think we are limiting it to that category.

DR. SHAPIRO: Larry?

DR. MIIKE: I think what we are all discussing is on page 15, lines 14 through 19, and that needs to be highlighted somewhere. It is buried right now because that is the whole point of why we had come up with this recommendation.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I agree with you that we could highlight this more but I do not agree that it is the only reason why this recommendation exists.

Now it is entirely possible that the appropriate solution here is to have a recommendation that is focused entirely at the phenomenon of investigators stripping identifiers off their already possessed samples and a second one that deals more
generically with the phenomenon of unlinked samples but I
do think that there is -- there is an appropriate space
in this report for something called special issues
surrounding the use of unlinked samples.

DR. MIIKE: I agree. What I am saying is
that the language on page 15 is not limited to samples in
the possession of the investigator. It is the issue out
there that are they stripping identifiers in order to get
away from IRB review. So it covers both instances.

DR. SHAPIRO: Bernie?

And then we are going to have to designate
some writing here. We actually have to write this up.

DR. LO: I would support the idea that these
recommendations should pertain to all studies on unlinked
samples and not just the ones where the investigator has
the sample and physical possession and strips them. In
the discussion that just took place it seems there are a
couple of reasons why we might want to do that and I
think that needs to be spelled out better in the
accompanying text.

I mean, on the one hand I think there are
commens concerns that using unlinked samples is a way to sort of
avoid confronting difficult ethical challenges. It is sort of too easy a way to sort of duck issues that should not be ducked and I think there are also specific concerns that are more technical concerns that if the person doing the delinking actually is one of the investigators, the delinking may be flawed. But I think the deeper concern is that knowingly or unknowingly investigators may use the unlinked samples as a way of failing to confront issues they ought to be confronting.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: In light of that I wonder if I could actually try out the two sentences I wanted to add and make sure that they do not offend anybody here.

DR. SHAPIRO: Let's try them out. Read them slowly.

PROFESSOR CHARO: Exemptions should not be granted when IRB review would assist investigators in avoiding group harms or when the scientific merit of the research is compromised by failing to use coded or identified samples with appropriate human subjects protections.

DR. SHAPIRO: Do you want to read the first
one again? I am not sure I fully -- I am sorry, Steve.

Then we will go to you next.

PROFESSOR CHARO: Exemptions --

MR. HOLTZMAN: My question was who determines.

PROFESSOR CHARO: The person who determines is the official at the institution designated to grant exemptions or not. The sentence reads: "Exemptions should not be granted when IRB review would assist investigators in avoiding group harms or when the scientific merit..." and so forth.

So it was an opportunity for the official who grants exemptions to say, you know, there is a group harm issue here that you have not spotted and an IRB discussion might help you with some design issues. I do not expect it will happen often but it would be the point of contact where that second opinion would be made available and it could operationalize some of the later recommendations.

DR. SHAPIRO: And you also, if I have understood this -- this is just asking a question. I understand now the first part. The second part deals
with a judgment of the scientific merit of what is going on. That is a different kind of judgment.

PROFESSOR CHARO: Right. To deal exactly with what Bernie was saying where as a commission there seems to be a sentiment that we should discourage the use of unlinked samples when better research would use coded samples and the unlinked use is tied only to a desire to kind of avoid human subjects protections burdens.

And again this is a way to alert people to the fact that it is not impossible to deal with the human subjects protections. You can use coded samples and frequently, for example, have the consent requirement waived. Something that investigators frequently do not appreciate and so assume that if they are using coded samples they are going to be stuck with the difficult process of locating hundreds of people.

So again it is a point of contact for kind of education about alternatives.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: I understand the motivation of what we are trying to do here and I am trying to think through its potential implications.
Standardly researchers order tissue cells and DNA from lots and lots of places, ATCC, Corielle, the local path lab, get blood samples. I do not know to what extent the majority of those are unlinked samples as opposed to unidentified -- come from unidentified specimens and I think we may have just introduced a level of review far beyond anything that we have contemplated before -- the necessity of review far beyond anything we have contemplated before.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: Actually this is very, very pertinent and it has been raised from the very first time this idea has come up. I think that based on Elisa Eisman's work that we can suspect that most of what they are getting is unlinked as opposed to unidentified, which means that this is an enormous number of protocols.

However, I think it is also fair to say that in the vast, vast majority of cases this requirement will consist of nothing more than a single sheet of paper that gets signed off by a single person. It will be diminimus in terms of procedure. It is a very limited oversight opportunity to catch the small number of protocols that
actually raise the issues that we discuss later on about
group harms and the occasional circumstances in which
investigators are stripping identifiers from available
samples.

The people who are simply taking stuff from
repositories and then filing a notice with their official
that they are going to proceed pursuant to an exemption
will be granted the exemption in a standard fashion, I
suspect.

DR. SHAPIRO: Arturo, do you have a question?

DR. BRITO: No. I just gave Alta a
suggestion.

DR. SHAPIRO: Okay.

Larry, and then Alex.

DR. MIIKE: I think this recommendation is
getting to be much too complex for it to capture -- it is
now -- if we start looking at group harms, et cetera,
this is going to be a review way beyond what we initially
talked about. This was is it justified and is it
scientifically valid? We are getting way beyond that.

DR. SHAPIRO: David?

Excuse me. Alex was first. Excuse me. I
apologize. I am not keeping my list here organized.

Alex, and then David.

PROFESSOR CAPRON: Two quick points. Alta, I

would prefer, since I have a sense that at some point we

are taking a break and you are going to go rewrite this,

to use language closer to Harold's language and make the

operative phrase "the review process" and then when first

introducing it say, "An IRB or other designated -- e.g.

IRB, other designated official," or whatever.

The constant use of the word "official" makes

me think that that may not be what is used. It could be

an IRB or something.

The second thing is I hope that once you have

done that you take Larry's comment into account. It may

be that what you are providing is an explanation that

could be in the commentary that -- as to what kinds of

considerations will go into making the decision and what

is the benefit of having that review process.

DR. SHAPIRO: If I could say a word before

David since David is really next but Alex's last comment

is very close to what I was thinking because I agree with

Larry. This thing is getting too long and too
unmanageable. I think having in the commentary, especially in my view the second half, namely the scientific review, but once I go that far it makes sense to do what Alex has said. I am actually worried about the scientific review by a single individual and I do not want to be drawn away from the single individual so I would much prefer that as we write that we put that in commentary and try to deal with it that way.

David, I am sorry.

DR. COX: The third time is the charm because I had the same point. I think that I would have in the following way: Researchers now -- and this is in some way Steve's point. You know, when they have samples that they want to strip identifiers from they just do it and, you know, they do not screw around with it. Now they are going to say, "What is this NBAC? What they are trying to do is make us go through these hoops. How come?"

They genuinely will not know how come and unless we put in a commentary why we want to do this is that no single, individual is going to understand what they should even be checking for.

So I think that the points that you make,
Alta, are ones that we all care about but that have it be in the commentary because we already have somebody checking that.

DR. SHAPIRO: Okay, Alta. Let's go on with our discussion and Alex made a good forecast. We will ask you to rewrite two but let's save -- those two sentences, I think, really are very valuable. The two thoughts that you had regarding this. I think they are a valuable addition to the chapter and we should certainly include it in the commentary but not part of the recommendation itself.

Is that all right?

Okay. Thank you very much.

Let's now go on -- we are going to be jumping around now. We are not going to go -- you will be relieved to know we are not going through these one by one. I would like now to turn to recommendation 9, which we have discussed a number of times. At least it is not clear to me that we have reached closure on this.

Now this is a recommendation which is -- I am sorry. I do not have the page right in front of me since I am going -- page 22. This particular recommendation
really is designed to make sure that when consent is being sought people have a reasonable idea of what it is their options are. Okay.

And the way that the recommendation is actually phrased, it is such options might include, for example. All right. So this is not prescriptive but it has got a might include and then for example. So it is obviously giving a lot of options to people. But I think it makes the point by going (a), (b), (c), (d), (e).

And (f) is something we have discussed a number of times and which there is disagreement amongst us. That is there is, I think, a minority of the committee that feels that (f) should never be allowed and I do not think we specifically need to discuss that again because we have been through that. I think there is a small minority of the committee that feels that way and so I do not want -- I do not think there is much to be gained by discussing that particular issue again.

But are there other issues here which anyone needs to clarify or speak about on recommendation 10?

Okay. Thank you.

Let's go on to a new recommendation. This is
new to me. And that is recommendation 10. Are you going back to recommendation 9?

MS. BACKLAR: On page 23, this is not exactly about the recommendation, there was a suggestion that the tiered consent form for the National Action Plan for Breast Cancer be used as an example. That is in the second paragraph of page 23. I just wanted to suggest that I thought it would be a good idea if we would have somewhere in this report some examples of this instead of just referring to it and not letting people see what it is like. Not in this section but somewhere.

DR. SHAPIRO: Would an appendix be all right?

MS. BACKLAR: Yes. Yes.

DR. SHAPIRO: Well, why don't we accept that and we will put it -- I do not know exactly where it ought to be put and which ones we ought to use but let's find some. I think it is a good suggestion and people might find that useful.

Let's go again back to recommendation 10. I found, myself, I could not understand recommendation 10 and what it meant. So I presume that at the meeting that -- part of the meeting I did not attend someone does know
what this is going to mean and can help me out and tell
me what this is supposed to recommend.

Larry?

DR. MIIKE: Yes. The language is confusing.

Whoever wrote this, is the intent is, I guess, to say
rather than permitting expedited review we are going to
treat them all as minimal risk? I think -- isn't that
what the intent is? I think that is what it means.

DR. SHAPIRO: What do you want to treat as
minimal risk?

DR. MIIKE: I am sorry. Instead of
permitting expedited review for minimal risk research for
collections solely for nonresearch purposes, it would be
"always treated for -- it would always be dealt with in
an expedited review basis if it is minimal risk."

Right now it is a permissive one but we are
just sort of saying treat it -- and I think that is what
it is saying.

Alta is shaking her head yes.

I do have a problem, and I guess it is with
the current regs. I cannot imagine -- the language is
kind of weird. It says, "Collected solely for
nonresearch purposes," and yet it is going to be used in
research --

(Simultaneous discussion.)

DR. MIIKE: -- is one of the reasons for the
recommendation.

DR. SHAPIRO: Alta, do you have --

PROFESSOR CHARO: It is, I think, a part of
the meeting that you were absent from and it --

DR. SHAPIRO: I was absent either actually or
spiritually or --

PROFESSOR CHARO: No. I think you were
actually. And Marjorie Speers from CDC was alerting us
to a peculiar ambiguity that exists in the regulations
governing expedited review. I think I am the one that
has to plead guilty to this completely impenetrable
language. I probably scribbled it at the table to fill
in the one actual hole in the regs when the easier
solution is to do a recommendation that speaks globally
and then explains in the text what the regulatory problem
is and a global solution is something like "all minimal
risk research that uses human biological materials is
eligible for expedited review" or something very simple.
There are four categories collected in the past for research, collected in the past for clinical, collected in the future for research, collected in the future for clinical. The regs handle three of those one way and one of those a different way. We think they should all be handled the same.

PROFESSOR CAPRON: Well, I think that without naming all four categories somewhere in there you have to say collected for whatever purposes or something to signal that there is something going on. Otherwise it sounds -- what is it explanatory of? You have to sort of, it seems to me, signal -- although collected for different purposes, all -- or for whatever purposes they were originally --

PROFESSOR CHARO: Why not just put that in the text explaining it to keep the recommendation really simple?

PROFESSOR CAPRON: Could you repeat what you think it would say?

PROFESSOR CHARO: "All minimal risk research using human biological materials should be eligible for expedited review."
PROFESSOR CAPRON: Again, I mean, so many of
the things that we write here are directive to OPRR or
someone for clarification purposes. From what you are
saying about this one, this is precisely such a category.
That they should either rewrite or clarify that all
materials and it seems to me that what you would be
emphasizing to them is that OPRR or whatever -- the
language we always use -- should interpret the
regulations or modify them if necessary to make clear
that for whatever purposes originally collected all
materials, blah, blah, minimal risk, expedited
review.

Do you see what I am saying?

Just if I read that I would know right away
there is some confusion about different purposes and I
can read the explanations of the four categories, which I
agree do not belong there, but that would signal what we
want done. OPRR clarification.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: You could either do that or
just insert after the words "biological materials" in
Altá's sentence the words "regardless of the
circumstances under which they were collected."

DR. SHAPIRO: I think we agree on the
substance of this and this is not -- recommendation 10 as
it is currently written does not say that. It says
something which we cannot understand but whatever it is
maybe we will save it for posterity as some kind of --
and so I think we really do know what we want to
accomplish here. We all agree with it.

I think that we need to be careful with the
language because all kinds of research uses human
biological materials so we want to just be careful that
we do not say something much more expansive than we had
in mind here dealing with our particular subject.

So would you and Larry like to work on this
10, rewriting 10 is that all right? Well, you can --
when we break you can decide how you want to handle that
but let's get a new 10 written here.

Okay. Thank you very much.

The next one I want to go to is 12. My
understanding is -- and please correct me -- that 12
seems to have been agreed on at some stage. I do not
know if it was discussed explicitly at the
Charlottesville meeting. But I am really quite unclear in my own mind what this says.

My recollection of the history here is that we wanted in the case of human biological materials to give some direction or ask OPRR to give some direction regarding what IRB's should think about when trying to interpret the terms, affects, adversely affects the rights and welfare of subjects. This is a very, very big term. It could include, in principle, almost anything you can imagine.

And it is my recollection, which could easily be wrong or distorted in some important way, that is that where we started here and what we were trying to do in that stage is to narrow the scope of what should be considered under "adversely affects the rights and welfare of subjects" in the case of research using human biological materials.

And my thought was, and again I want -- I hope I will be corrected -- was that what we were thinking of here was the psychosocial harms issues and the privacy issues as it is titled here and the other issues that are mentioned here. That is my recollection
of what we were trying to incorporate in 12.

As 12 currently stands it just says that the IRB ought to consider these issues, which certainly I do not object to but, of course, there is a long list of issues they might consider, of which we have somehow picked out two, and it does not seem to carry the connotation which I recall, which was that we wanted in this case for them to really restrict their view so to speak when interpreting these particular terms. This is just one of the things they have to think about.

But I could be completely wrong on this and if I am that is fine. If I am wrong on this I still do not like 12 because it does not seem to say anything. So either way I do not like it.

PROFESSOR CAPRON: I do not think this was restrictive. I think quite the contrary. This was enumerating there are things which might not occur to the average IRB when it says, well, someone is going to be looking at sample tissues. I mean, they are not going to a person's home. They are not, you know, injecting them. They are not extracting anything from them. What is the issue? And so why can't we just waive consent?
And this -- to me this says in determining whether a consent waiver adversely affects, the statutory language, affects the rights and welfare of the subjects an IRB should consider -- basically it is really three things -- whether the waiver would violate any state or federal statute or customary practice regarding entitlement, whether the study examines traits commonly considered to have political, cultural or economic significance, and whether the study's results might adversely affect the welfare of the subject's community.

So put that way, is that a little clearer? I mean it is really -- it is saying here are three things you should do that you might --

DR. SHAPIRO: Should be certain to consider.

PROFESSOR CAPRON: Be certain to consider.

DR. SHAPIRO: That helps. That helps me but how do other people feel.

PROFESSOR CAPRON: That is what I thought the intent was. Is that right?

DR. SHAPIRO: Okay. I do not have any -- it is really -- I think when I came to this I had just read Jim's new draft of chapter four, which I thought dealt in
a very, very helpful way with some of the psychosocial
issues that have come up in research of this kind and why
it is appropriate to think about them.

But I would have no objection to 12 if it has
got some bite to it, namely you should be certain to
consider this and that. Then I would have no problem
with it.

Steve?

MR. HOLTZMAN: Yes. Isn't 12 just really
trying to summarize what goes down on the page before
page 29 where we articulate four bullets that ought to be
in play in the IRB's mind? In other words, it makes
sense to me the way Alex has articulated it given the
text that precedes it.

DR. SHAPIRO: Okay. That is fine.

Alex, do you want to just make those changes
in the wording?

Is that satisfying to everybody else?

Alta?

PROFESSOR CHARO: Now I think consistent with
that we have had a running seesaw -- running seesaw? We
have had a --
DR. SHAPIRO: Now there is a metaphor.

PROFESSOR CHARO: We have had a running debate about the proper place to consider the issue of psychosocial harms. I would like to once again put in a bid for them to be clearly considered under the category of minimal risk and not under the category of rights and welfare.

If rights and welfare now thoroughly and completely has bite because we are talking about legal rights, we are talking about group harms, we are talking about special, you know, hot button issues, then the psychosocial stuff, which is considered under minimal risk in every other area of research that is considered by IRB's should be considered under minimal risk for this area of research as well. And that will just be a matter of reorganizing the discussion in the text and where that discussion takes place.

PROFESSOR CAPRON: Is that the stuff that is covered in number 11? I am not sure what you are saying. Or is it the commentary that you are worrying about?

PROFESSOR CHARO: Yes. No, it is -- there is text about psychosocial risk that both precedes and
follows 11 and the stuff that follows 11 seems to be linked to recommendation 12 about adversely affects rights and welfare. But I really -- I would really like to see it combined with the stuff on physical harms in the traditional understanding of minimal risk. I just think it makes it easier for everybody.

DR. SHAPIRO: This is a question of where the text comes and where do the recommendations come in -- is that --

PROFESSOR CHARO: No. It is more than that. The substantive -- the substance of the discussion in the text suggests that psychosocial harms are an issue of rights and welfare and not part of the minimal risk discussion and it makes it very confusing.

I mean, if there is no -- there is no risk except for psychosocial with regard to human biological material. That is the only one. And so -- maybe this is better handled in writing. I have got editing remarks all over the text but the way it reads now I find it extremely confusing as to what one is supposed to do with psychosocial harms and I do not think it should be confusing.
DR. SHAPIRO: All right. Why don't you just
make some suggestions and we will see how that flows in
that way.

Let's now go on to recommendation 15 where I
have a question and/or a suggestion. It just depends a
little bit on the discussion that took place last time.

Recommendation 15, which is now on page --
excuse me. Let me try and find the right page. 30 what?
On page 37, regarding guidelines for disclosure of
results and so on, and then it lists -- it says that
these results should be disclosed only if all three --
there are three conditions laid out and all three are
required for disclosure of results.

And I know that this was -- my understanding
is this was discussed last time at the Charlottesville
meeting and the issue of whether group or persons will be
involved seemed -- the discussions seemed to say that we
really wanted to focus on the individual. And I wanted
to make one -- suggest adding a word, which however might
be significant to some and I do not want to add it
inadvertently or without discussion.

And that is under item (c), which currently
reads, "There is readily available a course of action to prevent, avoid, ameliorate, or treat the threat to the subject's health." And I just want to add "concerns" after that.

And indicating that there might be important concerns that person has which might not directly impact only their health. It might impact the reproductive decisions they make, et cetera, et cetera.

But I do not want to get off on to the larger issue of group issues but just would like to add the word "concerns" if the commissioners do not feel that change is the sense of this in a way and that they would object to it.

PROFESSOR CAPRON: What about (b)? You have the same phrase there, "subject's health."

DR. SHAPIRO: I would -- I had not -- I just missed that. That is correct. I would also say "health concerns." But there may be a better way to do that and I will think that through. That sounds right to me. I am just trying to get to the case where there is a course of action available that will not affect their health but might affect their children's health, for example. And
that is not inconsistent then with what -- so, yes, Larry?

DR. MIIKE: Just conceptually I find it difficult to put concerns in (b), "a threat to the subject's health concerns." I mean, the other way -- I mean, it does not make sense. I can deal with health concerns in preventing, avoiding or addressing, et cetera, but a threat to the subject's health concerns does not make sense to me.

PROFESSOR CAPRON: Larry, the phrase is the same as in (c).

DR. MIIKE: But the verb is different.

PROFESSOR CAPRON: No. The phrase -- the full phrase is "the threat to the subjects" is in both. One is indicates a threat to the subject's X, the other is responds to a threat to the subject's X.

DR. MIIKE: Okay, then I would say that in (c) that I would take out the threat. I just find it conceptually difficult to --

DR. SHAPIRO: Let me work on the wording here and see if I can get some wording here because I think -- I take it we are agreeable on (c) and we want to look for
some wording here that is also consistent in (b). I do not -- I think there does have to be some change. I am not sure quite just how to change it.

So why don't I work on that and come back to the committee with that?

Okay. Any other thing on 15?

I would like now to go to 21. This is -- we are now sort of in a different area of our recommendations but this has to do with the suggestions or recommendations we might make.

Excuse me. Let me get the page number. Page 42, in the top of the page.

This currently reads, "When publishing research studies involving human subjects, journals should specify whether the research was conducted in compliance with the requirements of the Common Rule, even if the study was privately funded and exempt from these requirements."

Now we have had discussion in a number of different meetings about what journals should reasonably be expected to require and what has to be disclosed in the publication. And so I just want to open this issue
up to see who it is that is satisfied and/or dissatisfied with this recommendation.

Larry?

DR. MIIKE: We had a discussion on this and my main concern is that it goes beyond the topic of this report. I said that I would feel comfortable with this recommendation if we have some language that links it back to our mental capacity report so that it is a natural conclusion that we want to address all human subjects research and not just biological materials research. So I would be satisfied if there is some text that accompanies this.

DR. SHAPIRO: Okay. I think that is really easy to accommodate. We can certainly do that.

Alta?

PROFESSOR CHARO: I have just a very minor suggestion. Since there are categories of studies that are publicly funded but nonetheless not subject to the Common Rule, for example, state supported research at a state institution, I wanted to suggest that the last sentence read "even if the study was privately funded or otherwise not subject to jurisdiction of the Common
DR. SHAPIRO: If you were going to do that why would you worry about privately funded? Just say --

PROFESSOR CHARO: I agree. In fact, it could be simply say any research not subject to the Common Rule. I agree. I left the privately funded in because it is the most common category that people think of. It is kind of like back to the discussion that we had earlier about --

DR. SHAPIRO: Yes, that is right.

PROFESSOR CHARO: -- whether or not to put something in about that one reg.

DR. SHAPIRO: Yes, that is right.

Alex?

PROFESSOR CAPRON: We are saying journals should specify. Of course, it is the authors who we are really saying should specify. I do not know if we should say journals should require authors to specify. Is that really what we are saying?

PROFESSOR CHARO: Yes.

DR. MIIKE: Just to answer that, Alex, we originally -- I think this recommendation was originally
that editors should require that authors say whether or
not -- and then we came to the conclusion that what we
really wanted actually printed was whether it was done in
compliance with the Common Rule or not.

PROFESSOR CAPRON: Actually we said journals
should require that it be conducted and then we backed
off to say, no, they should simply require authors to
disclose.

DR. MIIKE: And indicate.

PROFESSOR CAPRON: Yes, and indicate. So I
prefer to say journals should require authors to specify

DR. SHAPIRO: Are there other --

PROFESSOR CAPRON: -- and Alta's language at
the end.

DR. SHAPIRO: Arturo?

DR. BRITO: This is very minor but this is
like on the tenth reading that word "even", if the study
was whether -- whatever language Alta uses here, there is
something about that word. How about just saying
"including studies that are exempt from these
requirements?" Something about the word "even" there. I
do not know. It is almost like a --

DR. SHAPIRO: Okay. That seems fine.

So let's see. The -- I just want to see what recommendations we have here now just to make sure that we want to say journals should require authors to specify whether research was conducted in compliance with the Common Rule and I guess our sense is now whether or not these studies were exempt from this requirement, something like that. Does that get the sense of it? Does anyone -- Larry?

DR. MIIKE: I think our discussion was that it was not so much that the authors would be required. That would be a corollary to when the report is -- when the research is published. There was some indication in the journal itself with that article that says whether it was in compliance with the Common Rule or not. And that if that was the case then we do not need to put in the requirement that authors need to do that because they would have to do that. Do you see what I mean?

The point was that we wanted the article to be explicit about whether it was done under the Common Rule or not, and if that is the case --
DR. SHAPIRO: You are not satisfied -- just
to make sure I understand what you are saying, Larry --
you are not satisfied with the author specifying. You
want it noted in the journal that they -- you want to be
able to read the journal --

DR. MIIKE: Well, I am not sure where I stood
in that originally but that is where we started and we
ended up with we are wanting it to be specified in the
journal itself whether it was the Common Rule was
followed or not and if that was so then we do not need to
put in the recommendation itself that authors had to
submit and say it because they would have to do that
anyway.

DR. SHAPIRO: I guess all our memories are
questionable. Certainly mine above all.

PROFESSOR CAPRON: I do not follow what you
are saying the conclusion is now, Larry?

DR. MIIKE: The conclusion is that the
published article indicates explicitly whether it was
done in compliance with the Common Rule or not and so if
that is the case the recommendation itself does not need
to have language that said authors must submit, et
cetera, et cetera, because that would have to be done as
a matter of course. We had that in the conversation we
had on the group discussion.

DR. SHAPIRO: I have it slightly different
but let's let others talk.

Steve?

MR. HOLTZMAN: I have a question about
current practice. When people write articles and they
use animals they always put in a reference that said it
was approved by the ILACC, institutional animal and
whatever it is, right?

DR. SHAPIRO: Yes.

MR. HOLTZMAN: Does that come about because
the regs say you have to specify that or is that simply
that journals have adopted the policy? So I think what
we want to --

DR. SHAPIRO: I think it is the latter.

MR. HOLTZMAN: Right. So I think what we
want to recommend is that the practice here in this case
be like the practice in these other cases. Diane has
cited a journal she is involved with. So why don't we
write the reg in terms of a recommendation to journals
that --

DR. SHAPIRO: Why don't you write that recommendation? It sounds good to me. Alex?

PROFESSOR CAPRON: While you are writing it, one argument for using something about private sponsorship or something here is that it helps to make clear what we are talking about. When it was just read as Arturo suggested, I have no problem with using "included" instead of "even if." But if you say "including those that are exempt from the requirements," it sounds odd. What we mean is including those with exempt requirements because of their sponsorship, i.e. they are privately funded, state funded or some other thing that got them out from the regulations.

Do you see what I mean? And if you do not know that is what we are talking about, the recommendation is a little bit of a head scratcher as you first read it through if you have not gone through the months of discussion we have done.

DR. SHAPIRO: On reflection I actually -- I agree with you on this because we -- for one reason,
expedited exemption is used for a 100 different reasons in this report and this might easily -- so I think if we do not state these things, the sense of this regulation may not be fully understood. It may take a few more words.

So, all right, Steve, why don't you work on that and then we will come back and take a look at it?

Eric?

DR. MESLIN: I was only going to point out to commissioners that staff has prepared a short note -- you do not have it -- that Sean Simon put together that at least provides a way out of this box. One is you could require that authors specify their compliance or noncompliance. But journals could be encouraged to adopt the practice that has already been adopted by 500 journals around the world, which is to be in compliance with the International Committee of Medical Journal editors, and it is also noted in the OPRR guidebook.

So there are, as Diane would point out, many, many journals that already do this as a matter of course. The commission could encourage all such journals to adopt what is already a common practice or a modestly common
practice so it may be a two parter.

PROFESSOR CAPRON: Why not put that in the commentary? That helps --

DR. MESLIN: We could put it in the commentary.

PROFESSOR CAPRON: And that helps -- yes, exactly.

DR. SHAPIRO: Let's put it in but let's -- all right. So, look, we will take a look at the recommendation again when Steve gets to it.

Okay. Let's now go to the oft neglected.

DR. CASSELL: The orphans.

DR. SHAPIRO: The orphans. The orphan drug so to speak of our report, which are recommendations 24 and 25. I will just read them for those who are here toady that may not have a copy in front of them.

Recommendation 24 says, "Because research using identifiable human biological materials sometimes requires that investigators have access to information in a patient's medical record, state and federal legislation concerning medical record privacy should include provisions for legitimate access by researchers who have
met all applicable review and consent requirements."

That is, I take it, a recommendation that is trying to get the attention of people at the state and federal level who are writing rules, regulations and so on regarding access to medical records and the privacy of these confidentiality records to remember that sometimes researchers might need -- might have legitimate reasons for access.

Comments, questions, observations?

PROFESSOR CAPRON: Remind me what particular problem this responds to. Which proposals are out there that would say you can get medical record access provided you are not also looking at biological samples, which is sort of what this sort of says it seems to me. Somehow people who are doing biological sample research are going to be peculiarly disadvantaged in getting access to medical records.

DR. SHAPIRO: Kathi?

DR. HANNA: I think this is in response to the fact that many investigators when trying to determine what their cohort is going to be will go to medical records and review medical records to determine which
samples they want to pull from a path lab.

The problem, according to OPRR, is that many investigators and many IRB's do not consider that part of the process to be human subjects research. They do not -- many IRB's think it does not become human subjects research until they identify the people that they are then going to go pull the blood sample or the tissue samples from.

So this is really just to remind them.

PROFESSOR CAPRON: I agree with that and I have had IRB's call me and ask me, and I have told them that process of trolling the records is to me the first step in research and needs to go through all the review and have consent or consent waivers.

This to me says the opposite and I would understand what you just said is to say should include provisions that limit access until researchers have met all applicable review and consent requirements. That would convey to me -- as I say, I read this and thought just the opposite, that somehow regulations were going to make it more difficult for people who were doing a biological sample cum record, medical records, research
to get to the medical records than people doing health services research and getting to the medical records.

DR. HANNA: Well, I think that -- I think probably there is an additional recommendation that is needed. I mean, because there is kind of three prongs to this. One is to consider the medical records review a part of human subjects research, which is -- I mean, OPRR has expressed to me that if we can make that more clear than they can that they would appreciate it because it is a very difficult subject for them to deal with. They constantly find IRB's confused about it. I do not think we have a recommendation in there about that particular aspect.

The second parts are that there have been, and there is an article in this week's Blue Sheet, Minnesota's privacy law has affected Genentech research where state laws have been passed that are extremely prohibitive and they do not allow legitimate access to medical records. So that is kind of step two that if the investigator goes through proper review and whatever they are finding in some states they have a hard time getting to the medical records because of state laws. So that is
PROFESSOR CAPRON: But that is not limited, I gather, to people who are doing biological samples research. So, I mean, there the complaint is that if the state has adopted a more restrictive law on the use of medical records than is appropriate, and you are going to have human services research people as upset as biological. Now that is -- that it seems to me is not our debate. That is the generalized debate. I mean, I am sure the people at the Mayo who have taken all sorts of steps are probably upset with the legislature in restricting them more fully than they think they should be restricted. To me, because you are doing biological materials research you should not have greater access to the medical records than anyone else. And if there is a problem with it, it is a problem across the board but it is not unique to biological materials research.

DR. SHAPIRO: I have got a couple of people who would like to speak.

Steve, and then Alta.

MR. HOLTZMAN: I do not think this is -- what
I am about to say -- inconsistent with what you are saying, Alex, and that is I think we are trying to lay out a framework here for the legitimate practice of research involving biological materials.

If in the context of medical privacy regulation people are erecting a whole other set of regulations which, as it were, inadvertently would result in people not -- who have fulfilled everything we have said not being able to undertake the research, it seems appropriate for us to note that and, therefore, to note that when they are erecting these things they should be cognizant of its potential impact in an area they have not thought of. I think that is consistent with recommendation 25.

There is another position which could say we are laying down the bare minimum, the sufficient, the necessary, but that you could be quite happy with stuff that was more robust than one view of the world.

DR. SHAPIRO: Alta, and then Bernie?

PROFESSOR CHARO: I think that the key here is recommendation 25. All right? Because one of the observations that has been made throughout this
discussion is that the research on biological materials takes place in conjunction with research on the associated medical records.

And a secondary observation that goes with that is that if you have different rules governing access to the biological material as opposed to the medical records it drives everybody crazy because they are trying to use both of these things together but they are subject to different rules. Not only different substantive levels of protection but often different procedures.

Twenty-five says to the extent possible we should try to make these things the same to keep everybody sane. I think that is a legitimate concern. I think it is possible to even drop 24 entirely and say in the text by way of background that it is getting harder and harder to achieve this kind of uniformity in approach between access to records and access to materials because we have got two divergent trends.

We have got state statutes, which up until now have, in fact, included access for legitimate research now being tightened up in the context of medical records privacy acts to the point that researchers may
well have difficulty getting into the records and yet
conversely at the federal level we heard testimony that
the proposal might be to make the medical records even
more accessible without IRB reviewer subject consent than
we propose with regard to biological material.

So we are working in a situation in which we
have got divergent state and federal trends and they both
in each direction differ from what we are proposing so
the keystone is that we think that ours strikes a happy
middle ground that might be the compromise for both
areas.

DR. SHAPIRO: Bernie?

DR. LO: Yes. I think in 24 and 25 we are
tackling a lot and I am not sure we are clear yet on what
it is we are trying to tackle. I mean, I agree with Alta
that on the one hand we probably want to say it is nice
to be -- it is reasonable to be consistent between
medical records research and biological records research.

I think we also have some substantive things
we are trying to say, which is that the two extremes
of -- one extreme is to demand individual consent for
every research use of medical records. We have got all
this kind of research, it seems to me, because we have
said we are going to allow under certain circumstances
waivers of consent.

So it seems to me that is a substantive point
which really contradicts some of the proposals now out of
congress.

Then I think there is the concern that Kathi
and Alex brought up that on the other hand the current
practice, as we understand it, a sort of trolling, I
think that was Alex's nice phrase, the medical records
and saying that is not really research, we are just
identifying subjects, can be very damaging to privacy
considerations and ought to be treated in just the same
way we treat the rest of the protocol under these
regulations.

But it seems to me that we should decide
whether we want to make just a very sort of general
statement saying that regulations ought to be consistent
in these two domains of research or whether we also want
to make a point, which I think is the core of our report
here, that we do not think that there should be
unfettered access but also we do not think that there
should be specific consent for each research use. And
that really -- those are the extremes of the privacy
debate.

DR. SHAPIRO: Let me try to separate two
issues here. There is the trolling issue. Let's put
that aside for a moment and come back to it because I
think we do -- may wish to have a recommendation
specifically about that -- what we can loosely call a
trolling issue and to make sure that people understand
when their human subjects research begins.

So let's come back to that issue that Alex
raised and Kathi also raised. I think it does not really
appear here one way or another in any specific way.

As I look at 24 and 25, or to put it more
specifically, if I look at 25, 25 says directly that
federal and state legislators, we would encourage them to
enact statutes on medical records research that are
uniform in their approach and consistent with these
recommendations and so on and so forth.

It seems to me 25 may have to be rewritten a
little and it really eliminates the need for 24 because
24, it seems to me, says that, you know, we want to have
legitimate access. Well, 25 says here is how you get
legitimate access. You get states and so on to enact --
now I am not saying the wording does not have to be
worked with a little bit but it seems to me we could
collapse 24 and 25 into a recommendation that simply
courages states and the federal government to consider
legislation that would provide appropriate level of
access to researchers who fulfill all the various
conditions, so on and so forth.

That seems to me like a hard
recommendation -- like a recommendation that certainly
should have a spot in this report. After all we want
people to do this. We do not know exactly what those
laws should look like. We are not writing the laws.
That is a very complicated issue on its own. We are not
going to do that.

But it seems to me that we could collapse 24
and 25, although it needs some rewriting, to do so
effectively.

Alex?

PROFESSOR CAPRON: I am basically in
agreement with that and the idea of uniformity. There
are lots of times when we talked both in the IRB context about taking into account community views, which are not uniform across the country, and when we talk in state law context about the so-called laboratory of the states, which seen in the most pejorative way is the right of the citizens of a particular state or their elected representatives to do foolish things and find out that they are foolish and the rest of us learn from that as well as learning from wonderful experiments.

So if the good people of Minnesota say that up here in the frozen north we take a different view of privacy than you do in Florida or California, then -- and they have enacted something that will drive researchers away from their medical records and have them flocking to Florida and California or some other place that has looser rules, I am not sure -- to go back to Steve's point -- that we are not setting the minimum requirements and that some state may say we have higher requirements and that is not -- that is not something on which I feel like we should break our lance particularly.

DR. SHAPIRO: I have something I would ask the legal scholars on the commission. It is my
understanding that at least in some cases on morally
contested issue the Supreme Court takes exactly this
position, that it sort of gets worked out in the states
which might have different views. Is that correct?

PROFESSOR CAPRON: That is quite correct. I
mean, Oregon's statute on assisted suicide -- it has not
gotten to a Supreme Court challenge but when it was
challenged in federal courts in a lower level it survived
that challenge and I think the sense is that Oregon did
not violate people's rights by doing that even if most
other states are not persuaded to go in that direction.

DR. SHAPIRO: Larry, and then Steve?

DR. MIKE: When the first drafts of these
two recommendations came out I was against them because
we were getting into an area of medical records which did
not include biological and I -- and then it got innocuous
enough, like what Alex says, "Oh, well, that is fine. It
is sort of like mom and apple pie. That is great." So I
did not really -- I did not care one way or the other.
We had them in there because we said, "Oh, we should be
uniform and all that."

If we keep 25 and get rid of 24 that is good
with me except I have a big problem with what if I am in the states. I am writing this legislation and all of a sudden I am told that "by the way all you medical records legislation should go look at the NBAC report and see how to deal with human biological tissues and make sure you conform to that" because that is the way the recommendation is reading right now.

If we are talking about that there should be uniformity or consistency between privacy issues and human biological tissues and medical records, that to me is a general statement that I can agree with.

I think the bigger issue or the one that we should focus on is this trolling issue because it is directly on point. These two if we make them innocuous enough I will go along with it but the way it currently stands it is sort of like telling the legislators pay attention to what we said on human biological tissues and make sure you do it for medical records, and that -- I cannot agree with that kind of a stand.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: The discussion about the laboratories of the states points out that there is an
ambiguity in the wording. Does uniformity refer to state and federal uniformity or biological materials and medical information uniformity? I think we have discussed the latter and I think we should come down with a position on it.

With respect to the former it is a very, very hot issue. If you look at the seven different bills on medical privacy you will see some have federal preemption and some do not. I personally think federal preemption is important but I do not think the commission has discussed it or should take a position on it and I think we should make the wording clear which uniformity we are referring to.

DR. SHAPIRO: Let's -- excuse me, Alta.

PROFESSOR CHARO: I am sorry, Harold, but I think the way -- I think there might be a way to make 25 -- eliminate 24 and make 25 simultaneously more innocuous and closer to what it is we are trying to do. And that would be to rephrase it to not encourage states to enact legislation. We are not going to take a position on whether they rewrite statutes or not.

States that are considering legislation are
encouraged to consider the advantages of uniformity in how we protect access to records and how we protect access to human biological materials. That is innocuous because it is not telling anybody that they have to do anything but it does allow us to send a signal that we think that for the sake of sanity it helps to have the same rules governing until you can identify a specific reason why there has to be a deviation.

And in the text we can also emphasize that we think that the compromise we came down with on biological materials is not too bad and is in and of itself a pretty good one to look at as a model for medical records privacy but this maybe is a way to not at all touch on issues of federalism and state laboratories, et cetera.

PROFESSOR CAPRON: So that is using uniformity in the consistency meaning between types of research?

PROFESSOR CHARO: Correct.

DR. SHAPIRO: I think there is a very useful recommendation hidden somehow in 24 and 25 because -- we will find it -- because I think this doesn't --

PROFESSOR CAPRON: It applies to the reader --
(Laughter.)

DR. SHAPIRO: That is like a Where's Waldo part of our report or whatever that is called because I think there is a lot of activity in this area and someone ought to be paying a little bit of attention to this or at least we ought not to write a report without reflecting that this is an issue out there.

PROFESSOR CAPRON: I want to say that I am comfortable with that recommendation provided that the text that appears as commentary on lines 12 to 15 accompany whatever recommendation. Alta said it is "sotto voce" in hers. To me it is the heart of the matter. I like the notion of consistency but recognizing that there may be identifiable differences and good reasons for special treatment of human biological materials.

I think in a lot of our report, Larry, when you talk about a legislator reading it, will be there are some unique -- and the time that your medical record has accompanying it DNA on a chip, which is going to be there before long where it is going to be part of your medical
record forever. The notion of people simply trolling that, you know, running 1,000 of these through their DNA analyzers and picking out the people who, you know, have proclivities to prolixity or something, and identifying all of them and keeping them off commissions, that will be the day that we should get worried.

DR. SHAPIRO: The -- let's just -- we will try -- Eric, maybe you and Kathi can try to put something together on 24 and 25. Let me return now to the so-called trolling issue.

Is it the sense of the commission that we want to find a spot in the report to say something about the trolling issue specifically? What is the opinion of the commissioners? Should we try to find the right spot to indicate that trolling is human subjects research?

David and Bette?

DR. COX: I think this is a very --

DR. SHAPIRO: It is not only fishing, it is --

DR. COX: I think it is very important that we try and put that in some place. This is a -- just in the context of patients as well as physicians, when
patients actually become aware that someone is trolling through their medical records they go berserk. And I think that -- I do not -- in every situation I have seen where they did not know that they went berserk so that means to me this is an important issue.

PROFESSOR CAPRON: Is that a diagnostic term?

DR. COX: That is a diagnostic term.

DR. SHAPIRO: Look it up under DSM-IV.

DR. COX: My kids know what that means and everybody knows what that means.

DR. SHAPIRO: Berserk is a West Coast term.

PROFESSOR CAPRON: I knew the term. I just did not know I was speaking doctor when I used it.

(Laughter.)

DR. SHAPIRO: It is not clear to me whether this means that we need to write a new recommendation in this area or find the right spot in which to put it.

Alta?

PROFESSOR CHARO: Bette was first.

DR. SHAPIRO: Bette?

MS. KRAMER: I am not sure if this is exactly the same thing but it is close to it. I cannot remember
whose name but he was a consultant to us back when we still had the two committees a long, long time ago from the University of Iowa.

He made a large point about the research that is done by clinicians on their own patients' records without having any sense at all that they were doing human subject research. I wonder if we need to incorporate that some place with this trolling as well.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I've got to confess I am very nervous about doing much on this because this is a morass in which there is wild variation in institutional understandings of what is an appropriate policy and an absence of clarity from OPRR to help rein in this diversity of approach. So what you have just described, Bette, is something that in some institutions would clearly be considered a violation of patient's privacy and in other institutions would never even go to the IRB because it would be considered exempt since it is kind of an analog to the notion of publicly available. As a member of the public I can see everybody's name in the telephone book. As a physician I already know what is in
every one of my patients' records. So in a kind of symmetrical fashion they assume that, therefore, it is eligible for an exemption because there is no new information being dug out.

I do not want to get into this because I am not sure that there really -- that we have had a chance to really understand either what direction has developed out of Washington and whether it makes sense.

I do think it is possible to note maybe early on in the first chapter that if people think it is confusing out there with regard to biological materials they ain't seen nothing yet because it is even worse with medical records and that some of the issues in medical records are quite parallel but that there are special -- there are some special aspects about medical records research that make them something that needs separate attention and go beyond the scope of this report but that we are aware of the fact that there are some parallels both in confusion and possible solutions, and maybe leave it at that.

DR. SHAPIRO: Bette, then Bernie and Alex.

MS. KRAMER: Well, you know, interestingly
enough, my husband, who chairs the IRB in his hospital, 
tells me that very often these doctors have no notion 
whatsoever that they have engaged in human subjects 
research and it is only when they come up with something 
that they then submit to a journal and the journal says, 
"Did you get IRB approval," that they now come running to 
him as IRB chair and say, "Quick, quick."

So that does -- that lends significance -- 
further significance, I think, to our request to the 
journals.

DR. SHAPIRO: Bernie?

DR. LO: Well, I would agree this is a very 
vast and confusing and very important topic but I would 
be reluctant to sort of get in too far into something we 
have not really talked about.

I would urge us to sort of limit ourselves 
and not try and look at all medical records research and 
appropriate access but to limit ourselves to the idea 
that before you actually get the samples you need to sort 
of figure out whose samples you want to ask for so to 
really link it to the human biological materials work.

I think the point that we need to try and
make is that sometimes the mere act of trying to look for potential subjects of research may violate privacy and undermine rights and welfare in ways that are just as serious as when you actually do the research. Both investigators and IRB's ought to think about this. That does not mean to say that all research -- you know, you need consent to do any sort of trolling but that part of the research plan has to be how you are going to identify subjects.

That is how it is at our institution. The identification of subjects is part of your research protocol and is subject to review like everyone else. That does not address the problem that Bette and others have raised that if you do not think it is research and do not go at all to the IRB you never -- the IRB does not get to look at it but that is, it seems to me, outside the scope of this report.

DR. SHAPIRO: Alex, and then Steve.

PROFESSOR CAPRON: I agree with what Bernie and Bette just said. I suggest that we go back to recommendation five and in the commentary somewhere around that recommendation make this point:
Recommendation 5.b says, "A full description of the process by which samples will be obtained." And, in effect, that is what we are talking about here. We are talking about the method by which you decide in certain research these are the samples I want or from this pool or whatever.

And I think we should simply note in the text exactly what Bernie said, which is that IRB's should recognize that the process of research really begins when identifiable records are looked at, that they need to adopt a policy on how that will be treated at their institution, and that people doing human biological materials research should operate consistently with that policy and we do not have to get into the whole deal.

I mean, I think those three points would do it and it is linked -- I think this is the appropriate point in the chapter to link it. I am talking about commentary and not additional recommendation language.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: I would like to understand a little better what we mean by "trolling" here if we are going to get into this and its implications so that, for
example, if I call up a repository to get a half dozen unlinked samples they are unlinked but I would specify a phenotype.

PROFESSOR CAPRON: This is looking at the records, not samples.

MR. HOLTZMAN: Right. But I specify send me six prostate cancer samples, all right, of the following Gleason score, okay, but presumably was tied -- if the repository is a pathology lab it is probably sitting on the medical record. So my question is did that trigger an IRB review though the research would then be with an unlinked sample?

PROFESSOR CAPRON: I think we need to make clear that that is a question the IRB will have to address. If that came to an IRB I would say, "No." The trolling that I think we are talking about is where the researcher goes and looks at identifiable records and says, "Let me look at all the patients who came in, in March." And goes through those and says, "These are ones of interest. Now I want the biological samples or now I am doing human services research and I want to follow through on the payment mechanism used for these people
and whether or not different payment mechanisms resulted in different levels of testing," or something like that.

DR. SHAPIRO: I think Alex has made a very useful suggestion because I am really quite anxious that we deal somewhere in the report with this and I think the commentary around recommendation number five is a very good spot to deal with it now that you have pointed that out.

Is that satisfactory for everyone that we will deal with it in that context and not try to -- and deal with it in a way that makes sense for the subject matter of our report as a much bigger topic?

Okay. Kathi, I am sorry.

DR. HANNA: I just wanted to add one more complexity here and that is -- I mean, you have -- this has been posed in terms of the trolling, the initiation of the research, but throughout the report we use the term, all over -- all over in every chapter, "connected to the ongoing medical records." So it is not just identifying the samples that you want to use. It is also making a decision after you have some samples and you have done some work on them that you might want to go
back to medical records.

So I think we somehow have to add that twist in as well that they might not have gone to the records to find the samples but now they have the samples and they want more information and they have to go back to the medical records. So that also should be considered. It might not have been considered human subjects research when they got the samples but now that they are going back to the records, and they are identifiable records, it is human subjects research.

MR. HOLTZMAN: They can only go back if it is linked and linked as human subjects research.

PROFESSOR CAPRON: And probably consent. But you used the term "ongoing records" and I thought we said if it is ongoing records it is human subjects research would consent. If every time I go into the hospital and tests are now being done on my blood and samples are being sent over to some researcher, we are beyond question of waiving consent and I do not know if this is going on and you are looking at my blood and you are looking at my records. Are we? I mean, that much is clear. The ongoing process.
DR. LO: I think there are institutions that

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PROFESSOR CAPRON: No, I am not talking about what happens now in the world. What we conceived of as the correct policy, if I am a subject in real time, what is happening to me now, my samples, my medical records are going on to some researcher who says he is doing human biological materials research in real time. I am a current patient. I am a research subject and all the usual panoply of protections apply.

If we do not say that in this report, and I think we do, then I am going to have to reread this chapter and figure out all the places I am dissenting.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I think that is probably true but I think you would be surprised if you were to think about why it is true and where it falls in our recommendations. It is in the practicability requirement. Because you could be coming into the hospital every week for some other clinical procedure and they are doing blood draws, whatever, and it could still be that the research that they plan to do on your blood
is minimal risk and it does not affect your rights and welfare to waive your consent but because we are now in the area in which it is happening in the future after our recommendations have been issued we have said so long as it is practical to ask consent from somebody as a sign of respect, regardless of the fact that there is no concrete harms associated, you are supposed to do it.

And it is only for the archived collections for which we anticipate great difficulty that we have said you can presume it is impractical so that is the thing. It is down to the practicability requirements insistence on respect even in the absence of harm.

PROFESSOR CAPRON: Well, I would say there is one additional factor there. Once the researcher has communicated to my physician that she wants my current tissue samples sent along, a portion of them sent along for the research that is ongoing, I am concerned that my clinician has now moved into the role of cooperating investigator.

In effect, there is a small possibility that some time when I would not have a blood drawn or I would not have a biopsy taken she will say, "Well, I know the
investigator needs another one because they need it monthly. Your condition -- if we were just doing this clinically I would not do it but I will do it, you know, it is no big deal," et cetera, et cetera. I mean, it is just --

PROFESSOR CHARO: You know, chances are your physician would not know either and it would be -- it would be a request sent to the blood lab. Your physician would not know. It is the investigator collaborating with the lab.

PROFESSOR CAPRON: Well, the links in the chain go on at some point. I agree. The additional test aspect is only one aspect of it but I am a subject in research. I am ongoing subject and, yes, I agree with you. There is no difficult getting my consent. I am right there. No reason to waive it. So you are right. The practicability requirement is the main one.

DR. SHAPIRO: Bernie?

And then we are going to -- Steve, I think you have a question or a comment or something?

MR. HOLTZMAN: No.

DR. SHAPIRO: No. Okay. Bernie?
DR. LO: Yes. I would just like to say I think the issue here if you are talking about not ongoing collection of samples but ongoing linkage to updated medical records. There is an issue of rights and welfare and psychosocial harms as well as practicability. I mean, I do not know -- I mean, I have to, you know, look through this and see where that really comes through but if it is posed here it is just a matter of, well, it is impractical to do it.

Well, it is clearly not impractical if I am an ongoing patient in that system so that we have to really bring out the objection of being that it is offensive to me that someone is getting all this information I did not even know about.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Well, it is not just in the practicability because we waived for the past and what we are saying is we are making the presumption that in the future the sample will have been collected with consent, which could include, for example, the right for its use for a study in a coded fashion, which can include the continuous update. All right. And that one could,
therefore, go ahead potentially with the study without reconsenting. Okay.

DR. SHAPIRO: Well, reconsenting and consenting are two different aspects. I understand what you are saying.

DR. LO: If I never had the chance to consent and the information flows, that is where the problem is.

MR. HOLTZMAN: Again, there is a very -- when Alex says, "I am a subject of human research," there is another view, and it is not said very strongly but there is another view that if it is coded sample, all right, and there is no reach through to me, and it is confidential, all right, I am not a subject of research even though information about that sample is being collected on a continuously updated basis. But it is a different philosophical basis about the way the subject in here is.

DR. SHAPIRO: Larry?

DR. MIIKE: A long time ago I think Dave and I were strongly stating that if they have access to my current medical records they damn well better let me know about it and get my consent.
DR. SHAPIRO: I agree.

DR. COX: Steve stated it, I think, very nicely. It is a very different philosophical view of how you are looking at it. It is diametrically opposed philosophical views.

DR. SHAPIRO: All right. Let me tell you where we are. We are going to take -- Bernie?

DR. LO: One last thing. I think Steve brought up a very good point that if we are doing -- if we are putting a lot of weight on prospective tiered consent in the future then it seems to me one of the things that people may not appreciate when they sign up for allowing samples to be used for coded studies in the future is this ongoing link and that may be another thing that needs to be brought out in this tiered discussion. I mean, I may well consent to that.

MR. HOLTZMAN: We are doing studies right now with coded samples, all right, for example, of markers of metastases. All right. These are only research studies but now you are up to two to 300 people in retrospective studies, all right, coded samples, consent was waived, all right, because it is minimal risk. We do not want
those individuals really to know that this is going on because then you would get into the issues of will we inform you, how is the work going, the marker, how is it developing but it is critical to have the outcome data on those folks.

So what we are mandating here, in effect, if you are going to go with the practicability argument is those studies will always involve in the future telling people are doing the following kind of assay on a marker gene and that, therefore, you are -- they will know that they are involved in this study which has a potential kind of result.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: Are we basically done with the recommendations?

DR. SHAPIRO: Yes. I want to go on to -- I want to take a break in a few minutes.

PROFESSOR CAPRON: Okay. Could I suggest that we all look at recommendation 3 and ask whether it is now redundant of 1(c). I mean, there is a little bit of fancier language in (c) that could be -- in 3 that could be moved into (c).
DR. SHAPIRO: Yes.

PROFESSOR CAPRON: But basically I think the reorganization made it duplicative.

DR. SHAPIRO: Thank you.

All right. Let me just see where we are now. We are going to take a break. There are really six recommendations of the 25, or whatever number it turns out to be now, which need some rewriting.

There is recommendation 2, which I have asked Alta to work on; recommendation 10, which Alta and Larry will work on; recommendation 12, which Alex will work on; 15, which I will work on; 21, which Steve will work on; and 24/25, however that works out, Eric and Kathi will work on.

Let's take at least half hour so it will give people a chance to work this through. We will see what we can write out and we may even be able to get some things reproduced.

For those of you that are not involved in writing, have deep thoughts. Read some of the materials we distributed on your arrival here. Thank you very much.
Let's try to reassemble -- let's make it at a quarter to 11:00, 10:45.
(Whereupon, a break was taken from 10:10 a.m. to 11:18 a.m.)

DR. SHAPIRO: Okay, colleagues. Could we reassemble, please?
Okay. We have here some alternative wording. There are some typos I can see already but in any case we have some alternative wording for some of the recommendations we were considering. So let's just -- we will just go from the top of this page to the bottom. I think they are sort of as these recommendations come in any case.

So let's go then to what is now revised recommendation 2 and let me turn to Alta and/or Bernie to speak to this.

Alta, do you want to --

PROFESSOR CHARO: Yes. Read it and see if you like it.

DR. SHAPIRO: Read it and see if you like it.

PROFESSOR CAPRON: No. Somebody read it out loud.
DR. SHAPIRO: I will read it out loud.

"Institutions deciding whether to grant an investigator's request for an exemption from IRB review of research should consider:

"(a) why the investigator is using unlinked rather than coded or identified samples." Obviously there is a typo there.

"Whether the links will have been removed by a disinterested third party;

"Whether subjects remain personally identifiable despite the absence of links;

"And whether the research poses a significant risk of group harms despite the absence of links."

Alex?

PROFESSOR CAPRON: Well, this reintroduces the notion of the disinterested third party and I thought we had spent a lot of time at the last meeting -- and Kathi is shaking her head and she is usually my barometer on whether we did it because she probably read the transcript -- getting away from that specific language. And Steve argued and convinced at least me and I thought all of us that what we should be concerned about was the
way it was expressed on page 14 of the latest draft, which is the difficulty of making the linkage at the end because the methodology might be a disinterested third party. It might be some other protocol that is followed. So I do not see this --

PROFESSOR CHARO: So just strike (b). Just delete (b).

DR. LO: And see if (c) captures it.

PROFESSOR CAPRON: Well, (c) is a statement of present fact.

PROFESSOR CHARO: What exactly is the concern? I thought you were getting to the point saying last time that the reason you --

PROFESSOR CAPRON: No. Because it is not whether it is the disinterested -- whether the -- a method -- it is the way it was expressed here that the procedures are sufficient to make it extremely difficult. The procedures -- it is a linkage between -- it is not a statement that the subjects remain personally identifiable. You would say, no, you look at it and they are not personally identifiable. It is whether it is going to be sufficiently difficult to make them
identifiable. That is to say have you used a really good coding methodology?

PROFESSOR CHARO: There is no --

PROFESSOR CAPRON: Or has your lab assistant done it and she can go back and tell you who this person is because she remembers, it was so distinctive, that was Ms. Jones with these odd looking fibroblasts.

PROFESSOR CHARO: See, Alex, I think actually the procedure is less important than the outcome. What you care about is --

PROFESSOR CAPRON: And the language here is --

PROFESSOR CHARO: It is about the outcome.

PROFESSOR CAPRON: -- the procedures are sufficiently -- are sufficient -- I do not -- I thought you were making a minor rewrite of this and I thought our discussion --

PROFESSOR CHARO: I could not make a minor rewrite on it because we were getting all balloxed up over who was going to make the decision, which is not something we can talk about.

So when you rewrite it, to avoid that, what
you really have to focus on is either the information the
information has to deliver to this unknown person or the
criteria for making -- what the unknown person is
supposed to be considering in making the decision.

PROFESSOR CAPRON: Well, Bernie suggested --
excuse me. Larry suggested and I agreed, and then Harold
agreed with that comment, that the things about group
harms and scientific justifications sounded like
commentary. I expected to see a much more minor rewrite
that stayed much closer to the language that we went into
the discussion with. This seems to me to be a major --

PROFESSOR CHARO: Maybe we should take
another crack at it. I have got to say that I really
dislike the original language and found it confusing and
found it focused on procedures and not on outcomes and
maybe we need an entirely different third alternative
that we can all agree on because my editing that I had
privately on that one basically went through the entire
thing making major changes.

So maybe we just need to have a different
person take a third crack at this one maybe on e-mail.

PROFESSOR CAPRON: What you had read was two
sentences and I thought at the end of that -- at -- as additional sentences and then at the end of that discussion I thought there was general consensus around the room that those were to be in the commentary. You have put one of them in. I guess we will have commentary on the other one, the scientific.

PROFESSOR CHARO: I did not read everything I had going on.

PROFESSOR CAPRON: Okay.

PROFESSOR CHARO: The question is what do we really care about here? I guess I have misunderstood because I thought what we cared about was why you would not go ahead and exempt the use of unlinked samples from IRB review, which suggests that you would have to answer the question of what are you worried about. What are -- why would you need an IRB review if it is unlinked?

Well, there are reasons and the reasons include that the people are still identifiable or that the scientific and that is what number -- that is what (a) actually goes to, that there are better ways to do this with coded samples as opposed to using unlinked, and you want to make sure that investigators are alerted to
the fact that there is a way to do it with coded. I just
-- I do not understand the focus on procedures as opposed
to outcomes.

PROFESSOR CAPRON: I am saying that I thought
the language, which I do not think I wrote -- I am not
defending my own language and it is not perfect. I am
sure it could be edited. The language on 14 speaks of
procedures.

It says -- and it ties together the procedure
with the outcome of that procedure -- "The procedures are
sufficient to make it extremely difficult for the
investigator or a third party to link the results of
analyzing a sample with the individual from whose
specimen the sample was taken."

This -- that is a more accurate description
of what you are concerned about than that the subjects,
as you put it, remained personally identifiable despite
the absence of links. That to me sounds like a current
description of the fact. We could use their social
security number as the coding and they are still
personally identifiable.

PROFESSOR CHARO: This is not a coded. These
are unlinked. There is no code here.

PROFESSOR CAPRON: All right. You did them in alphabetical order. That does not -- that makes them still -- in other words, you look at it right now and say you went in with Able, Baker and Caine, and you left them as Abe, Baker and Caine, and anybody looking at this can see that as opposed to the state -- what is wrong with that statement here? It just -- you say that it used to be not directed to outcome.

This is language, Alta, that is directed to outcome. Your criticism seems inapplicable I guess I would say.

DR. SHAPIRO: Larry?

DR. MIIKE: I am satisfied with Alta's changes except for (d). I do not think we need (d) but (a), (b) and (c) seems straight forward enough to me.

DR. SHAPIRO: You do not like (d). Did I understand you correctly?

Well, the purpose of this particular recommendation, just so I can rehearse it in my own mind, is to help people decide whether to exempt from IRB review a particular unlinked sample and it has been the
sense of the commission that we want someone to go
to through some procedure here before exempting them from
the regulations of the Common Rule in this regard. That
is the intent as I think we all understand it and we all
agree with that so we need a recommendation of some
type.

This -- the way -- if I understand the way
this is written, Alta, and you can help me here, you
started off with the vocabulary "institutions deciding
whether to grant an investigator's request." It implies,
of course, that they have some procedure in back of this
all to do this.

PROFESSOR CHARO: They all have to have one.

DR. SHAPIRO: They all have to have one and
they have one, and whatever it is, it is. "For an
exemption from IRB review should consider that as well as
deciding whether to grant this they should consider in
this case (a), (b), (c), (d)." And you are -- if I
understand not Larry's comment but your's, (b) is not
critical. Did I hear you say that?

PROFESSOR CHARO: yes.

DR. SHAPIRO: You are willing to say it. Put
it this way: You are willing to say it. Okay.

PROFESSOR CHARO: And if I may, Harold, on (c), all right, (c) could be rewritten to more clearly capture what Alex wants without focusing on an investigator going into a lengthy explanation of its procedures by having (c) be whether research results could be correlated with individual subjects despite the absence of links.

It is my point about we are focusing on the outcome. It does not matter what procedure the investigators use, what we care about is the outcome. Right?

PROFESSOR CAPRON: What we care about is describing that outcome here and it seems to me that (b) and (c) combined should refer to a process, which may be a disinterested party or whatever. A process, the result of which is that it would be extremely difficult to identify the individuals with their samples.

PROFESSOR CHARO: So that (b) and (c) could be deleted and the substitute would be whether research results could be correlated with individual subjects
despite the absence of links.

DR. SHAPIRO: No, I do not like actually the word "correlated" but let's not stick on that. That has got a meaning in statistics that has nothing directly to do with what we are talking about here. I think I want to now go to (d) because one of the considerations here that Alta and Bernie have proposed is whether the research poses significant group harm and that would be a consideration of whether or not to grant exemption.

Larry did not prefer not to have that.

How do people feel about (d) quite aside from the language that we use to describe it? We can still continue to work on that.

PROFESSOR CAPRON: I think (d) should go with the consideration of lack of maximum benefit from the research as factors which this institutional process are going to use in deciding whether the choice to go unlinked rather than coded makes sense. In other words, I do not see it as the separate consideration.

DR. SHAPIRO: You want to combine it in some way with (a)?

PROFESSOR CAPRON: In commentary.
DR. SHAPIRO: In commentary.

PROFESSOR CAPRON: No. (a) is the substantive --

DR. SHAPIRO: Right.

PROFESSOR CAPRON: -- requirement but it

seemed to me that the previous discussion indicated in commentary we would say that the process should take into account the notion that the design of research would reduce the benefit because people could do the coded research that they think they cannot do, which would be much more valuable research. And, secondly, that the process could also take into account would there be significant risk of group harms and again could suggest ways of avoiding those harms.

DR. SHAPIRO: Alta?

PROFESSOR CHARO: I am afraid I cannot go --

this does not work for me because if (a) is aimed at the group sense that there are times where you could get more scientific benefit out of working with coded samples, it has nothing to do with the relative degree of risks, and the reason why I would like to urge that (d) or some version of it stay in here is because it is the only way
to operationalize the subsequent recommendations about group harms.

Imagine somebody wants to use unlinked samples. They are going to use all of the intercity kids from Baltimore to test for a proposed aggression gene. Not an unlikely scenario.

Wouldn't it be nice if when they have to request an exemption that the institution have an opportunity based on these criteria to say, "This is the kind of thing where maybe we do not want to exempt it from IRB review. We would actually like to have a conversation about the phenomenon of group harm."

This is a way to operationalize those recommendations and by talking about posing a significant risk of group harm from trying to use language that signals that it should not be used trivially, it should not be used frequently, that it is there to catch the occasional case that we are worried about later on, and that this is the great advantage of using the exemption mechanisms that it provides a point of contact that can allow for a distinction of that small minority of cases where the exemption really is not appropriate and IRB
review really is helpful.

DR. SHAPIRO: Well, two things -- David?

DR. COX: So I think that one is not going to be able to solve the problems with group harm, okay, in an easy way but if we do not state it somewhere that at least it is something we want people to think about then we have got a problem. So I am in favor of it being stated in this simple way in this place.

The -- but in the text to make it clear if I was an IRB person, I would say, "Great. So how the hell am I supposed to figure this out? What is a significant group harm?" We state that is a thorny issue but all we are saying is that we would like people to at least think about this and it is an important consideration about whether something should be exempted or not.

If we do not have that in our recommendations somewhere then I agree with Alta that it is going to be difficult to implement anything.

DR. SHAPIRO: Let me suggest the following because I think we -- there may be some disagreement on the group harm issue as to whether it ought to be mentioned here but I think we share the common objective
here. Let's continue to work on the language here and we will produce something which tries to reflect some of these concerns.

I continue to have some -- I have no concerns with the substance of this. I do have some concerns with the language of this. So we are just going to have to work on that. Let's not try to do this around the table right now but understand in the substance we will try to get a recommendation that deals with language.

Yes?

MR. HOLTZMAN: Just a quick question. That recommendation, I believe, would also go to not just unlinked samples, which are seeking the exemption but could also be in play in the case of unidentified samples, right?

PROFESSOR CHARO: No. With unidentified samples there is no human subjects. There is never any point of contact with an institution.

MR. HOLTZMAN: But if you are concerned about the institution getting a whack at the issue of group harms that would equally be in play you should be equally concerned in the case of unidentified samples.
PROFESSOR CHARO: It would be lovely to be able to do so but there is no mechanism for it.

DR. SHAPIRO: Arturo?

DR. BRITO: Isn't that issue addressed in recommendations 18 and 19?

PROFESSOR CAPRON: Not 19.

DR. SHAPIRO: It states it in part but does not deal with review. Right. It encourages people to do things.

DR. BRITO: Right. I was responding to what Steve just said.

DR. SHAPIRO: No, I understand.

DR. BRITO: Okay.

DR. SHAPIRO: This does not require review, that is all.

DR. BRITO: I agree with Alta and David, and whoever else, that this definitely should be included in here irrespective of the language we end up using.

DR. SHAPIRO: All right. We are going to go ahead and redraft some language here containing these. We will take a look at it in its redrafted form. Whether we do will do it today or not, I am not sure. And then
see whether -- where agreement stands on that issue. We may come back to it.

DR. MIIKE: Recommendation 18 goes to investigators no matter what kind of research they are doing.

DR. SHAPIRO: Right.

DR. MIIKE: And the question for me is that why then do we need in this particular case to reemphasize it again so that in an expedited review or an IRB review they are going to look at the whole same issue again.

DR. SHAPIRO: Well, I mean, I think there is an answer but it may not be convincing. The answer is that at least some commissioners feel that they would like in this circumstance to get -- not have just the investigator think about it but have to talk with -- to some other third party. I mean, that may or may not be convincing but I mean that is the idea.

PROFESSOR CAPRON: It does seem, however, ironic that we would end up with a situation in which the IRB apparently would be reviewing risk to the group with unlinked studies but we do not, I think, have a
comparable recommendation for coded or identified samples.

We do have an encouragement to the investigator always to think about the issue and we have a requirement that it be part of the consent process and we might simply say, "Well, the IRB does not have to think about it. It will be in the consent process," and if the people who are subjects could not care less -- but this suggests that the IRB has a role and that is what would be different.

PROFESSOR CHARO: Actually it is not exactly that because remember there is nothing here that says anything about what happens once the IRB review takes place. The point is that there is a subset of research with unlinked samples that like research with coded and identified samples should be seen by an IRB, and then they will or will not take -- they will or will not get very upset about this. That will be up to them but the point is simply that with coded and identified there are group harm issues. They are already there for an IRB to see. With unlinked samples, unless the exemption is denied, the IRB never sees it.
So it is not about forcing an IRB to take it seriously or to say -- or to have a certain finding. It is only about making this like coded and identified samples something the IRB has an opportunity to see.

PROFESSOR CAPRON: No. This says they should consider it. It does not say --

PROFESSOR CHARO: Consider whether to grant the exemption. That is all. It does not say they have to consider it and whether or not to approve the protocol. It is only consider it and whether or not to grant the exemption from IRB review.

PROFESSOR CAPRON: They should consider it.

We are telling them you should do this.

PROFESSOR CHARO: No. That they should consider -- no, wrong. Alex, it could be the department chair who makes the decision about whether or not to grant an exemption, not the IRB administrator, and not an IRB member. So the chair of the psychology department at Amsterdam University says, "You know, this research strikes me as posing a significant risk of group harms. I think rather than granting the exemption that I am allowed to give you, member of my department, I am going
to say you have to go to the IRB." That is all. It does
not say a thing to the IRB.

PROFESSOR CAPRON: Well, it would be odd if
it came to the IRB and they are not, in effect, told the
reason you should evaluate this is because it considers
group harms. Whereas with the other we do not say the
IRB should do it. I guess we just assume that the IRB
will be aware of it and will do it.

I mean, otherwise why is it on the table in
front of us? You are sitting at the IRB, something comes
in, it has unlinked samples, and you say, "I thought we
had an exemption from unlinked samples." "Yes, but this
time," says the chairman or the process person, "We
thought you should consider this because we read it in
the NBAC report that where it involves significant risk
of harm to a group to which the subject belongs --"

PROFESSOR CHARO: Right. And then they can
do with it exactly what they would do with any other
protocol coded or identified that comes to them that
raises these issues. They may be very solicitous. They
may be quite callous. It is entirely up to them.

DR. SHAPIRO: Arturo?
DR. BRITO: When I read this I am thinking that the investigator -- this reviewer is going to tell the investigator, "No, you need to go through the IRB." Am I not interpreting that right because that is the way I am reading it and that is why I think it needs to be in there. But what you just said, that is not the way that you are reading it.

PROFESSOR CAPRON: I am saying -- I am just thinking the steps through.

DR. BRITO: Right. That is what I am saying. So the --

PROFESSOR CAPRON: The IRB -- the investigator, the process, whatever it is --

DR. BRITO: Right.

PROFESSOR CAPRON: -- the institution tells the investigator, "We are not giving you an exemption. You have got to go to the IRB," period. Or no, he comes to the IRB, you know, he is sitting there at the IRB. "I have got an unlinked study." Usually somebody has got to say, "The reason he is here is so we can look at the risk to the group and decide something about it." Otherwise why do we make him go through this process? Does that
seem -- I mean, I am just thinking practically. I am not trying to be highly theoretical about this. Otherwise why do we make him go through the process? Because the IRB is supposed to consider this.

DR. SHAPIRO: I understand that. I think that whether or not we want to add a special consideration for the coded and the identified samples is something we can deal with as the report goes on. It is my own view that this is still a viable thing to do right here. I would like to retain it. Whether we want to add something later, we can certainly do that, and -- but let's work on the language before we spend any more time on this? We are spending too much time on this particular thing. And you will have time to submit comments later.

Bernie, the last comment on this because I want to go to public comment.

DR. LO: First, I think we should have something that just addresses the threshold issue of should it, you know, even be exempted. With regard to the concern about the discrepancy between unlinked versus linkable -- linked samples, I think one way to get around
that is with recommendation 5 put some text saying that among the other things they should consider when the IRB looks at a protocol is this notion of group harms where it is applicable.

The other thing, I guess, is do you want to have it straight up, though, as to whether people want to take the original language from two, which Alta did not like, having to do with procedures to ensure that -- I mean, if people like it, that could replace both (b) and (c) it seems to me.

DR. SHAPIRO: Well, we are going to rewrite the language but if you want to see -- how many of you prefer the original 2 with the small change?

Larry?

DR. MIKE: In my mind if you just take Alta's rewrite as (a) and (c) only, it is what the original language was.

DR. SHAPIRO: Do people have any strong views about the structure of the -- the original structure or the alternative structure of the recommendation? We will get the substance of it out there one way or another. No strong feelings. All right.
Alta, you and I will write this recommendation and we will see what happens with it.

Okay. Let's now go to public comment because we scheduled that for 11:30 and people have been waiting patiently.

Let me remind everyone who will be participating in public comments, our rules are five minutes and when the five minutes are up I will indicate so and ask you to bring your remarks to a close as quickly as possible.

The first person to speak to us today is Daniel McConchie, who is from the Center of Bioethics and Human Dignity.

Mr. McConchie?

I hope you do not mind standing.

PUBLIC COMMENT

DANIEL McCONCHIE

MR. McCONCHIE: No problem.

DR. SHAPIRO: Good.

MR. McCONCHIE: Thank you, Dr. Shapiro, members of the commission and guests.

My name is Daniel McConchie, Operations
Director for the Center for Bioethics and Human Dignity located just north of here in Bannockburn, Illinois.

With the astonishing number of recent advances in the research on stem cells, there is real promise for the future of medical treatment. As an advisory commission, you have the duty to support research that has the potential of bettering or saving the lives of millions of people worldwide as long as that research does not better or save some human life by harming or destroying other human life.

This country has long sought to curb these sorts of utilitarian notions. For example, we do not allow the carving up of one life in order to transplant the organs and save several others. The still existent funding ban on destructive human embryo research serves to stem the same utilitarian mentality. This precedent is useful to guide us and avoid the enticement to sacrifice some human beings for the benefit of others.

With that in mind, it is important, in fact imperative, that you oppose human embryonic stem cell research while encouraging research into adult stem cells. There are many reasons one can argue in support
of this position. In the limited time I have, I will bring up three points.

First, obtaining the stem cells an embryo possesses necessitates that we destroy a human being in the early stages of life. Because we should not further our quest for medical treatment by sanctioning the destruction of one group of humanity to promote the benefit of another, we must avoid any activity that necessarily demands the taking of life. We are all placed at risk whenever any one group, especially a weak, under-represented group, is singled out for discrimination.

Second, because a large portion of the population of the United States sincerely believes that human life begins at fertilization, many people may oppose receiving or providing treatments derived from research built upon the destruction of human embryos. This could result in the refusal of treatment by patients who are not willing to better or save their lives at the cost of embryonic life, and the similar refusal by health care professionals to offer such treatment.

Research into and perfection of treatments
using adult stem cells does not carry the same stigma
attached to embryonic stem cell treatments. In fact,
emphasis on research into embryonic stem cells could
taint all stem cell treatments in the minds of many
Americans and therefore actually hinder the sick and
dying from considering legitimate treatment options.

Third, it is important to note that little
will be lost by opposing only embryonic stem cell
research. Adult stem cells have a greater probability of
use in medical treatments in the foreseeable future.
Biotechnology is much further away from being able to
turn embryonic stem cells into usable medical treatments.
Two main obstacles, immunological incompatibility and
inability to direct the differentiation of cells into
desired tissues, may be less problematic or not at all
problematic with the use of adult stem cells.

There are these and other moral and practical
reasons for avoiding human embryonic stem cell research.
There is a way to support stem cell research without
doing violence to the earliest stages of human life. As
members of the Commission, you have a responsibility to
exercise your ethical duty by encouraging new technology
that promises medical benefit while restrained unbridled utilitarian notions.

We are not faced here with a choice between conducting research on human embryonic stem cells to develop medical treatments and forgoing the possibility of having treatments at all. Rather, we can pursue medical gain via a moral and publicly acceptable form of research, or via research that destroys human embryos and will be rejected by those patients who refuse to discriminate against any form of human life.

I encourage the Commission to be a balancing voice in this debate and encourage stem cell research that is not dependent on the destruction of human life.

Thank you.

DR. SHAPIRO: Thank you very much. And thank you very much for submitting the comments in writing. It is very helpful to us.

MR. McCONCHIE: Thank you.

DR. SHAPIRO: We will make sure those commissioners not here today gets copies.

Questions from commissioners?

Jim?
DR. CHILDRESS: Thank you very much and I understand that the center has prepared at least one publication or another statement that if you could share that with us that would be helpful, too.

MR. McCONCHIE: Certainly. In what form?

DR. CHILDRESS: That you have written that you could present to Dr. Meslin and we could have it as part of the commission's work?

MR. McCONCHIE: Oh, okay. Sure.

DR. CHILDRESS: One question. I just want to make sure where you stand and where the center stands on the question of the use of tissue from electively aborted fetuses as away from the destruction of the embryo as part of the process of obtaining stem cells.

If we are in the context of the other possibility or another possibility of getting tissue from electively aborted fetuses where there has been a separation between the abortion and the procurement of tissue, is that considered also -- do you consider that also problematic or equally problematic?

MR. McCONCHIE: Yes, we would for the same type of reasons that we would oppose using fetal tissue
in order to use in let's say transplant cells as recently
did in the Parkinson's disease patients. Based upon the
same concepts that you are using an immoral means to
further -- even though it is an attractive treatment
option you are still using an immoral means to do so.

DR. SHAPIRO: Thank you.

Diane, and then Steve.

DR. SCOTT-JONES: Thank you for your very
clearly written testimony. I would like to just ask a
couple of questions. How long has your center been in
existence and could you say a little bit about the
training of the persons who are the staff at the center?

MR. McCONCHIE: Certainly. We have been in
existence for just about five years. The training of the
director, he is a graduate of Harvard University -- his
name is Dr. John Kilner -- with a Ph.D. in bioethics.
The research people that are associated with it, we have
an advisory commission who is a list of, I believe, 12
people from different disciplines, including law,
science, academia, all of whom have Ph.D.'s or medical
degrees, or J.D.'s. And the people who work on the
staff of the center either -- other than the secretarial
level -- either have a master's degree or a Ph.D.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Thank you for your remarks.

The Jehovah's Witnesses believe that there is a biblical prohibition on the transfusion of blood. I was wondering how we should think about that from your perspective in terms of research into transfusion. It seems to me a similar argument to the one you are making against ES cell research.

MR. McCONCHIE: The argument against the research would be in the way it is obtained. The arguments that the Jehovah's Witnesses make for transfusion of blood is based upon their idea of the soul and that by a blood transfusion you dilute your soulness and are no longer capable of salvation or no longer redeemable.

The grounding in which we do in this has nothing to do with the idea of soul or anything of that fashion so I do not necessarily see the correlation that you are referring to.

MR. HOLTZMAN: If a Jehovah's Witness was standing in your place and we were considering whether or
not there should be federal funding of transfusion research, it seems to me they would be mounting an analogous argument, albeit in a different biblical basis, to the one that you are mounting against ES cell research and I am asking a policy question of how a commission such as this should take account of the kind of objection you are making or that Jehovah's Witness would be making in the formation of public policy.

MR. McCONCHIE: The primary arguments that I tried to make here was to address a lot of the pragmatic concerns that should be concerned with. The fact that by pursuing embryonic stem cell research, the fact that you will have a portion of the population who have a serious ethical problem with this, you are going to have those people -- especially when you have an alternative or an apparent alternative in the use of adult stem cells, seems to be that you will be encouraging a form of research that could taint later treatments.

When -- so in a policy issue I -- I mean, I have not thought of this explicitly but just off the cuff it would appear to me that the primary issue that you are concerned with in blood transfusions is something of a
more personal nature. If you are going to do research into doing blood transfusions that is not -- that is something that Jehovah's Witnesses reject outright, the idea -- the ability to do that.

And I do not see how that would taint other legitimate medical treatments in their minds when in this case use of stem cells would possibly cause people not to take upon certain treatments that would otherwise be legitimate had you gone down the adult stem cell route.

DR. SHAPIRO: Thank you. Any further questions, commissioners?

Thank you very much for being here today. We appreciate it very much.

The next speaker is Dr. Peggy Connelly from Wheaton, Illinois, who wants to talk to us about access to medical records.

Thank you very much for coming here.

PEGGY CONNELLY

DR. CONNELLY: You are welcome.

Thank you for allowing the testimony.

I urge you to use your influence to enhance
rather than diminish protection of human subjects, particularly medical patients who are especially vulnerable and often coerced into research not because of any malicious intent but because of lack of information on the part of medical staff or hospitals.

In the introduction to chapter 5 it stated that policies and guidelines governing human subject research ought under certain circumstances to promote investigators to have access to sufficient identifying information assuming that adequate protections are present.

The history of human subjects research, past and current, should be convincing enough to make it evident that there is little point in protecting human subjects if the basis of it can be the assumption of protections. Where protections are present they are not always understood and often times they are deliberately ignored.

It was stated by Professor Charo that there is wild innovation and institutional understanding of human protections. Professor Capron mentioned that there is a question about what is happening to my tissue
samples in medical situations. And the comment was made that if these guidelines are enforced that researchers may have difficulty getting access to medical records.

I direct a research program that has about 130 students a year in different research institutions. I am also a member of a hospital ethical committee health system board of directors, ACUC and IRB, and have a fair amount of experience reading research protocols and grappling with some ethical issues.

I see a lot of research that is of dubious scientific merit. Sometimes this is an attempt to get a degree. Lab supervisors are not always aware of the OPRR, the Belmont Report and other things that guide human subjects research.

There are physicians that feel that they are increasingly coerced into placing patients into research situations without adequate informed consent.

Often times researchers are unaware of the guidelines. Hospitals feel exempt and the people generally in my experience in hospitals and medical situations that hand out the informed consent are not
given any training in the law or in the application of it
and again this is a point where patients are coerced into
medical research or coerced into giving up their rights
to protect their own information.

There are two things that I would ask you to
consider. One is that in the introduction if you would
consider rephrasing the line that says "assuming that
adequate protections are present" and replace it with
"when adequate protections are demonstrated to be
present," I think this would offer protection.

The other thing is if you could consider a
recommendation that would allow patients to have an
option of flagging their records like they do for an
advance directive or a DNR that would prohibit access to
their medical records without specific informed consent.

Mr. Holtzman, I am glad to see that there is
a representative of the pharmaceutical industry here.

At one of the sessions I attended this year
at the Association for the Advancement of Science and
Biochip Technology and Pharmacogenetics, one of the
perspectives that was given by an industry official was
quite disturbing and he said that originally the
pharmaceutical companies were not interested in
developing the assays that would do the diagnoses for the
biochip technologies but now they realize that if they
did both genetics research to develop the products and
the assays to diagnose the difficulties they would have
access to patient records that would be useful for
patient research but also for direct marketing to people
that had those sorts of maladies.

Thank you very much.

DR. SHAPIRO: Thank you very much for your
thoughtful remarks.

Any comments or questions from members of the
commission?

Alex?

PROFESSOR CAPRON: Well, just so that you
understand a little further, the concerns that you raise,
I think, are relevant to more than this report and we are
working on additional reports. Any further
substantiation you have of the description you give of
the undergraduate or graduate level students, and
research, and labs being unaware, any problems that your
IRB has found after the fact with research that was done
would be useful for us to get because we do need to illustrate the kinds of problems that arise and I appreciate you bringing them forward.

As you were reading it I recognized the problem with the word "assuming" and I was going to say we substitute "provided that" but your wording certainly gets to the same point.

DR. CONNELLY: I could give you a couple of brief examples now or I could write them and provide them later.

PROFESSOR CAPRON: If you could, I think, write them and we could then use them more easily in any report.

DR. CONNELLY: Okay.

PROFESSOR CAPRON: I appreciate you coming forward.

DR. SHAPIRO: That will be very helpful to us. I apologize. I know that is an extra burden on you but it would be very helpful to us.

DR. CONNELLY: No, I am delighted to it and obviously you do not want a copy of this but tomorrow I will bring you a legible copy.
DR. SHAPIRO: Thank you.

Any other questions? Diane?

DR. SCOTT-JONES: My question is very similar to Alex's. If you could provide us some data on some of the statements that you made it would be very important. For example, you said that many are concerned that they were in studies by coercion. If you could document that. Also, you said that some of the research you see is of limited scientific value. If you could provide some way that we could know what percentages of studies that you examine you would put in that category, it would be very, very helpful.

DR. CONNELLY: Okay. I would say I am talking more about the protocols that we send back for further work rather than actual research outcomes but I will do that.

DR. SHAPIRO: Thank you very much.

Any other comments or questions?

Thank you very much.

We are going to break for lunch shortly but I want to give recommendation 10 another shot and see, Alta, if we fair any better on this one than the previous
This is revised recommendation 10. It is really, as we requested, very different from the previous but it gets to the point, which I think many people had in mind, and it reads as follows:

"All minimal risk research involving human biological materials regardless of how they were collected should be eligible for expedited IRB review," which was -- I think fairly represents the discussion we had. At least that is my recollection of the discussion. Does anybody have any further comments or questions about this?

Alex?

PROFESSOR CAPRON: I had thought that it was possible, Alta, that we were going to make this conform to our other recommendations, which are framed in terms of the Office for Protection from Research Risk should through interpretation of the regulations or whatever make clear that all blah, blah, blah. Was that not a possible --

PROFESSOR CHARO: I did not recall that but there is no problem with it. In fact, on this and also -
- I guess it is just this one. This might be something we might want to think about incorporating back into recommendation one which covers a variety of regulatory interpretations and modifications. It could either be stand alone or could be back in one but either way the OPRR directive would be fine.

DR. SHAPIRO: Let's leave that issue until we work on the text and so on.

Tom, welcome.

DR. MURRAY: Thank you. Thanks to United Airlines for fixing the electrical fault on the airplane and the taxi driver for stopping and asking directions after we had gone five miles in the wrong direction. I am glad to be here.

(Laughter.)

The language of the revision seems to me much more clearer than the written version I had prior to today and I think Alta's suggestion of possibly moving this might be sensible because when I came to this recommendation I really had the feeling of having read a novel and having the plot line change without any warning because this was a section on waiver of consent and all
of a sudden I am reading a recommendation about expedited review. I just think at minimum we should move it.

DR. SHAPIRO: All right. Then we will proceed with this recommendation as revised. I think whether it appears in one or elsewhere, I think Alex's suggestion should be incorporated into it. I think it is just much more straightforward -- much more straightforward that way.

All right. It is now -- we will not have time before our breaking for lunch to go through the rest of these. Let's try to -- let's see. I said most of us are going to probably eat right here in the hotel. Is it reasonable to allow an hour for lunch and reassemble at 1:00?

PROFESSOR CAPRON: Has any arrangement been made with the hotel? Are tables to be held?

DR. SHAPIRO: I think there is plenty of room. I do not think it is an issue for us.

PROFESSOR CAPRON: I do not know.

DR. SHAPIRO: That is what I was told. I do not know either.

PROFESSOR CHARO: Harold, just a point of
order.

DR. SHAPIRO: Yes.

PROFESSOR CHARO: Were you expecting to go back to the remaining four recommendations after lunch before moving on to stem cell?

DR. SHAPIRO: Yes.

PROFESSOR CHARO: Thanks.

DR. SHAPIRO: Because I want to -- as I said before, this is the last time we are discussing this report here as a group. There will be various withdrawal pains and everything.

(Laughter.)

So we will come back to that.

(Whereupon, a luncheon recess was taken from 12:04 p.m. until 1:20 p.m.)

* * * * *
AFTERNOON SESSION

DISCUSSION CONTINUES ON DRAFT REPORT

DR. SHAPIRO: Okay. Let's reassemble and begin our discussions. I want to turn our attention now to revised recommendation 12, which is on that single sheet, which you all ought to have a copy of.

And I think, at least from my reading of it, Alex has succeeded in capturing what we intended on this but, Alex, do you want to make any comments?

PROFESSOR CAPRON: No, correct away.

DR. SHAPIRO: Correct away. Does anybody have any corrections, questions?

Bernie?

DR. LO: Just I like this. My only suggestion is a minor one. It is under (a) to add "privacy or confidentiality" because I think a lot of these issues are actually confidentiality issues rather than privacy issues.

PROFESSOR CAPRON: Well, I just used the language that was there.

DR. SHAPIRO: That is at the end of (a). Okay.
Do you have that, Kathi?

Any other comments or suggestions?

Okay. This is recommendation -- the next one is recommendation 15, which is one that I reworded very, very slightly so it is really a very small change. And if you look at recommendation 15, I do not have the page number in front of me.

PROFESSOR CAPRON: 38.

DR. SHAPIRO: It is 38. (A) is unchanged. (B) instead of saying the "finding" indicates "a threat to a subject's health." It is written, "A finding has significant implications for the subject's health concerns." And then (c) is "there is readily available a course of action to ameliorate or treat these concerns." I did not think we needed to have avoid and so on, and prevent in there. As a matter of fact, it seemed sort of a little unnecessary. So I think it is very straightforward. It was not intending anything new here beyond what we had discussed.

PROFESSOR CAPRON: And we will have commentary explaining.

DR. SHAPIRO: Right. Those concerns could
extend beyond your own personal health.

Okay. Any -- I do not want to rush it.

Let's go on to recommendation 21. Steve, I think this is also fairly straight forward but you may want to say a few words about it.

MR. HOLTZMAN: Just for clarity of the corrections and the typos in the line -- third line after "Common Rule" delete the "slash" and insert a "period."

And in the last line "privately funded or" and then delete the word "others."

MR. HOLTZMAN: I think the intent --

PROFESSOR CHARO: So, Steve, in the first line after the word "that" you want a comma?

MR. HOLTZMAN: What did she say?

DR. SHAPIRO: A "comma" after "that" is the suggestion. "Journals should adopt a policy that, --" is that what you mean?

Steve says he is not going to fight you on this comma.

(Laughter.)

PROFESSOR CAPRON: I think the "a" in the
first line should be "the." It's "the policy that." It is the definite article.

DR. SHAPIRO: Any other comments, questions, punctuation, et cetera?

MR. HOLTZMAN: Did we catch the intended sense?

DR. SHAPIRO: Yes. It seems that you have.

(Laughter.)

DR. MIIKE: Just for clarification, it says that you adopt a policy when publishing that authors must specify. I think what we still mean here is that whatever is being published you be clear somewhere in the publication or in the little note before that about compliance with the Common Rule.

DR. SCOTT-JONES: My comment is similar to Larry's and it has to do with the word "publishing." It actually is "when reviewing the results" because it is not at the end when this is published but when it is reviewed that there needs to be the statement and it is taken into account during the review process.

DR. CASSELL: Change it to "published" and you solve that problem. "Should adopt a policy that when
published."

DR. SHAPIRO: There are other comments, let's just see, before we decide anything final.

Tom, you had a comment?

DR. MURRAY: For 20 and 21 the discussion leading up to it talks about two different things and does not clearly distinguish between the two. Mainly, number one, whether journals' policies with respect to whether research was conducted ethically -- and that is addressed, I guess, in recommendation 21. And the second thing is the manner of publication and the impact of that manner of publication such as the presentation of pedigrees on privacy and confidentiality. I guess that is supposed to be addressed in 20; is that right?

DR. SHAPIRO: Excuse me. Can you tell me what the page is?

DR. MURRAY: 41.

DR. SHAPIRO: Okay. Could you -- I'm sorry, Tom.

DR. MURRAY: That is okay.

DR. SHAPIRO: I did not follow it.

DR. MURRAY: I will try again.
DR. SHAPIRO: I am sorry.

DR. MURRAY: The paragraph beginning on line 13 --

DR. SHAPIRO: Right.

DR. MURRAY: Conflates two things. First, whether journals' policies with respect to publishing research that is conducted ethically and how it will take that into account, and that I think is what recommendation 21 is intending to deal with. The second issue is that the manner of publication could have an impact on privacy and confidentiality. For example, the publication of pedigrees.

DR. SHAPIRO: Right.

DR. MURRAY: Those are just two different things --

DR. SHAPIRO: Right.

DR. MURRAY: -- in 20 and 21. They also need to be separated in the text because the text kind of --

DR. SHAPIRO: Okay. I understand.

DR. MURRAY: -- runs them together without being clear.

DR. SHAPIRO: Okay. That is very helpful.
We will certainly do so.

I hope, as I said earlier this morning, that these are very important, that kind of suggestion, and I really want to encourage everyone to any suggestions like that. We do not have time to discuss them all here today but please put them in writing in however abbreviated form and get them to us so we can really think about it carefully as we produce a final version of the report.

Diane?

DR. SCOTT-JONES: Eric had shown me some expanded text for that same area that Tom was talking about and in the expanded text there is still that same concern that the two issues that Tom mentioned are still not separate and they really should be separated.

DR. SHAPIRO: We will do so. Thank you very much. I have not seen that particular text but we will do so in whatever the text is that we have.

DR. MURRAY: If I may follow-up, in recommendation 21 do we want to ask journal editors to take into account the issue of the manner of the presentation of the research because all we are telling them in 21 is was the research done in accordance with
the Common Rule. So we are simply -- to the journal
editors we are simply addressing the kind of the
research.

We are not addressing at all -- we are not
asking them even to look at the manner of the
presentation of the research and its impact on privacy
and confidentiality. We need to decide. I would be in
favor of just directing them to take the privacy and
confidentiality into account as well and I think some of
their own statements are in that direction.

PROFESSOR CAPRON: If we do that are you
suggesting really that belongs with recommendation 20 as
a second sentence then, which is -- because that now says
plans for disseminating, which sounds like the plans made
by the author and then you could have a sentence saying
journal editors should consider the adequacy of such
factors or whatever in the publication of research
results.

DR. MURRAY: I have no problem with that. It
is simply a question of whether you want to lump them
together by the concern they treat or whether you want to
lump the two things together by whom you are addressing
them to because 20 is addressed to researchers and 21 to editors.

PROFESSOR CAPRON: Personally I would vote for the topic and having the two actors addressing the topic. Twenty-one is such a different kind of recommendation and it basically is a disclosure of how you conduct the research and it ties into commentary, which Kathi is writing, which we do not now have, that makes reference to the journals' policies on a comparable issue.

DR. SHAPIRO: I mean, I agree with that regarding separating these issues. It should be in -- that thought that Tom has just expressed should be in 20 if we are going to include it but let me ask -- that is a separate idea because certainly in part of that recommendation it flows very nicely but I just want to make sure the commissioners are comfortable with that recommendation.

Arturo?

DR. BRITO: I am not sure I agree that 20 only refers to the authors because if you read the text before it and then follow it, plans for disseminating
results, that -- to me that implies that the editors are also already responsible so I am not sure that anything needs to change there, Tom.

If you read the description right before, the paragraph, it says, "Journal editors have an ethical obligation to publish." You know, lines 18, 19 and so on.

DR. MURRAY: It is ambiguous. And I think it allows the reading that you have just given it, Arturo. Maybe we should just clarify that this is instruction both to the researchers publishing and also to journal editors.

DR. BRITO: Within recommendation 20.

PROFESSOR CAPRON: I would strongly suggest -- I think Arturo is quite right about the material on lines 18 through 22 on page 41 and I do not think that that is germane to recommendation 20 and it would probably be helpful to separate the two ideas. That has to do with recommendation 21.

When we were talking about 20 earlier and talking about plans I believe we thought that part of the plan literally before the research is done should include
some thought to this. Now you will not know everything until you get your data because you may have some surprises in the data but you should think this through and have a plan. In effect, the journal editor would be saying "as executed does the plan come up with reasonably protective results or should the data be conveyed in a way that it does not compromise their scientific utility but perhaps protect some of the interests that would otherwise be at risk."

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Would we simply capture both if we wrote in 20 something along the lines of authors and publishers of results of research on human biological materials should attempt to minimize the potential harms to individuals or associated groups?

DR. MURRAY: I think that captures what I thought would be a good clarification of 20.

MR. HOLTZMAN: And, Alex, your point about plans, that could come out in the text.

DR. SHAPIRO: I think I sense around the table agreement that either using that language or some equivalent language that we do want to specifically in
the recommendation acknowledge both the author and publishers’ responsibilities here in addition to what we might want to straighten out with respect to the text. There is also the thought that rather than deal with a single paragraph that refers both to 20 and 21 we should deal with the issues that 20 deals with and then have additional text for 21. We will proceed along those lines unless someone wants to raise objection now but I think we understand the principle here.

Arturo, do you have another question?

DR. BRITO: Yes. I just want to make sure that with what Steve just said that dissemination of results is not lost here somewhere because I did not hear that said.

DR. SHAPIRO: Yes. We will not lose that. It is an important part of this. It is a key part of this.

Okay. Thank you very much. Now will go to our orphan recommendations, 24 and 25, which we discussed earlier today and in which we decided we would try to collapse what we wanted to retain. This was not an attempt to summarize everything that is currently in 24
and 25 but what we wanted to retain of those to try to
collapse them into a single recommendation. Let's see if
that works.

Alta?

PROFESSOR CHARO: I will read it out loud
just because I found a couple of small syntactical errors
at the end. "State and federal legislators are
encouraged to draft medical record privacy laws that
protect patient confidentiality and autonomy while still
maintaining appropriate access by researchers.
Legislators should also take into account the advantages
of applying similar rules to research on medical records
and to research on human biological materials.

DR. SHAPIRO: So you took out "govern" and
you added "to research" at the end of the line?

PROFESSOR CHARO: Yes.

DR. SHAPIRO: Comments, questions, concerns,
if any?

Okay.

PROFESSOR CAPRON: Are we addressing, Alta,
in the first sentence just all kinds of research then?
This dose not make it -- this is not -- "appropriate
access to biological materials."

PROFESSOR CHARO: I think --

PROFESSOR CAPRON: Because we really have not
spent time doing the whole medical privacy thing.

PROFESSOR CHARO: Yes. I understood the
conversation this morning as being a little bit vague
about what exactly we wanted to say about medical records
research. The first sentence is about medical records
research, not about HBM research. All right. And in the
discussion with Harold and Kathi and Eric the agreement
was to make a stab at something that spoke to medical
records research in a way that would be acceptable to
everybody given that that is not the focus of the report
overall but that it is an absolutely necessary adjunct to
HBM research.

DR. SHAPIRO: What I am concerned with here
is -- and maybe a small word change would take care of my
concern as I read this -- what I am concerned with is
getting the attention of legislators when they are
drafting medical record privacy laws. And rather than
say -- and to make sure that they at least think about
appropriate research access in that context, whatever way
they are going to come out on it, just so they do not
forget about it or just by omission not deal with it.

Now that is -- Alta, would it do injustice to
this to say "state and federal legislators are encouraged
when drafting medical privacy laws --" I mean, I just
want to get when. Rather than telling them to go draft
something, which is not what we are saying because we
have not discussed that. But say "when drafting or when
considering or when."

PROFESSOR CHARO: Yes, that is fine. One of
the reasons it came out this way was because of the
discussion earlier that we did not want to give the
impression that currently there is inadequate access
because, if anything, currently there is excessive access
and so we have been dancing this line but there is no
question we can draft it so that it says "when state and
federal legislators draft medical record privacy laws in
order to protect..." let's say, "...patient
confidentiality and autonomy, they encouraged to
nonetheless maintain appropriate access." Something like
that.

DR. SHAPIRO: Something of that nature would
be fine. Now let's get the second aspect of that. Now there is also then the second sentence -- excuse me.

PROFESSOR CHARO: Alex was flashing hand signals at me but I did not understand them.

DR. SHAPIRO: It is probably a basketball play you are supposed to run next.

PROFESSOR CHARO: I am sorry, Harold. I interrupted you. What were you saying?

DR. SHAPIRO: That is all right.

The second sentence is also asking them to think about something, not to do -- think about doing something. Namely that -- to take account of the advantages of applying similar rules to research on medical records and to research on human biological materials. And that I presume is really because it is very difficult in practice if you have different rules here. These are often the same people doing different things at different times and that is a sense of this so I am just asking a question.

PROFESSOR CHARO: That was my sense of why this would be here.

DR. SHAPIRO: All right. Okay. Let me now
return to where we go from here before we start looking
this afternoon at the human stem cell research. As I
said, this is the last of our community consultations on
this issue. We will have a lot of drafting to do. We
will submit, of course, everything to members of the
commission. We eagerly request that you look at it
carefully.

The next thing you will receive will be a
draft of the entire report from beginning to end and I
ask that you -- there will be a fairly demanding time
limit on getting back to it, something like a week,
something of that nature after receiving it so that that
is the kind of time frame we need in order to try to
accommodate any concerns that you might have.

We will then produce a final draft -- a final
report. Of course, as I said earlier today, if at the
end of the day any commissioner objects to any particular
item here they are certainly welcome, indeed encouraged,
to provide an appropriate notation. We have not thought
how we will handle it but in some appropriate way. It
will be quite obvious to those reading the reports that
one or more commissioners agreed, disagreed on one or
more of the issues that we have in front of us.

And so there is -- we have a lot of work to
do just to accommodate the things that were said today. When you get the next draft if there is any changes or things that I feel in any way are -- I do not expect this -- different from what we have focused on today they will certainly be highlighted because I certainly do not want to start inventing a new report now or any aspects of it.

The one issue which I am going to try to get back to commissioners before you get a draft is on what the eventual way of dealing with what we call recommendation 2 is. That is still somewhat up in the air in my own mind as to exactly how we will deal with it and I do not want to take more time this afternoon since I want a little chance to think about it but we may, in fact, get back to it even as early as tomorrow morning. So we will try to do it before we leave town.

But it is unclear to me, for example, whether 2, which deals both with the issue of investigators who strip identifiers and what, if anything, they are required to do in that context, and deals with the issue of group harm in some way, in this case looking at risks
surrounding an exemption, may very well work out as I have tried to think about at least quickly over the lunch hour as to try to -- we may be sort of confounded by trying to deal with those together.

It may be, in part, for the reasons that Alex raised earlier on that the group harm, whatever we want to say about that, ought to be as part of recommendation 18, which deals with that in a broader context.

PROFESSOR CAPRON: Or in conjunction with it.

DR. SHAPIRO: Or in conjunction with it. Not necessarily in conjunction with it. Whereas the stripping identifiers could be dealt with as a separate issue. But that is unresolved and we will certainly have to get back to you separately on that.

Yes, Diane?

DR. SCOTT-JONES: I think it would be important to take a look at all the recommendations that have some reference to group harm and I have noted that there are two -- there are -- also 12 because it mentions cultural and political issues that have a bearing on group harms and then 18, 19 and 20, all of those have
something to do with group harms, and I think we should try to think about them together and make sure that we are speaking in a consistent manner.

DR. SHAPIRO: That is very helpful. We will either try to put them together or reference them in some appropriate way so the reader can really get the set of them together in ways that is helpful. We will certainly see. Maybe we can rearrange it that way.

I know that many of you, including myself, may have additional comments. I hope you have additional comments regarding organization editorial issues of any kind that concern you about the report. Please put it in writing and get it to us -- I would like to say tomorrow but soon because we are very, very rushed to do this now. I think this has been on our plate long enough and we will have to say what we are going to say and then get on with something else. Despite the fact that Steve says he is going to have withdrawal symptoms we cannot keep talking about this.

Jim?

DR. CHILDRESS: Along those lines let me just say a word, if I could, about the revised chapter 4 that
you received, I think, after you got here.

There have been several criticisms we talked about at the last meeting in Charlottesville and I think even once before. Particularly about the structure of the discussion in terms of balancing interest, conflation of wrongs and harms and the like. And following that meeting and actually following the Belmont meeting, Bernie Lo suggested a way to restructure it in terms of drawing on some of the things already in place like the Belmont Principles.

So what I tried to provide in doing this restructuring and rewriting was actually including most of the materials that were already there, I only dropped probably about three or four paragraphs all the way, tried to rewrite and provide a kind of flow. I think there will be several areas where I think people will want to add or modify things.

I guess one of the main things that Bernie and others and I have talked about here would be to make sure that now in the next revision that we make the connections to all the important material in chapter 5 because there are ways in which we could slightly
elaborate here or there in chapter 4 to connect both the
recommendations and the text in 5.

So from my standpoint that is probably the
biggest deficiency at this point though I am sure you can
identify others as well.

DR. SHAPIRO: I am very glad that Jim has
pointed to chapter 4 since that is new in very
significant ways. It is not brand new but I think it is
-- in my own view, I read it as carefully as I could
yesterday and thought it really flowed very well despite
the fact that there is a number of notes in there
indicating where other things have to be added and dealt
with that are not in there right now.

But if you do have to prioritize your own
time as to what you can spend time on I would suggest
right now that chapter 4 would be the first priority and
then chapter 5 and, of course, hopefully you can get to
the whole thing but chapter 4 is extremely important for
you to turn your attention to as quickly as possible.

I am sure Jim will be here. If any of you
get a chance to do that either late today, Jim is here
and Eric is here and could certainly talk to you about
Okay. Let's now shift gears and pick up our discussions regarding human stem cells.

PROFESSOR CHARO: For the record I am going to recuse myself at this point of the meeting.

RESEARCH INVOLVING HUMAN STEM CELLS

DISCUSSION OF DRAFT REPORT

DR. SHAPIRO: Thank you.

We have -- first of all there was an awful lot of material that was provided in your books this time. I do not have the list right in front of me but there were materials from Lori Andrews on two different topics and some -- a paper on the FDA issue, an interesting set of -- it was a memo plus a paper, I think, on fetal tissue and that legislation, what it says and what it does not say, and so on. There is just a lot of information there. I hope that you will all read that as carefully as you can over the next short period of time.

I am going to want to turn in a few minutes to the actual chapter on conclusions and recommendations and begin discussing that and spend the bulk of our time
discussing those issues but I want to pause to see if there is other kinds of information that you feel we need to provide you with in order to help you reach conclusions about this.

That is what you have includes some very detailed information on certain aspects of it and less detailed information on other aspects of it, and we do not have uniform needs for detail here on all the issues. At least I do not think we do but there may be issues or information that you would like to have that we do not have or we have not presented you with and we may not have. And, if so, would you please let us know because pretty soon we are going to run out of time to get more information together but we still have some time left.

So please let me or Eric know if there is other information that you would like to put together.

Eric, will you remind us who is going to be here tomorrow morning?

DR. MESLIN: Yes. Lori Andrews will be here and Dr. Sander Shapiro will be here. Professor Andrews is a lawyer who will be speaking to the state survey that she presented to you in the briefing book and Dr. Shapiro
is an IVF clinician who will be providing information about policies and practices from his perspective.

DR. SHAPIRO: One issue which I am very eager to know a little more about, and since I have to apologize I am going to have to leave early tomorrow, and I do not know exactly when Dr. Shapiro is going to be testifying, and I have heard such widely different estimates of what so-called success rates are in an IVF clinic that I do not know what to think about this issue and it is of some relevance to understand this and I do not -- perhaps there are no good data in which case that may be the answer but I know even around this table I have heard very, very different estimates in the material we are getting.

I listened to a talk the other day of someone claimed the best clinics were now 70 percent successful and so on, which is way out of what I understood to be the case. I have no idea if it is true or untrue. I have no independent, you know, verification of any of these numbers.

DR. MURRAY: They were referring to collecting the fees, I think.
(Laughter.)

PROFESSOR CAPRON: Actually Tom's point is correct although there is federal law that requires reporting information.

DR. SHAPIRO: Right.

PROFESSOR CAPRON: One of the things that law was intended to do, and I am told is not really enforced, is to get people to report comparable results because there is achieving fertilization, achieving pregnancy, achieving live birth, and there is a lot of room for differences based on that.

DR. SHAPIRO: I think I have probably not listened carefully enough to some of the statistics that I have gotten but I just -- maybe tomorrow morning it will be a chance to at least get an opinion or clarification on some of those issues.

Arturo, did you have a question?

DR. BRITO: Well, if you are asking about general topics, and it may be covered somewhere in the body, I have not had a chance to read through it all, of course, but Friday actually from one of the public testimonies the issue of tagging stem cells came up,
which we have raised before but it seems to be a very --
even more important now.

And I was just curious if we could have some
information on the feasibility of tagging stem cells and
what kind of stem cells can be tagged and following those
stem cells.

The reason this came up is because that way
if stem cell research is allowed that way it will allow
individuals to choose whether or not they could use that
information or the stem cells for their own common good,
make choices for themselves. And I do not know how
anyone else feels about getting more information on that.

DR. SHAPIRO: I need to know -- I do not
fully understand the question because I do not know
enough.

DR. BRITO: Okay. Well, with the issue of
tagging stem cells -- by tagging the stem cell you can
actually follow it and say in its utilization for a
clinical reason, for instance where that stem cell
originally came from. Did it come from an electively
aborted fetus? Did it come from --

DR. SHAPIRO: I see. I see.
PROFESSOR CAPRON: The source.

DR. BRITO: The source of the stem cells, right.

DR. SHAPIRO: Yes. Larry?

DR. MIIKE: On that line I think somewhere in the science part it should address the issue. Is that -- my understanding was that -- and Steve and Dave can answer the question quite easily -- is that these cells have pedigrees that you know where they came from and that you can trace them that way, and that it would be important scientifically that you know what the source was.

DR. SHAPIRO: David?

DR. COX: If somebody wants to keep track of them it is easy to do it. If somebody wants to not keep track of them it is easy to do that, too.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: They came from somewhere. You can demand or require that there be a label as it were on the bottle. Now if you are asking for something that is more intrinsic labeling in terms of at the time of creation you put in a marker gene I do not think you
really want to go there. I do not think it is necessary because you can mislabel the marker in the same way if your concerns are mislabeling.

DR. SHAPIRO: Excuse me, Bette.

MS. KRAMER: I had a question and maybe it can even be answered here at the table. The references to developing stem cells from adult stem cells --

DR. SHAPIRO: Yes.

MS. KRAMER: -- is that scientifically feasible? I mean, where is that?

DR. SHAPIRO: I can -- I will not speak as a scientist but I have asked this question of quite a few scientists. I will just tell you what I have heard and David and others here, Steve and others, who know more about this can say more because this is an issue that has come up over and over again in the public testimony, and it came up again today in the public testimony again.

And most of the information we have here is from animal models. Not all but most of it. And what I hear is that it seems from the animal models that the embryonic stem cells are -- have much more flexibility and capacity to help scientists answer the questions that
are before them.

It does not eliminate the possibility these other stem cells could also be used at some stage. They are much harder to get hold of. If they are inside the brain it is not an easy matter to get it. And that it is not -- it remains less sure from the animal models as to just how -- in what way they can be used as substitutes for. That is what I am told.

MS. KRAMER: So, Harold, is it two problems?

Is it the source, the derivation problem, and then the potential use problem?

DR. SHAPIRO: Mm-hum.

MS. KRAMER: So it is two problems?

DR. SHAPIRO: Right. But there are others here much more capable of answering this question than myself. I should not have even tried.

Steve?

MR. HOLTZMAN: Here is a way to think about it, Bette: What somatic cell nuclear transfer Dolly showed is that you can take a committed nucleus and by putting it in the right kind of environment, namely the environment of an egg, all right, that environment
effectively said let all of the DNA free in order to be able to express all of its potential, which effectively an ES cell, an embryonic stem cell, has all of that potential.

So when you take a committed cell and leave the nucleus in it and now you are trying to take that cell all the way back to that pluripotency you are postulating a scientific program in which we understand all of the environmental factors and can recreate them to take them back to that state.

Currently what you have seen in some of the publications is the ability by putting certain things, proteins in that environment, to get it partially back there, right.

Can we eventually get to where we understand that whole, as it were, environmental program that unleashes that potential? Yes.

Is it around the corner? No, I think is basically the answer to that question.

So effectively you can think of the Dolly-like experiment of saying we do not know how to do that but we know an egg knows how to do it so we will take
advantage of the egg being able to do that.

DR. SHAPIRO: Larry?

DR. MIIKE: One last comment on that, I think that in the past that in the research agenda it should not just be dealing with embryonic stem cells because you will be looking at the whole range and that it seems as a common sensical thing to me that part of the research agenda would take a relatively differentiated stem cell and try to reverse engineer it back because that is the only way you are going to understand the forward and backward process. So at least some kind of description about that I think would tend to alleviate some of the people's fears that everybody is just going down the embryonic stem cell route when the whole research agenda can cover more.

DR. SHAPIRO: Well, again, I mean, what I am --

PROFESSOR CAPRON: Some of that is in chapter 4.

DR. SHAPIRO: Yes. Some of that is in there, right. What I hear from the scientists I have spoken to is -- I have just asked them what they think just from
the point of view of a scientist putting all the other
issues aside -- it is that we ought to pursue an agenda
in all these areas. There is no reason to exclude one or
the other from their perspective and all could yield
results which to some extent are partially unique.

Eric?

DR. MESLIN: And that was an issue that was
also brought up at the Friday meeting of the religious
scholars. They raised that question about various
sources of various research activities, including
research into alternatives.

DR. SHAPIRO: Eric?

DR. CASSELL: But at this time if I
understand correctly, at this time there are no sources
of stem cells that are pluripotent in the same way as
embryonic stem cells and as far as we know there is
nothing that will have that as an end result next month
or in six months. So that we do not get the business of,
well, let's stand on one toe because it is just about to
happen when it is not really about to happen. So we
really have to face the issue we have.

DR. SHAPIRO: Correct.
Arturo, and then Alex.

DR. BRITO: This issue raises another issue about totipotency versus pluripotency that was brought up Friday and has been brought up before, and I think that is where a lot of uneasiness comes from. So we need to address it in those terms, whether we are talking about adult stem cells or more adult stem cells because it is truly questionable.

When we go back about four months ago when Harold Varmus was presenting from his point of view, he made a big distinction between totipotency and pluripotency. Right now that distinction is still there. I am not sure whether it is going to be there in the future and I think there is a lot of uneasiness coming from it.

DR. SHAPIRO: Well, my recollection, Arturo, of that -- just that testimony was that Dr. Varmus was speculating that at some time in the future one might be able to move up and down this whole scale and that at that point, you know, a lot of our ideas might change about just what to do but that that was a project a long time in the future. That is my impression of what he
said. I am just talking about his testimony now and not about what the world said.

Steve?

MR. HOLTZMAN: Well, this comes from an ambiguity in the use of totipotent. Totipotent can mean all cell types of the organism. In which case ES cells are totipotent. It gets used in the second sense to mean can it create an organism. The ES cells are made from the ICM which does not contribute to the placenta, which is necessary in order for the organism to evolve. Okay.

DR. SHAPIRO: Right.

MR. HOLTZMAN: So if you then -- so it is very clear in what sense they are totipotent and they are not totipotent. There is an avoidance politically now of using the term "totipotency" because of its systematic confusion with can it create an organism. Okay.

So whatever Varmus is talking about going back up the chain, you are going back up stream of an ES cell, a back up stream of an ICM cell.

DR. SHAPIRO: All right.

DR. BRITO: That distinction is -- we need to be really very specific on just exactly what you just
said.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: Two separate comments. One in response to Arturo's comment. The interesting thing in the future is going to be if we have the ability to move up and down it poses enormous difficulties for people whose arguments rest on the potentiality argument. And so the very forces that say let's deal with adult cells rather than embryonic cells are pushing towards the development of a technology which will then make huge questions.

If all you have to do is add a chemical to this fully differentiated adult stem cell to go all the way back to -- in Steve's just second sense of the word "totipotent" -- a cell that would have the ability to generate an organism then you have a potential organism in every stem cell in our body and that is the issue.

Responding to Eric, I quite agree that we should not be dancing on the point of a toe but it does seem to me that if we end up making some differentiations and aim towards saying some issues are not yet ripe and we do not have to get there yet, which is a view that I
favor, it is in part by saying that the argument for
having to use a particular type of cell is, in part,
based on the notion its therapeutic applications will be
so wonderful. And if those therapeutic applications have
not even been shown to be possible in a controlled way in
an animal model and if there is other valuable research
that can be done with other forms of ES cells that do not
raise all the problems with another type, it seems to me
it is possible to say what is sauce for the goose is
sauce for the gander.

Just as we are not going to say we will hold
up all of this work until we can do adult cells. We also
could say hold up some of this work because the arguments
in favor of using that particular type of ES cell rests
upon capabilities which are not yet at hand.

Is that clear? You look a little puzzled?

DR. CASSELL: Well, I am a little puzzled
because what -- the distinction I was getting at is that
the intent not to have to solve our problem -- because
next month there is going to be -- is the thing I am
trying to avoid. So that we do not have that.

The issue you are raising is a more complex
issue and I think further down the line. I think there
is no way at the present time for our audience -- there
is no way we can avoid for our audience the fact of
dealing with embryonic stem cells at this time.

PROFESSOR CAPRON: Right. But if we draw as
we have been in the tentative recommendations here
distinctions between, for example, discarded IVF embryos
and discarded fetuses as sources versus research created
embryos or somatic cell nuclear transplant embryos as
sources. And if we were to say research should go
forward or may go forward with the first couple of
categories and someone says wait a second, you cannot
achieve an autologous organ transplant using those, you
have to create the embryo from that person's cell, we are
not at that point yet. We do not know how to create the
organs in mice yet.

So let's make sure that we do not -- just as
we do not hold up all this research to wait for the
adult, let's not say that it is appropriate to go forward
with certain research because we have to do that right
now in human cells in order to achieve a therapeutic
privilege. That can be done still with mice or whatever.
DR. CASSELL: I agree 100 percent.

DR. SHAPIRO: Okay. Let's go --

DR. CASSELL: Maybe 1,000 percent.

(Laughter.)

DR. SHAPIRO: Careful now, Eric. Careful.

Let's just go back to my question. We might

just move to the recommendations and start discussing

them substantively since that is what we are aiming --

that is what we are sliding towards in any case.

But let me just ask -- I will not ask for any

answer right now but if any of you have additional

information that we could put together that would be

helpful to your own considerations of these various

issues, please let us know very soon because within a few

days really we are going to lack the capacity to have

time to go out and accumulate this information.

We have given you a lot so far and I think my

own judgment is since I found it extremely useful at

least from my own considerations but if there is other

things, let us know and let us know quickly.

Let's go now to what is chapter 5.

Tentatively chapter 5 at least. We will have to see how
all this works out when we start putting this together. Which is currently entitled "Conclusions and Recommendations." I want to just for purposes of our discussion, although we are going to have to move back and forth around these issues in many different ways, I want to go to our conclusions/recommendations, which begin on page 6. Okay.

This is -- obviously this is tentative and it is for purposes of generating discussions. The commission has not decided exactly where it wants to be on all these issues. As I understand the way this has been put together, recommendations are things that actually require action and conclusions are conclusions we have reached -- I mean, if we decide to sign up to these -- but do not require further action.

So if we look at this first one, which is on page 6 -- and for purposes of those who may not have it in front of them, I will read some of this. The conclusion is that research involving the derivation and use of human stem cells obtained from fetal tissue should continue to be eligible for federal funding. Now that does not require any action. That is just an assessment
we have made or at least a suggested assessment we have made.

There are then two additional -- not two additional. Two recommendations that follow that, which are sort of summary in their form right now, and which would require action if we decide to go that route. The first one is such research should be conducted only under appropriate oversight and institutional review. A comprehensive framework which is already in place in this country.

And, second -- this is not clear what the action is there now that I read it. But there is a second very important issue, which is just summarized by a few words, which is, in fact, a much more complicated issue than I actually appreciated. And that is that we would recommend a clarification of current laws.

This is an issue at least in my recollection was first raised by Alex when he suggested that whatever the interpretation of the fetal transplantation legislation, we ought to recommend that it become specific with regards to the particular issue that we are discussing here.
Well, I -- that sounded as appropriate in the first instance as it does right now. However, it is a lot more complicated than I appreciated because the law is actually written and so on for transplantation of tissue which is certainly as far as basic research goes not what is going to happen. And so I think there is a very serious and complicated issue of knowing just what actual changes in not only some federal laws but state laws would have to take place in order to accomplish this.

I do not think that we will have the chance to really do that in any detail but this clarification of current laws will have to be specified with some considerable substance behind it in order to point people to those areas where people who draft laws will have to -- will know where to go and what to look at and what we have in mind.

So I do not propose that we draft the legislation. I do not think we have the capacity to do that or the time to do it but we will certainly -- this four words here involves -- to clarify that requires a considerable effort, which we, I think, must do.
PROFESSOR CAPRON: I would suggest either now or perhaps at the next meeting that we have before us the provisions of the NIH Revitalization Act that placed restrictions on the fetal research and that we just go down them and say whether or not we agree.

There are two, I think, that bear particular attention. One is the issue of directed donation and I think there we simply need to be clear that there is not the same concern with directed donation. In other words, you could have that provision, and I would see no reason not to parallel the transplantation act, as there is with the -- as there was with the fetal cell transplant. Because with the fetal cell transplant the notion was that someone was going to produce a fetus so that those very cells could go into her father's Alzheimer's affected brain or Parkinson's affected brain or something.

Here if and when autologous transplants ever come into the picture you will not have to have created your own fetal line of cells, it is a matter of getting your cells fused into an existing line of stem cells, as
I understand the likely technology, or of creating this not through the fetal route at all so that is not really an issue.

The second issue is the one of the payment and here I think we may need to spend a little bit of time because there are two sources of law. One is the trans -- the Revitalization Act and the transplant -- fetal transplant specific -- what I take to be an absolute prohibition on all sorts of payments to anyone. And the other is the National Organ Transplantation Act. And I guess the third would be if there are any specific state provisions, which there may be, in fact, in about 20 or 30 states on this as to tissues as opposed to organs.

And the framework here is made complicated by the fact that IVF clinics in some of the excess embryos that they are talking about may be talking about gametes that they paid for, that they incurred expenses for. If we are talking about a reproductive project then we would be talking about those gametes probably having been paid for by the couple whose reproductive project it was. But do we feel the same about prohibiting
payments there as we do in the fetal area? So I think we
are -- because we are going to need to think about not
only the application of our recommendations vis-a-vis
aborted fetuses but also vis-a-vis the IVF.

So I would suggest that we do that. I agree
we will not end up writing the statute but I think we
should specifically address -- and my sense is that the
careful kinds of concerns that people had and that they were
persuaded to overcome in the case of the fetal transplant
area apply here to the use of the fetal tissue for
embryonic or embryonic germ cells or whatever they are
called. And that we ought to address those concerns.

We ought to recognize the validity of those
careful concerns and the sense that they are ameliorated at least
by these protections against this becoming an industry in
which people are encouraged to do abortions for this
purpose or whatever.

So I hope we will endorse the adoption of
similar specific rules and be quite specific in our
discussion as to why.

DR. SHAPIRO: I think, at least from those
commission members that I have heard from are very
sympathetic to that and really want that to happen. I think we may have to find a way to get an initial stab at this before our next meeting and share that with commissioners just to get started on this because we will not be able to obviously approve it but I think we will need to get started because it is -- one thing I had not appreciated is just how much complex this is and I learned a lot from reading the materials, some of which you wrote.

PROFESSOR CAPRON: Yes. Ellen Flannery's revised draft of her memo -- and I do not mean just the latest revision but the difference between this one and the one I saw previously, she is now much clearer that Harriett Raab's discussion is, in effect, almost sort of -- not quite misleading -- but she is very clear that the only way, and I agree with her, the only way that the present statute would apply would be in those instances in which one was getting to the point of transplantation.

DR. SHAPIRO: Correct.

PROFESSOR CAPRON: And as you say, that is not in the cards for most of the work that is going to go on in the near future.
DR. SHAPIRO: That is right.

PROFESSOR CAPRON: Ergo if we think those protections are desirable we should recommend them for this area.

DR. SHAPIRO: Yes. I think, I completely agree with that. I do not know how other commission members feel. I mean, I do not know what the alternative is we have. I think we absolutely must do it as far as I can tell.

But let's try -- and so that is very, very helpful, what Alex has clarified here, and that will essentially sort of -- that broad and really quite difficult issue will come in where lines 15 and 16 are in some combination of recommendations and text in some kind of combination.

But let's go to the conclusion here. That is the first statement here. Namely that the question is whether we are willing to -- whether we agree with this conclusion involving the derivation of the use of human cells obtained from -- should continue to be eligible for federal funding.

I understand we are going to have to have the
appropriate oversight and protections. That goes without saying. But let's just assume that for the moment and we will be able to articulate that in a way that is -- put it this way: If we can articulate it in a way that is acceptable to commissioners, would the conclusion -- would commissioners feel comfortable with the conclusion? Larry?

DR. MIIKE: Just based on the past conversations and testimonies we have had we have got to address the issue of elective versus spontaneous because we mean elective here.

DR. SHAPIRO: Correct. And that is -- as a matter of fact, as I have gone through this chapter, it does not make an adequate distinction on exactly this issue. The word "abortion" for example is used as if there is no distinction between those two and I think we have to be quite clear that we are talking about elective here because otherwise there is really not an issue.

DR. CASSELL: Elective or spontaneous.

DR. SHAPIRO: Right. Elective or spontaneous, right.
And the issue of definitions, in general, in this report have to be dealt with extremely carefully. There is a lot of -- including in this report until we get it straightened out -- kind of loose use of words like pluripotent, and totipotent, and stem cells, and embryonic stem cells, and adult stem cells, and so on, and that is -- it turns out in this area things are very sensitive to how you handle these definitions and we have to do it consistently and carefully, and that is not yet something that is accomplished.

The science -- as I mentioned to you before, the science chapter itself has been reviewed and we have received detailed comments back from two people. One is Professor Thompson. The other is Professor Silver. Those were extremely helpful. It is still out to other reviewers. And we have attempted to incorporate their -- many of their discussions in the draft you have but it is still out to at least one but perhaps more than one, two other reviewers we are hoping to hear from very shortly. So we will be quite sure that we get that right.

Eric?

DR. CASSELL: I would like to make what is
going to sound like a silly comment but I am serious about it. I would like us not to use initials to stand for like ECS and so forth because that is a habit that has come up in medical literature in the last 20 years and in this area people begin to get distant from the definition and now we need the precision and those initials move you away from precision. So in any other place that is the way it is but here I think we cannot afford to do that.

DR. SHAPIRO: I have no objection to that.

PROFESSOR CAPRON: There is a related question. Are we going to continue to use embryonic, which is fine with me. You know that the NIH and everybody is eluding that issue and just saying "pluripotent human" or "human pluripotent." I mean, it is human embryonic stem cells because that is where the issue lies.

DR. SHAPIRO: That is what I would like to use.

DR. CASSELL: You want to use?

PROFESSOR CAPRON: Human embryonic.

DR. SHAPIRO: You cannot use it for fetal.
When it comes to fetal, you know, obviously these stem cells are derived from fetal tissues there is a two-step procedure so to speak. I understand that.

PROFESSOR CAPRON: As I understand it, they are embryonic cells still in the gonadal ridge and they are called embryonic germ cells. It was not the absence of the word "embryonic." It was the absence of the word "stem" that -- the mouse work had called them EGS instead of --

DR. CASSELL: Right.

PROFESSOR CAPRON: But the memorandum we got from Ellen Flannery, like the memorandum from Harriett Raab, we saw "human pluripotent stem cell research." It is cute.

DR. COX: Too cute.

DR. SHAPIRO: Is that an editorial comment, David? "Too cute" means we should use "human embryo."

DR. COX: Yes. That is what I mean because the -- if -- I mean, we would not be having this discussion if the word "embryo" was not there.

DR. SHAPIRO: Jim?

DR. CHILDRESS: Eric Meslin reminded me or
motioned over about one of our important moments at the
hearing on Friday that I think all the participants who
were there will recall, and that is when Gil Meilander
urged us even if we voted for a different position than
he would take, and he would be very conservative on this,
at least be truthful about what we are doing and by that
he meant very careful attention to using words that
really would be understood as they should be understood
in the public debate and not to try to hide the issues.
I think part of what our discussion here is pointing in
exactly the way of doing that.

DR. SHAPIRO: I think that is right. I
actually feel pretty strongly about that because that has
caused some mischief before and no use repeating that and
we might as well be straightforward in whatever it is we
recommend and the recommendations will just stand or fall
on their own weight.

DR. COX: There is nothing that can be more
harmful than obfuscation of these issues because --

DR. SHAPIRO: Cox's law, right?

DR. COX: That is axiom number one.

DR. SHAPIRO: Thank you.
Okay. Again I want to just focus once again on this conclusion to make sure that people are assuming the appropriate protections are in place and so on -- something we will have to talk about in more detail -- comfortable with. And as usual I will take silence to mean comfortable.

DR. CASSELL: Comfortable.

DR. SHAPIRO: Yes. Or some other -- thank you, Eric. Thank you.

Let's turn now -- and of course there is a lot of work to be done on that particular recommendation but let's turn now to page 8 in which it deals with embryos remaining after infertility treatment. Again I do not want to get caught up on the particular words that we use but we want to use David's encouragement to be as plain and as straightforward as we can in all the language that we use.

That conclusion is "Research involving the derivation and use of stem cells derived from embryos remaining after infertility treatment is ethically acceptable for federal funding given an appropriate framework for oversight and review."
This is what we used to call sometimes case two to use Professor Fletcher's topology which is another paper that you have that we presented in your book.

This is followed with certain recommendations, although let's not get to those just yet.

DR. CASSELL: I am comfortable with that, also, but I feel strongly that in the science chapter we have to make it clear what those things really are. What they are in practical terms? What happens to them if they are not used and so forth so that people know exactly what it is we are talking about. So we are not talking about that abstraction called an embryo left over, which is not -- you know. So we -- the temptation to joke is impossible. So that -- so we know exactly what it is we are talking about.

DR. SHAPIRO: Okay. It is not clear. I do not think we have to settle right now whether that would go here or somewhere else.

DR. CASSELL: It can go in the science chapter itself. It does not matter.

DR. SHAPIRO: Okay.
DR. MURRAY: I have a question, I suppose, at this point about the conclusion on page 8 that actually derives from a report of NBAC's view, which appears on page 3, lines 13 through 15, in a sentence that reads, "It is NBAC's view that there is no compelling ethical justification for distinguishing between the derivation and use of human stem cells."

Now I have missed some of the discussions that the commission has had about this. I was quite surprised to read this sentence. In part, because I had -- my -- I paid attention, I thought, to what the Fetal Transplant Panel had said and they seemed to place a significant amount of importance on the distinction between where the cells come from -- you know, where the cells are derived from, that is the decision to have an elective abortion, and the subsequent use of those cells.

And it seemed to me there might be people for whom it would be at least a comfort if the Federal Government would fund perhaps the subsequent use of those cells which had been -- if they had been derived at other times by the people with private money. That is cell
lines that have been once established might be usable in the same way that tissue from an abortion which has already happened for other reasons might also be usable.

I mentioned this to Harold at lunch. We had a brief discussion about it. I just want to signal my -- I would at least like to have that explained to me, how it is that we reach that view because it is not my view.

DR. CHILDRESS: Eric?

DR. CASSELL: Well, I think we can go back a step and say that it has been offensive to some people to imply that somehow those cells having gotten here by the magic of being produced off site represent no ethical problem whereas the garnering of them did represent a problem. That is offensive. And for myself, I believe that there is not an ethical difference between their production and their use.

In part, because we are looking towards federal funding of the production of those cells and that that -- when we are clarifying this we are trying to move away from the pragmatic situation of how that actually came about up to now towards the situation of would the Federal Government fund the production as well as the use
of stem cells from those embryos that were initially

intended for in vitro fertilization.

DR. SHAPIRO: Steve, and then Alex.

MR. HOLTZMAN: I would like to second Tom's

thought and then try to provide an answer. The reason I

want to second your thought is because we encounter and

reject the complicity argument in the case of the fetal

in our work, right, and we analyze it as complicity as

three components. One of which we will just put aside,

which is the negative connotation. The two operative

components are the causality, all right, and what is

called here the symbolic association, all right.

And I think the argument had been made that

there is no demonstrable causal relationship between a

decision to abort and the creation of the cell

downstream. Whereas in the case of the ES cell you have

to, to get to the ES cell, have to destroy the embryo.

And I think that is where the salient difference will

lie.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: To take one further step

in the same direction, Steve, abortions happen one to two
million times a year in this country. There is nothing — there is no reason to think that people are becoming pregnant to create aborted fetuses.

The same is not true either of the creation of embryos or their use by people to create embryonic cell lines. Those embryonic stem cell lines would not be created if people were not actively engaging in the steps that lead to their creation so that the person who is using them, and I tried to address that on the last -- next to the last paragraph in that four-page memo that you have at your place in responding to the view that Harriett Raab put forward.

If you just imagine someone saying, "Okay. The government allows me to do the research with them but not create them so I cannot hire someone in my lab who is going to create them but I can set up a lab across the hall, have them create them and then take the money it requires to run that lab and pay it in terms of purchase prices for those embryos that I am getting from that process." And it is just -- "The stem cells from that process," rather.

And it just is a -- the linkage is not --
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this vague notion of complicity. A woman has an abortion and you later use her dead fetus to create a cell line.

But rather the whole activity of creating those embryonic stem cells only occurs -- and as Steve says involves this step of destroying the living cell, the living organism rather, because of your purchasing of them. And it just -- the linkage is just so much closer.

It may be that Harriett Raab, as a strict legal matter, is correct and I think Alan Flannery says, "Yes, it is reasonable to have concluded that." But I think as a moral matter it is very hard to defend that position and that is why that sentence is on page 3.

DR. SHAPIRO: Steve, I think you wanted to say something else.

MR. HOLTZMAN: I agree with Alex. I do not know if we are going to want to grapple with this or not but that critical difference which allows us to reject the complicity in the case of the fetal but keep it intact in the case of the embryonic stem cells, all right, plays -- cuts against potentially the way we have conceptually organized this. Because the four cases, the logic goes like this: It is okay with fetuses. Leftover
embryos are like fetuses. In other words, no one created
them in order to be able to get to the cell.

But what is built into that and you think --
take your words, no woman gets pregnant in order to
create these cells -- and we all agree that abortion is
not a good thing. It is a tragedy. It is a failure of
good social policies and good families, et cetera, et
cetera, all right.

We have built into our conceptual framework
in thinking about it that the creation of an embryo other
than to create a child is a bad thing. In other words,
the destruction of that embryo in the same way in which
the destruction of the fetus is a bad thing. All right.

And I am -- we -- because we are coming off
that paradigm of the reproductive act and the goodness of
reproductive frustrated. And I can imagine, all right,
many ways of creating embryos in which reproduction was
never in play to begin with.

And if you start from that paradigm, whether
with the thought experiment, which is not purely a
thought experiment of the ex corporal -- the ex
corporally maintained ovary that produces eggs, or you
start with the paradigm of somatic cell nuclear transfer of the somatic human nuclei into a nonhuman embryo, which never could be reimplanted, never would become a child, you might draw very, very different conclusions and a very different way of organizing this but we have built our conclusions in effectively into the organization of the four cases.

PROFESSOR CAPRON: Wasn't that what Harold Varmus invited us -- the thought process he invited us to do when he was with us? And again if you did not get it in the materials, I addressed it in the last paragraph of my Hasting's Center article. I quite agree.

I still think that there is a difference here, Steve, when it comes to saying whatever your view of legitimacy of it, it ought to apply to use as well as derivation. I mean, that is not the complicity argument. That was to use your very helpful division. That is a causation argument.

DR. SHAPIRO: And I think on this issue, I think as the discussion just indicated, there are differences between these two cases and there are differences in the arguments that you would make.
You cannot sweep them both together into a single argument and I think you can get them together in a number of different ways as a matter of fact. There is not one single way to do it. And you could reach conclusions regarding what we should perhaps calling case one and case two but actually say what we mean. But anyway for shorthand here there are different ways to arrive at case one and case two if one agrees with that but they are not the same.

I do not think there is any argument that would make them the same in both cases, that is the fetal tissue and the excess embryo, and we do need to -- whatever arguments we use we do need to make them separate and it is one of the weights of Tom's argument or observation that he made that is, I think, quite correct.

And the issue of whether one thinks of it as a frustrated procreation effort or something else, there is all kinds of ways to go with that. That is only one possible avenue by which to approach it.

Larry?

DR. MIIKE: One of the things Steve said was
that creation of an embryo for research is a bad thing. I do not subscribe to that viewpoint. I never have. I do not think that we actually had to state that even in our cloning report. We talked about creation of a living human being.

My concern about -- and you know I am against creating embryos for research purposes at this current time for reasons I have stated before but I do not think that in the abstract it is a bad thing.

DR. SHAPIRO: I expressed similar views in the first meeting we had on this but I also have the same conclusions you have on this issue that I do not think it is appropriate for -- it is certainly not at this time in any case.

Okay. I am sorry, Eric. Eric?

DR. CASSELL: In terms of that it is a practical and important matter that we do not confuse the cases.

DR. SHAPIRO: Right.

DR. CASSELL: Because one of the reasons for oversight knowing we now have begun to add in the idea that oversight is necessary in order that they are not
confused in the situation where that takes place. We have to make it clear in order -- so that everybody knows what we are talking about. This is a particular case and that is what we are talking about.

DR. SHAPIRO: Let me just focus our attention for a few moments on what is listed as recommendations at the bottom of page 8, top of page 9. It is my own interpretation -- it is my own reaction, I should say, to the first of these recommendations is that it is incorrectly stated since there is not a current ban or at least that is the general -- the accepted view that there is not a current ban to use existing embryonic stem cells.

This recommendation is either not necessary or should read in a somewhat different way. At least that is my understanding of it. And, frankly, my own view is that particular statement, I do not believe, is necessary but we can get back to that later. I think it just -- my own view is it could just be eliminated.

But there are two recommendations or partial recommendations on the top of page 9. One is a very definite action item that would be required in order for
this to all happen. Namely that Congress should rescind, in part, its ban on the use of federal funds to support research involving the derivation and use of embryonic stem cells. In this context meaning from the source referred to here as the embryos remaining after infertility treatments.

And the second recommendation there is federal agencies supporting research in this area should develop and maintain a system of national and local review of such protocols. I, myself, am unsure whether it should be national oversight and local review or some other combination but I mean some kind of system of protection which we will get to later on today or early tomorrow and discuss exactly what that should be.

But the key issues here -- the key recommendations which would flow from this conclusion would be that it would require Congress to rescind, in part, its ban on the use of federal funds in this arena and, second of all, that we would recommend some appropriate national oversight and local review or some combination of those things, which we would have to specify later in the report. We could not leave it at
that level of generality.

How do -- I think they flow very directly from the conclusions so I do not think they introduce anything new but are there any comments, questions, issues that they raise in people's minds?

Steve?

MR. HOLTZMAN: Yes. A general question.

When we speak about oversight and review and protocols, are we referring to -- I know we are referring to the derivation of the ES cells such as in parallel with the fetal being transplant -- about the conditions under which these are received. Are we also advocating a "RAC-like" mechanism for protocols using ES cells as well?

DR. SHAPIRO: Well, I have my own answer but -- my sense and my view of this is that given the system I have in my head, which is yet to be discussed, the answer is yes, it would cover derivation and use. That does not mean in my view that every protocol would be reviewed at a national level like the RAC was but that -- we would have to sort of circle back here after we understand what the oversight would really mean and what we decide in that area. That is my own thought but other
people could have different --

MR. HOLTZMAN: And the rationale for -- I understand the rationale for the derivation if I just look at the fetal -- at the transplant laws and an understanding of that. What is your sort of brief answer to the rationale for oversight of the use --

DR. SHAPIRO: My brief answer is that this is an area which is at the very least morally contested and we would want to build confidence that public oversight over the -- any research that would take place in this area. That is in a word what I have in mind.

Eric, and then Bette, and then David.

DR. CASSELL: Add to that, certainly in view of the issues raised by our witnesses on Friday there are social concerns about the use of this research and oversight will be necessary to know where these cells -- what are these cells being used for, where are they going, and where are the benefits of the research going?

DR. SHAPIRO: Yes, Bette?

MS. KRAMER: I quite agree. I wonder, would you limit it in any way, either by time or would you have that open ended?
DR. SHAPIRO: I think the -- oh, you mean the review process?

MS. KRAMER: Right. Would that go on indefinitely?

DR. SHAPIRO: I do not -- nothing, I guess, goes on indefinitely but I did not have in my mind myself saying for a year or two years or three years or four years. But that could be addressed if we go down that route. That could be addressed over time as we gain experience but I did not have any -- myself, any time limit in my mind.

David?

DR. COX: You are saying if a panel has the name "stem cell" on it, it does not become an immortal panel?

DR. SHAPIRO: We will wait and see. Science has to tell us.

Do you know of any committees that are not immortal?

David?

DR. COX: So, I just wanted to bring up the - - to say that I actually am very much in favor of this
idea of review of both use and derivation because of the points that have been made. But more -- but to carry another concept forward in that same vein, the -- it is looking at what the real utility of this is in terms of treatments. I have been struck by our testimony from different people that this possibility of treatments is what is really driving all of this forward.

In fact, Tom, that is the argument, okay, by which the -- and I am not saying it is a trump card but it is the argument by which this use of the extra embryos was proposed by a lot of testimony because of this potential benefit that, in fact, swings the pendulum.

Whether one buys that or not, you sure as hell want to figure out if that benefit happens. And I would say that the longer one goes on doing things and does not see any benefit, okay, the more my view would change in terms of not being able to have benefit be the argument any more.

So I think that this review of the use not only of how people are using it but what the outcomes are is -- would sway heavily on me in terms of -- in an ongoing review of this process -- what I would do.
I think that it is not going to be -- we are not going to make a decision and then that is it forever. I would really be very much in favor of this ongoing process and it is the process and the results of it that decide what you do in the future.

DR. SHAPIRO: Other comments or questions?

The next part of this -- and, of course, we can circle back to any part of this but we will just keep going through just to get ideas on the table for further discussion and consideration -- deals with a section on need for informed consent, which is -- begins on page 10 and then ends up with a recommendation in the middle of page 11, which reads, "Individuals or couples receiving infertility treatments should be given an opportunity to consent to the research use of embryos remaining only after the infertility treatments have ceased."

There may be better ways to phrase that.

PROFESSOR CAPRON: Kathi described for us at the last meeting, I believe, that some of the embryos that could be suitable sources might be those that are not suitable for reproductive purposes but it would be while the reproductive project is still continuing. So I
think we do not want language like this.

DR. HANNA: And I would suggest that since we are going to have Sander Shapiro here tomorrow to ask him some very detailed questions about what the process is there.

PROFESSOR CAPRON: It seems to me that the category we are talking about are people who have decided not to use particular embryos for whatever reason, either they are done with their project or they have been told that the embryos are not suitable, and then the alternative at that point is some other use, either discarding or some other use of the embryos, including research, is in prospect for them and that they would consent at that point.

DR. MIKE: I thought part of the testimony was that the issue came up when they were going to discard the embryos. That was the usual point in time which they asked them.

PROFESSOR CAPRON: But they may not be discarding them because one of the choices that could be presented to them, not with the ones that are not functional but with the ones that are functional, but
they do not want anymore, is would you like to give them
to another couple that wants to have a child and for some
reason does not have the embryo.

So it is -- whatever point where they are
either going to discard or no longer make their own use
of the embryo that their consent -- that this alternative
would be presented to them as part of a consent process.

DR. SHAPIRO: Steve, and then Larry.

MR. HOLTZMAN: Well, I would like us to
articulate clearly the logic because the rubber hits the
road here with the word "after."

PROFESSOR CAPRON: We have got one in.

MR. HOLTZMAN: Well, but that is the
separation in the fetal -- the fetal is from the
motivation to separate the decision to abort so if we are
adopting that as a model here then we need to clearly
state that we are adopting that and effectively why we
are adopting that. Why do we think it is important that
the decision to have that embryo go to the creation --
for research -- all right -- be separated.

DR. SHAPIRO: Bernie?

DR. LO: I think there are other
considerations that we need to highlight in this recommendation. Consent in this situation can be very problematic for a lot of reasons. In terms of the relationship of the woman to the IVF physician, concerns about financial incentives. And I think what we really want to do is to make sure this is really a free autonomous decision and there are lots of subtle and not so subtle pressures that can be brought to bear here.

And I think that it would be important to spell out, as for example the Human Embryo Research Panel attempted to do, sort of conditions under which this consent would be ethically valid. It is not just the timing. It is sort of the manner in which the consent is obtained.

Again I think it would follow the rule that you want to make sure that there is somehow no connection between the decision to donate and other decisions having to do with infertility treatments. So certainly the notion of giving a financial discount or some other consideration for the donation of the embryos could potentially be a very compelling motivation to donate embryos and I think we want to try insofar as possible to
exclude that as a motivation.

DR. SHAPIRO: I think my own reasoning on this is, I guess, similar to what Bernie was just expressing. I think we should try to the extent possible to separate these issues and decisions from other important decisions that go into the nature of these fertility treatments, the number of embryos produced, the amount of superovulation that takes place.

I want to cut down, I mean to the extent that one can do it, any other motivation for producing embryos other than helping the couple with their project in this case focusing on infertility treatment and so on and that is an inexact science and clinical practice as it currently stands now.

And so I am trying to sort of do what we can.

In my head I am trying to do what I can -- do not say this language has got it right -- to do what I can to make sure that there are no inappropriate incentives in there that would actually do things that are not related to the treatment -- infertility treatment or related to some other objective sort of quasi-hidden
from the subject. That is what I had in mind.

MR. HOLTZMAN: It is just a really tough area because remember when you superovulate the woman you do not get embryos, you get ova, and she is allowed to sell them to the highest bidder, as many as she wants.

DR. SHAPIRO: Yes.

MR. HOLTZMAN: And we are not touching that.

DR. SHAPIRO: That is right. That is correct. We all get ads in newspapers. We see them all.

PROFESSOR CAPRON: Particularly for --

DR. SHAPIRO: That is right.

(Simultaneous discussion.)

DR. MURRAY: Now, Steve's observation, I just want to emphasize that is -- I take it that is a report of the law, not a report of what is ethically desirable. Is that fair enough?

MR. HOLTZMAN: It was also a report on if we are going to go to the underlying motivations that are going to support or a logic that is going to support these kinds of distinctions, we might wish to observe that their grounding implicates other social practices.

DR. SHAPIRO: I agree with that.
Bette, do you have --

MS. KRAMER: No. Just what Steve said got by me. I am not -- I do not know exactly what you are talking about.

MR. HOLTZMAN: There is different ways of grounding and trying to separate this -- the decision to have the embryo used in a certain way as opposed to for reproduction. If you locate the locus of that moral concern in the embryo, much as was the case in the fetal regulations, you can deal with that alone.

If, however, you start to locate the locus of the concern in terms of things like how the woman is treated, the super ovulatory regime, the notion of separating it from pecuniary interests such as Bernie articulated, then what you are really going to find is that it is less an issue about the embryo than the role and conditions under which certain practices having to do with very defining issues in our lives such as reproduction, which includes the production of ova and sperm, that are equally implicated.

And it so happens we have not touched that in this report and we have this funny situation that ova and
sperm can be sold to the highest bidder in as large
amounts as you want.

DR. SHAPIRO: Kathi?

Excuse me, I am sorry, Bette. If you want to
follow up, go ahead.

MS. KRAMER: It was precisely that that I
wanted you to spell out that --

MR. HOLTZMAN: The latter? That that is
ture?

MS. KRAMER: Right. I guess I did not know
that and also the fertilized -- the embryos themselves?

MR. HOLTZMAN: No. You cannot sell those.

You can sell your ova.

MS. KRAMER: What happens? Does the couple
who --

MR. HOLTZMAN: The woman who is
superovulated, the ova are collected and they are IVF'd.

Before they are IVF'd.

MS. KRAMER: Right. I realize that. But in
the case of a fertilized embryo that a couple is no
longer going to use, if they donate those to another
couple, is there -- can they receive a payment for that?
DR. HANNA: They can only receive reimbursement for any costs incurred from the procedure or the transport or the transfer. That is all.

MS. KRAMER: But that is -- I mean, that is very vague. I mean, what part of -- the IVF -- the whole IVF treatment is a very expensive process. So what portion of that treatment can they ascribe to the production of that embryo that they are now going to donate to this other couple?

DR. HANNA: If they are paying a storage fee and they are paying the storage fee while the couple -- the recipient couple is located they could possibly be reimbursed for the period of time that they are paying for the storage. It is that kind of cost.

DR. SHAPIRO: Okay. I have a lot of people on the list right now.

David, then Trish, Alex, and Bernie.

DR. COX: So I think Steve is correct in that we are not dealing with the issue of the eggs and the sperm. I could actually care less about the sperm. I care a lot about the eggs because I actually personally view the eggs as an organ and that we do not sell other
organs and I do not think we should sell eggs. I would
like to see that issue addressed by our commission.

DR. SHAPIRO: Trish?

DR. BACKLAR: In a way that is exactly what I
want to talk about because I am very concerned about
using women in this way. I think this is going to be a
very difficult and tricky part of it. Once we look and
hear about people, individuals or couples, who are
planning to have children but, in fact, you have got to
go to that source of eggs and how we deal with that is
going to be extremely important and we cannot get away
from not addressing that.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: Well, I think the only way
we can address this without taking on a huge subject,
which is the whole reproductive subject, which is ripe
for someone doing something with it, it has been -- as we
know from the cloning report -- the scandal of American
biology as it were, biomedicine, is to emphasize that if
we are talking about situations in which the IVF embryos
or the so-called spare embryos from a reproductive
process, then we are talking about those which have not
been purchased at least on the face of it solely to

generate embryos for research.

So the limitation -- I mean, all the
complications that arise, David, in the purchase of
embryos and the use of these college students as a source
of them, and so forth, and so on, are subsumed under the
fact that that has taken place in a process which is
subject to whatever controls the American Fertility
Society or whatever it is called, the American Society
for Reproductive Medicine imposes, or state law imposes.
You see what I am saying? I mean, I -- otherwise, we
have to write a whole separate report.

If we were talking about the creation of
embryos for research purposes directly and solely then
the people would be out in that marketplace buying ova
the same way that the fertility docs are buying ova and
then we would be deep into it.

But here because it is a secondary situation
I think we have to describe the situation a little bit
and I do not think we have to deal with it as fully. I
do not think we can possibly in the scope of a report
that is due in a few months.
DR. COX: I would like to think about it because I would like to be extremely creative on this point.

DR. SHAPIRO: Bernie?

DR. LO: Let me just raise an issue which I think is going to be difficult and we will have to face. As I understand from the meeting last week where the religious leaders came and spoke, a very important theme was the theme of justice and distributive justice and sort of fair allocation of burdens and benefits.

I think most of us intuitively would agree with that but this is one of those points where the desire to follow those sort of ethical precepts runs directly counter to other important ethical precepts.

So in a sense one way which you can make both -- make the burdens of this research more equitably distributed and to try to ensure that the fruits of the research are distributed in a just way, is to allow payment to those who are now worse off under the system as a way of recompensing them for taking on additional risk.

And what you fall into here, it seems to me,
is the old sort of paternalistic trap of saying that this is such a grave concern that even though there are many women who may say I would, you know, be willing to run the risks of superovulation to enable myself to get the money to either pay for the IVF treatment or to do other things. We are closing that off in our desire to sort of remove the taint of financial consideration from these decisions.

I support that as well but it is hard to have both. It is one of the situations where the ethical principles are in conflict and it would be nice to do them all at the same time but it is going to be very tricky.

DR. SHAPIRO: Arturo?

DR. BRITO: I want to respond to something here because I think it is not real clear here what was said about distributive justice. The issue is not distributive justice with what to do with human embryo stem cell research, et cetera, but it had more to do, as I heard it -- maybe, Jim, you can help me with this -- but most people that talked about distributive justice or the beginning of the argument was basically concerns
question of utilization of any public resources for this purpose when we have so many other unmet health care needs.

Is that correct, Jim?

DR. CHILDRESS: Yes.

DR. BRITO: Okay. I am sorry if I said something incorrect this morning or did not explain it right. But not -- we are not talking about that religious leaders there were saying, well, it is not fair that, you know, if it is private funding and it is going to be available for certain segments but we are talking about any use of public funds for this.

The only time this came up about the distribution of the benefits from this type of research or if we are going to go ahead and do this anyhow then we maybe should have some federal funding for oversight of this somewhere in that context.

So I do not know if I --

DR. CHILDRESS: No. I think you are correct in reporting it. There were several subthemes of justice, though, that could be pulled together and I think what Bernie was doing was saying if we are going to
emphasize social justice we have to recognize the way in which it may run in contention with some other concerns on a more generalized level than simply what was said last week if I understood Bernie correctly. And I think he has rightly identified the tension between the risk of exploitation versus respecting autonomy, say to set it up that particular way.

DR. SHAPIRO: I would like to make a point in this distributive justice issue that you just talked about. As I look at the language of what we have here so far, and I have not looked at it that carefully, I suppose, it talks not about whether one should do this but it talks about whether such research should be eligible for federal funding, which means you put aside that particular aspect of distributive justice, which is an important issue.

I mean, I completely agree with all those people who think it is important but that is a matter of priorities in health care research and whether this -- whether you -- there are lots of things that we could do that we do not do because they are not considered important enough and so on and so forth, and this could -
- you know, some people could say this might fall in that category.

I just do not know. I am not -- I do not think that we are being asked to make that decision because that involves lining up all the health care alternatives and all the other public responsibilities we have and making a decision. So we are not -- so that aspect of it, I think, we are just passing on and that is what the "eligible for" is meant to convey. Perhaps we do not do that very effectively with the language here.

DR. COX: This is a critical point, Harold, that I really think needs to be emphasized because it is an argument that is made all the time about one type of technological research versus another, is that if you did not do any of this research there would not be any poor people in the world. I mean, I have heard this argument in numerous meetings.

So it is not about that is not the decision that we are making here. We are just putting it on the table for that debate about, you know, whether funds should actually be spent on it.

DR. SHAPIRO: Let me just move on a bit. I
do not want to claim at all that we have resolved this issue here but those have been very helpful comments but I do want to get before we break -- to look at the conclusion, which is on page 11. And that conclusion says as follows:

"At this time there are no compelling reasons to provide federal funds for the purpose of making embryos specifically for the generation of stem cells. More research should be done on pluripotent stem cells..." Let's not worry about just which way we describe these and focus on that. That will have to be done carefully everywhere. "...derived from aborted fetuses and embryos remaining after infertility treatments to determine the extent of need of these additional sources of embryos for research."

I am not sure that I like the whole language but you get the point.

Alex?

PROFESSOR CAPRON: I would favor -- I do not know how close what is written here is something that would be in black letter when we get done but I would favor the second sentence not being part of the
conclusion. I mean, it seems to me that the argumentation that must be given for this is more than that sentence and that sentence does not need to be privileged among the arguments.

One of the other arguments was the one I was suggesting to Eric, which is there are two reasons that are given here for this research. One is that creating embryos is necessary just for the denominator. You just need to have a large number of these cells and you are not going to be able to get enough. I guess there is three.

The second one is somehow those cells would be controlled differently. You would have more control over them or something.

But the third is that only when you are creating a cell would you have the opportunity to create it with -- to make autologous transplants or something, which is when you would be doing directed transplantation. And we do not know that we are anywhere near having a capability that makes that sensible and so there is a whole other set of arguments as to why it is not compelling.
I would prefer to see all of those arguments gathered as commentary to explain why it is not compelling.

DR. SHAPIRO: Other kinds of comments or suggestions about how we can focus and improve this? Steve?

MR. HOLTZMAN: What is the grounding of the argument we are going to use that says that in the case of all embryos that we need a compelling reason?

DR. SHAPIRO: I will certainly give you my answer if you want that but does anyone else want to -- as to why we should have this --

MR. HOLTZMAN: No. When we have this, we are putting together all embryos into a single bucket, and now we are saying there is a need for a compelling reason to change this and I am wondering what is the argument that we are going to use that says that they should all be bucketed together, number one. And, number two, that we need a compelling reason.

DR. SHAPIRO: I am not clear on the bucketing together what you are referring to here. I just want to be clear.
MR. HOLTZMAN: Well, just to say embryos will include embryos created by SCNT.

DR. SHAPIRO: Yes.

MR. HOLTZMAN: Right. It will include embryos -- well, will it include embryos where it was made with a hybrid? Are we going to include those as well? I am just asking. Are we going to put them all together, number one? And, number two, the single compelling -- what would be the -- why is it the case that we need a compelling -- I will stop being obtuse.

Okay.

DR. SHAPIRO: As opposed to a reason?

PROFESSOR CAPRON: Why is the standard sufficiency instead of compelling rather than --

MR. HOLTZMAN: Exactly. Okay. If you take seriously the materials from Dworkin, for example, and we seem to be building some arguments around this notion of a detached view, as he calls it, or some others would use different terms, all right, then the issue is whether the act, all right, goes against, all right, the inviability of life, all right, and then one can imagine a number of
different kinds of circumstances in which an embryo comes into creation, some of which more than others arguably are in violation of the notion of the sanctity of life. That is the gist of that whole line of thinking which I think Eric over the time has been saying let's stop staring at the embryo and looking for the source of its meaning and role in how we view it, all right, at the embryo instead. Looking at its context in our lives, including how and why it was brought into creation. We are adopting an intellectual framework and putting them all together and saying that we are going to take the embryo -- quay embryo is definitive -- and look for -- therefore, you will need compelling reasons for research purpose embryos.

DR. SHAPIRO: Okay. Larry?

DR. MIKE: I agree we do not need the word "compelling" but I am just looking at this in terms of if we have access -- if there is access to aborted fetuses and excess embryos in IVF's, given the stage we are in realizing the promise of this research that is ample opportunity to move to the next step to try to prove a stronger case.
I am looking at it from just a straight forward balancing and practical test. There is enough concerns expressed by many people with different points of view that are worried about this whole area all together. So I look at it as a step-wise fashion. There is now, compared to four or five years ago, more concrete evidence of benefit and we are now saying let's give enough of an opportunity to see whether that -- we get closer to a realization of that before we just sort of open the gates and say, "Hey, great, you know, there are some benefits now. We can do everything -- we should do everything we can."

DR. SHAPIRO: Eric, David?

DR. CASSELL: That is my response, also, what Larry said.

DR. SHAPIRO: David?

DR. COX: This comes back to the argument of -- especially in the case of using animals -- to basically realize the promise by which that -- we are proceeding with this in the first place.

As a scientist, Steve, I really understand your frustration. Just actually last week I thought of a
really cool experiment that would involve doing human nuclear somatic cell transfer and making an embryonic stem cell that I would like to do myself. But even though that science is a driving force on one side, all of this testimony from people in our society is a driving force on the other side.

So until I can see some of those results happen in animals that is what I have come to just for myself.

I hear, Steve, your argument and I understood Harold's argument -- Varmus' very clearly in that, well, maybe it is not really life itself, it is how we generate life. But, I mean, that does not even pass the red face test for me.

The -- now -- and that is -- and I do not say that lightly to sort of, you know, not consider seriously the possibilities but for me that is just not even on the radar screen. I mean, life is life. And now is an embryo life? I do not know but the process of making an embryo is not what I am talking about. I am talking about the embryos.

DR. SHAPIRO: Tom?
DR. MURRAY: I have more a sort of question than I have a comment. If I understood Steve correctly, Steve said that our recommendation -- not our recommendation, the draft recommendation on page 11 conflated to two things. And one of them has been in the draft, is what -- why do we have -- why do we demand sort of a higher level. We called it compelling. Maybe we use different language of a higher level of argument or proof before we would permit the creation of embryos for this purpose, and some people have responded to that.

The other question was, I think what Steve asked, was why do we put together that the embryos that might created by different sorts of purposes, some of which would seem to be not at all viable and others of which might be. And I do not know if that is a distinction people wish to go further with or not so I just pose it as a question.

PROFESSOR CAPRON: Some of which, in theory, may be viable or not but we do not dare do the research to find out if they are viable.

DR. SHAPIRO: Bette?

MS. KRAMER: Wouldn't it be sufficient for us
to say, much as Larry suggested, that at this time we have created the opportunity to go forward with the research and while these other questions may have to be addressed in the future that is going to be dependent on the development of the science, and just let it go at that. I mean, I do not think that is copping out at all.

DR. SHAPIRO: Other comments?

Larry?

DR. MIIKE: Just in response to Tom's question. At the religious scholars meeting I did ask Ed Pellegrino that very question. I said, "Would you differentiate between a fertilized egg that had no chance of becoming a human being?" And he said, "Well, there is no certainty about that." I said, "Yes, there is. There are women who have defective cytoplasm that they grow to a certain point and the egg always dies." And he said, "All right. Then I see no difference between them." Well, I do. I see a difference between those but he said he did not.

DR. MURRAY: Just to clarify, Larry, that for -- again it is always from the point of perspective, predictions. Ed Pellegrino saw no difference between an
apparently fully viable embryo and one with cytoplasm where there is no chance. He said, "Morally there is no difference."

DR. SHAPIRO: On the issue, first of all, of compelling let's not get hung up on that. That is just a word. I do not think we have to deal with compelling myself.

My own view on this issue, and it just -- I think that among the commissioners there is undoubtedly different ways they have reached -- for those who agree basically with this stance, there are probably quite different sets of reasons amongst people.

As I have expressed myself before at the commission meetings, I am closer to Larry's view so I will not repeat it. Namely that I, myself, do not see the big ethical differences here between some of these cases that other people see and think about but I come to this conclusion out of respect for the fact that I am not the only one that is involved here.

And in trying to echo back and to give some consideration to different perspectives on this issue that is essentially where I come out on this. And
recognizing that there are lots of different views in our
society about this and looking for those areas or for
those set of recommendations that might be both helpful
to the country overall in going ahead and respectful to
the extent possible of the fact that there are different
perspectives on this issue.

But if I were arguing it myself in ways that
I would find fully satisfying, purely on ethical grounds
that I find convincing, I would come to a different set
of conclusions than reflected here.

Jim?

DR. CHILDRESS: Just to add a thought to
that. Without taking a stand on the substance of the
issue, now it does seem to me that we have to distinguish
it as Harold just did between the kinds of reasons that
we individually personally would find satisfactory and
the kinds of reasons that take place in a public context
of justification and some of those will be more
political. Some will be more cultural. Some will be
more ethical, however we define them. But we do have to
attend to the range of views there.

PROFESSOR CAPRON: Excuse me. Looking at the
chart that your assistant -- your graduate student provided.

DR. SHAPIRO: I do not know -- let's make sure people have that.

PROFESSOR CAPRON: It is attached to --

DR. CHILDRESS: I would urge a great deal of caution on that just as a draft at this point of that part of the discussion so I would not recommend focusing on that. This will be tried out on a lot of other people, including the participants.

PROFESSOR CAPRON: Okay. What I wanted to ask because the chart does not quite get at this in any case, the conclusion, with which I also agree, Harold, would obviously, one, where if our report makes any difference in a sense of what response it is going to get, it has to appeal to more than ourselves.

The question would be are there any -- of the people who are articulating opposition to this work but who recognize some value from it, who draw comparable lines on arguments of a religiously differentiated view that says when you are dealing with an entity which in their view is not yet a person but is a human being, and
therefore is entitled to different treatment than just any other group of cells or lab animal. And a lab animal of a sense and sort gets different treatment than an amoeba or something. I mean, so all these gradations.

But this particular gradation that they would say since the entities that we are dealing with here do not explain the difference, does the fact that we are talking about entities where the choice is to reach into the discard bucket and take out an embryo that is on its way to death but isn't yet dead at that moment, and would say, yes, it is permissible, it is less of an offense to a sense of protection, it is less of a threat to humanity than developing a process in which you create these entities for that purpose.

Is there any religious echoes here?

DR. CHILDRESS: I would ask my colleagues and I will also have to refer to the transcript to be sure on just from the discussion we had on Friday. I have a vague recollection that in terms of the kinds of categories that say Pellegrino used in terms of moral gravity that there be certain kinds of distinctions that would be present but again not fully elaborated.
But then again the view, for example, expressed by Rabbi Tendler in Orthodox Judaism that the extracorporeal embryo has no value at all. It is the location in the womb that would provide it value. It gets back to a different view of the context but context is something we have focused on here.

But I am not sure. Maybe Eric, Arturo or Larry could refer to some specific part of our discussion that might address Alex's point.

DR. MIKE: Well, first of all, also there was the Jewish opinion that anything before 40 days was really not something to worry about. But, Alex, it was interesting to me -- and I do not want to focus on Dr. Pellegrino but he was the one that gave this answer, even given all of that he also came to the conclusion that if it goes forward we should have oversight in the private sector and if we fund in the public sector then, of course, we have to have oversight in the private sector, too. So even while he is absolute and adamant, he sees that if something goes forward he still would like to have safeguards. And I do not think he would see that as being complicit in the underlying objection that he has
to it.

   DR. CHILDRESS: Though he does intend to
   provide a memorandum on that particular topic, the last
   one that Larry mentioned.

   DR. SHAPIRO: Arturo?

   DR. BRITO: From my own notes something that
   Dr. Pellegrino stated, and this may help a little bit, is
   exactly this: "The fetus and embryo have the same moral
   status and rights towards protection." And then in
   reference to IVF spares he further went on to say that
   embryos created specifically for research have the same
   moral status.

   Now with that said, the three representatives
   of the Jewish faith said exactly this: "Forty days and
   implantation were key times."

   At the end of this when Eric Cassell
   summarized this in what I counted as nine points that we
   all agreed upon, everyone in that room, no one said they
   did not agree with this, is that regardless of the final
   outcome, it required the respect -- outcome meaning what
   we -- our recommendation that we make -- it required the
respect for human embryo and that it is important to continue to look for alternative sources.

So I do not know if that answers your question or not but basically there is the whole gamut of where the embryo -- the moral status of the embryo is but everyone agrees that there are -- that it is -- because of the benefits that it really muddles even in their own mind, and this is -- what I got is it muddles in their own mind what to do with this now and that they are willing to concede to some degree that we just have to respect the human embryo regardless of what we do and -- but it is best to try to look for other ways of doing this kind of research.

PROFESSOR CAPRON: Because obviously I would like to have any -- other than narrowly pragmatic support for the conclusion that I think Harold articulated and Larry articulated and Eric agreed with, and in the fetal area we know that some people who are against abortion say the complicity argument means no research with the fetal remains.

But others who are against abortion say if we are convinced that the procedural protections are
adequate then we think that certain approved types of research are valuable enough to allow the use of the fetus.

Of course, a third category says do not see any problem, a dead fetus is just like any other dead body. Do not worry about it at all.

But in that middle category you have some people who would be against abortion and I am just wondering if there is any recognition in the community that when you are dealing with these tiny IVF embryos which, you know, Margaret Farley was making statements about, when they are not created for this purpose but are rather on their way to discard anyway, the argument is comparable to the fetal remains argument.

And so that you -- that what we are worried about is a systematic program which creates the risk of coming to regard embryos simply as a commodity and that would be a risk some people would argue if you start a program in which you are creating embryos for research purposes or, you know, for decorative art purposes or, you know, whatever, I mean it just gets offensive and they say do not go down that road because that diminishes
respect for human life.

Whereas here you are not diminishing it and that is what I am looking for and maybe staff should just search high and low to find any articulation of that view with assistance from Jim and others who know the religious literature, the ethical literature.

DR. SHAPIRO: Eric, and then the other Eric.

DR. CASSELL: From Friday's discussions the idea of not going down that road that you were talking about where you are creating embryos, everybody was very clear about that who cared about it. There were, you know -- and some that did not. But where there was concern everybody was clear about that.

Respect for human life everybody was clear on.

The reason the other embryo that was on its way to be -- you know, that is on its way to just dying becomes a possibility is not merely for pragmatic reasons or practical reasons, it is because its situation is ambiguous.

The conception of it -- excuse me. That is not a good word. The idea of it previously as an embryo,
this is a living embryo, does not really hold up because if it is not going to be implanted -- and we are talking about this little speck. It is not living in the sense that people previously conceived of it especially when it was merely a black and white argument against abortion.

At the present time the problem comes -- as I -- to repeat, not merely for practicality but because of the ambiguity inherent in that entity.

I hope that when we hear from the IVF person tomorrow we are going to know a little more about that. We are going to find out a little more about that entity and understand better why it is ambiguous.

DR. SHAPIRO: Eric?

DR. MESLIN: One note of caution. I would not want commissioners to rely exclusively on the meeting on Friday as evidence of widely held views in the public. There were ten or more individuals who shared similar commitments to some issues and had different commitments to others.

At the same time there were at least two or three examples. One, Ron Cole-Turner, a Protestant theologian, and Nancy Duff, a colleague in the same
tradition, and Demetrios Demopulos, a Greek Orthodox
priest, who I think described very well the paradox,
Demopulos in particular, that he was in.

And, in fact, Arturo may want to speak to
this but when asked how can you hold what appear to be
conflicting views on the one hand opposing the
destruction of human life, yet on the other hand
acknowledging the importance and, in fact, the waste that
might occur by not taking advantage of and making use of
already aborted tissue, gave what I thought was a
wonderful response. He said, "That is a true paradox and
it may be inconsistent but I happen to hold inconsistent
beliefs."

And we will share with you their full
testimony. Each of them providing no fewer than five or
six pages.

The other point, and it is in your briefing
books, is the survey that Lori Knowles did, which shows
at a public policy level how other national commissions
and bodies have also struggled with this.

So while we may not find in response to
Alex's question any public opinion poll that you can turn
to that will give you an empirical answer, the struggling that those folks did publicly on Friday and the outcomes that national commissions and other bodies have struggled with publicly should situate you right where you are, and that is on the -- in this sort of paradox position that Demopulos was in.

DR. SHAPIRO: Eric?

DR. CASSELL: And further it is like finding that everybody is uncertain, and on one view there is nothing to be said about that and what can one say, everybody is uncertain of it, and the other view is the uncertainty is the fact.

And in this instance Demopulos also said, "Well, a Greek Orthodox loves it when they are in a paradox." That is what he said. That is the best place he can be is in a paradox.

But, in fact, the very fact of the uncertainty and the paradoxical situation is the fact that we face and it makes the solution -- I think it makes for the ultimate way of getting out of it rather than making it impossible to resolve.

DR. SHAPIRO: Thank you.
Any other comment on this particular issue right now?

Let me make a suggestion. Let's take a break for 15 or 20 minutes. Then let's -- I would like to then talk -- spend some time talking about possible oversight mechanisms or some suggestions in here and we ought to talk some about that and see what we feel about that.

Let's take a break for about 20 minutes. Let's try to reassemble at 20 to 4:00.

(Whereupon, a break was taken from 3:23 p.m. until 4:00 p.m.)

* * * * *
EVENING SESSION

DR. SHAPIRO: Colleagues, could we reassemble, please?

Colleagues, I would like to focus the remaining time and energy we have this afternoon on the issue of national and/or local oversight and/or review of research in this area if such research, federally funded research, is to go forward.

There is a recommendation in your report, which is really on page 17, about how such a mechanism might look. I would say a few things about it. One, I do not think you should take the term "ethics advisory board" seriously. That is obviously -- it should be in quotation marks if anything. We certainly -- at least speaking for myself -- certainly do not want to use that term. It has a lot of baggage associated with it, which is not necessary to take on. So if this was a good idea all together we would have to develop another name.

But the proposal on 17 really in some sense is almost like an accrediting body you might say, that is as I understand it how it is laid out here, that some type of national organization and national board would
have to sort of approve local IRB's capacity to review
protocols in this area.

This tends to have a national -- as
structured here in a very loose way, tends to have a
national group to sort of credit, you might say, IRB's
but the local -- the review actually takes place at a
local level, and there is various characteristics of that
review and so on which is laid out here.

So this is, I think, an incredible idea that
was put together by Eric and others on the staff, and the
question is not only what do we think about this but what
are the mechanisms we should think about in terms of
oversight. Should it be just local? That is one way to
do it. Should it have a national review component or
not? If so, should it be an oversight component or some
other kind of authority that you might want to give it.

It is very much an open issue as far as I am
concerned.

Larry, and Steve?

DR. MIIKE: I just want to ask a clarifying
question. The second proposed recommendation in the
middle of page 17, is this kind of research subject to
human subject protection?

DR. SHAPIRO: Is this kind of research subject to human subject protection? I think you have too many subjects in there. But anyhow that is the question.

MR. HOLTZMAN: And the related question tied to that is assuming it was not and that it will be conducted in many places which are not associated with hospitals, those places do not typically have IRB's.

DR. SHAPIRO: Well, lots of places have hospitals that are IRB's.

And I do not know the answer to the question you asked, Larry.

Bette?

MS. KRAMER: Well, since we are writing this can't we require it?

DR. SHAPIRO: Oh, yes. We can require anything we like. Sure. We can recommend anything we want.

MS. KRAMER: Right, we can recommend.

DR. SHAPIRO: We cannot require anything.

MS. KRAMER: It seems to me it would be more
efficient to have it be a national body because you are
going to want to have a -- you are going to want to have
people on it who are abreast of the latest in science and
why not do it once instead of having to do it in 50
states.

DR. SHAPIRO: Well, you mean have a --
something sort of equivalent to the RAC? If you want a
research protocol in this area you submit it to some
national body.

MS. KRAMER: Right.

DR. SHAPIRO: That is one possible model.

Eric?

DR. CASSELL: I like that, also, because --

DR. MESLIN: We cannot hear you.

DR. CASSELL: Sorry. I like the idea of it
being national rather than just local -- rather than
local because the issues in this, I think, the body ought
to be accumulating experience with this. The thing is a
constantly moving field so that the people have to be
knowledgeable. It just would not do to have the usual
IRB handle this.

I want to say parenthetically I am interested
if we have something that describes the British oversight mechanism, if we could see that sometime, maybe even within a day or so.

DR. MESLIN: There is a description in Lori Knowles' paper about that. We can extract parts of it if you would like.

DR. SHAPIRO: Bernie?

DR. LO: I think this issue is really important so I think it is good that we are dealing with it early on.

I have a series of questions and I guess one big question is sort of what is the goal of this review? I think there may be a number of goals. One is obviously to prevent ethically problematic research from just sort of continuing without some deliberation. But, secondly, I think there is also sort of a publicly reassurance goal of demonstrating to the public that we are -- that the country is sensitive about problems, potential problems with this research, and that the review is tangible and can be sort of looked over by whoever is interested in doing it.

I think the more you decentralize it the
harder it is to really know what is actually going on.

It seems to me a third goal Eric sort of suggested was to accumulate sort of a body of wisdom coming out of specific cases, specific protocols, so that over time if things go well certain issues which now seem controversial or uncertain will become more settled. We have gone through it and we have gone through the arguments, and we have seen how it works.

So I think that given -- if we think that those are some goals we are trying to achieve then the balance between local and national starts to tip, it seems to me, in the direction of a national arrangement.

DR. SHAPIRO: Thank you.

Larry?

DR. MIIKE: On that issue I would agree to have a national review board but I think that there should also be built in some learning experience for the IRB's so that there is a process in which the IRB's, that is the institutions, are somehow involved in it. I do not know how exactly to do that but I think it would be a mistake to bypass the locals if only just for the issue of familiarizing themselves with that research.
On the issue about the human subjects research, I guess -- whether it applies or not but it occurs to me that even if it does apply, so much of those oversights are for the protection of humans, and where is the human in here that we are going to protect? So what is the relevance of that review process?

DR. SHAPIRO: Eric?

DR. CASSELL: We have two humans. At least we have the progenitors of this entity that has to be -- that have to be protected, consent is required and so forth, confidentiality and all those things. And then we have the embryo itself and there the issue is an issue of respect and protection in the classic sense is not the same as respect but that is a real thing.

DR. MIIKE: I understand that but I am just thinking in terms of what actually is on the books and what we are proposing.

DR. CASSELL: What is on the books is different and I do not know what is on the books.

DR. MIIKE: I mean, what is on the books. I wonder if we are proposing a human biological materials study. How relevant that is to the kinds of interest
that we are concerned with in this particular field?

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Well, I think those arguments, Eric, are important arguments and the question then is if we are going to be proposing any kind of oversight how will it differ with respect to the creation of these cell lines versus research using the cell lines once they are created. Are those -- your point about there are two people involved. It does not seem at least prima facia that is the case once you are talking about a protocol to do research with cells that have already been created.

DR. CASSELL: Well, I think that my answer to that is I do not know the answer to that and that is one of a set of issues that an oversight organization deals with, trying to figure out -- remember we did talk about the fact that we did not want to see them -- we wanted to see distributive justice in the way the results of the research is used and there is a local way of doing that as well as a further out way.

We wanted to make sure that it is not used primarily in a money making sense that the cells once they get out there are not merely a way to make money.
There are a number of social issues. Now on the other side of this -- on the other side of that are people who would argue entirely differently about it. That is a subject for discussion. Those are things that have to do with the use of those cells after they have been harvested.

DR. MIIKE: Could I butt in just one last time, Harold?

Eric, all I am raising is I am not contesting the issue about oversight. I am contesting the issue about using the human subjects research model as the oversight mechanism.

DR. CASSELL: Very -- I do not know.

DR. SHAPIRO: David, and then Bette?

DR. COX: So for the reasons that have been stated, I am in favor of a federal level rather than a whole bunch of individual local levels. The one thing about the review, and this is what Steve brought up, is I think that there is a real distinction in terms of the questions to be asked in a review in terms of whether you are creating new cells or whether you are using already existing ones.
And my main issue for people that are already using the existing ones, at least in the context of federal funding, and I have not thought this through for nonfederal funding, but it would be to collect data on what the results were. What is it that people wanted to do and what was the results?

Now that is difficult to do in the private sector but certainly in the context of federal funding we do it all the time. That is the trend that what you do is you let people know who is working in a particular area and what is the body of knowledge that they found.

Certainly if we are going to focus on this -- is the promise being realized? That is a way of collecting data and finding out about it.

The -- I do not like the idea, though, of having separate types of goals for reviewing this in the public versus the private sector so that is the -- the -- my critique of my own idea.

DR. SHAPIRO: Bette?

MS. KRAMER: I have a different feeling about it. It seems to me that in the recommendations that we are considering making that we are asking society to make
a dramatic change in its acceptance of something that is
very morally charged and is objected to by a lot of
people. It has been historically objected to by a lot of
people.

And that, therefore, it behooves us to come
up with a mechanism by which society is going to be
assured as much as it can be and it is going to be kept
informed and is going to be assured that it is going to
be -- that the whole process of a scientific
investigation is going to be monitored properly and that
society is going to be informed, as I said, as to whether
or not -- whether or not the concession to allow this
work to be done is going to be justifiable in terms of
the rewards that will come back to society.

So I think it is a different model from, you
know, IRB's and local supervision. I think it requires,
you know, the very best talent in terms of the appraisals
that will need to be brought to it.

DR. SHAPIRO: Bernie?

DR. LO: There is an issue that David touched
on, which I think we need to sort of confront head on,
and that is sort of the scope of this national panel.
Is it confined to federally funded or projects seeking federally funded or do we think this type of oversight ought to extend to privately funded research in this area, as is the case, for example, in England? That would seem to me to be a very big departure from the current practice of a lot of implications for sort of what is the grounds on which you would have this kind of level of --

DR. SHAPIRO: Let's come back to that issue. That is a very important issue.

Just listening to the comments around, it seems that at least everyone who has spoken believes that this type of research, now talking about derivation and use, should be reviewed at a national level, sort of the RAC type thing.

Now let's focus on that for a few minutes just so that we can get alternative views out on the table on that issue. It is a local versus -- there is a lot of arguments have been given so far about why local review would not be adequate at the current time. Maybe at some future time. And that we need some national review of the research in this area -- proposed research
protocols.

Is there different views on this? Now would be the time to tentatively propose them.

Bernie?

DR. LO: Well, I think the concerns that many scientists in the field would raise would be the prospect of inordinate delay.

DR. SHAPIRO: Right. I understand.

DR. LO: And the -- you know, to some extent there is going to have to be a trade off between kind of the review and sort of transparency and public accountability as sort of the quid pro quo of the price for federal funding. But I think it is important in terms of how we design it that it not become so cumbersome that, in fact, it serves as a disincentive to do this type of research under this arrangement. In fact, you know, drive people who are interested to sort of seek private funding to just avoid a kind of bureaucratic quagmire.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I have a question just to clarify what is written in the document on page 17. As I
read it quickly, it seems to recommend the national board
but a national board that certifies local IRB's so the
local IRB's would still do the work. So is that what we
are all discussing?

DR. SHAPIRO: No. I think everyone who has
spoken --

DR. SCOTT-JONES: It seems that people are
discussing something different.

DR. SHAPIRO: I think that people have
suggested that is a bad idea. I think that everyone who
has spoken so far does not like that idea and would
rather have something which is more akin to the RAC type
process as a -- than what is here.

So I think what you are hearing, Diane, is
people who say this ought to be reviewed at a national
level in a RAC type process. We can talk about the
process in a moment. And they actually do not like the
idea of having these two separate levels, one of which
accredits and one of which reviews. At least they do not
like it for now. That is now I am interpreting the
comments.

Trish, and then Alex?
DR. BACKLAR: I am wondering if this RAC-like body -- if one could approach scientists generally to see if they would be interested in endorsing this just as they did endorse -- it was the scientists who really brought about the finding of the RAC, right? Am I wrong or right?

DR. SHAPIRO: Yes.

DR. BACKLAR: So I think it would be very interesting for us to try and -- I do not know if we have time but I would like us to think about what we might do in terms of getting some response from people who will be doing this kind of work.

My second point is that I think that the local IRB still might have some part to play because people would need to know maybe to the directed to the RAC by the local review boards. That might be a more -- there may be a way to deal with this that might make it more efficient and not have the kinds of delays that, I think it was, David was concerned about.

DR. SHAPIRO: Alex?

PROFESSOR CAPRON: To respond to your question, I like the certification/accreditation role as
a tactical move but probably not as a strategic move.

That is to say the notion of our establishing, as we sometimes do in a report, a position on an overall subject which we will plan to get to in a later report, the notion that there should be a process beyond what we have today for finding out what IRB's are really doing and how well their procedures are set up to pass on research protocols.

This is an area of particular sensitivity. It is likely that some of the IRB's that will review this will not really have a grasp on how to do it. But if they had to go through a process of sort of meeting certain standards and showing that their outcomes are reasonable, it would be fine by me.

But I can well understand people thinking that is too big a topic to bring up here.

On the RAC-like role, yes, of course, I endorse that. It is what I have been pushing right along. The question of whether the present regulations cover, of course, the definition of human subject on which the regulations turn is the human subject means a living individual about whom an investigator conducting
research obtains, and then all this stuff about data and information, samples.

Then the part B of -- subpart B that is applicable to research that involves human *in vitro* fertilization, and this would be research that involves human *in vitro* fertilization, are additional. So it does not seem to fall under the main part. It is covered but I certainly agree with those who say we are really talking about a new and particularized research framework not basically building on this.

It does seem to me that within that, the notion of the local establishment having to review it first makes sense. I mean, there are certain processes that if carried out well are better carried out at a local level in terms of certifying that all the concerns about consent that Bernie said are so difficult have been really addressed in fact and not just on paper and so forth. There is no way a national group can do that very well.

So I see the combination of local review and national oversight as making sense.

DR. SHAPIRO: So if I understand that, Alex,
for this at this time you really would like these proposals to be approved by a local IRB and then sent forward to get final approval from whatever.

I would also be interested in finding out if people have any view on how such a national group should be assembled. Who should -- you know, who should be on it? Who should decide who is on it? Where --

PROFESSOR CAPRON: You should decide.

DR. SHAPIRO: I like that. I like that.

(Laughter.)

DR. SHAPIRO: I will put all of you on the list.

Larry?

DR. MIIKE: Hasn't the NIH director just begun to constitute a body that would seem to match that?

DR. SHAPIRO: Yes. That is if you want to have it at NIH. That is one possibility.

DR. COX: But I have another issue that comes up from the scientific view is if whether this is a -- as Bette suggested and I agree -- a way of sort of keeping track of what people are doing and seeing what the results are or going further, which is, in fact, what the
RAC was, which was assessing the scientific quality of the proposals and whether they were meritorious enough to proceed.

I think that I believe that to consider something in the latter form is dead on arrival just because there is going to be so much stuff to be done at least in the context of using already existing lines. Perhaps in the context of making lines. But I think that to really say what is the group going to do -- so it registers. It says what people are going to do but is it going to have a scientific evaluation or not in terms of if it makes sense.

I think that is something that we need to pay attention to what the scientific community is recommending in this regard.

DR. SHAPIRO: Well, is that meant to say, David, that you think that in at least -- I mean, Steve has asked this question a number of times already. Namely should the review process be different for use and derivation? I think you are suggesting and I thought you said that in the case of use that should be handled at the local level. I think you said that. And maybe just
register at a national level for the purpose of keeping track of but not for approving.

DR. COX: Yes. If one has -- so I do not know whether I want that to be local or federal. I think that in terms of speed to have that be federal just does not seem like it is going to work. You are going to have a massive amount of stuff. How even locally people are going to decide on the use, though, I think, is going to be difficult but that is what we are talking about in a way, is what is the use. And so is that going to be a scientific measure of use? Is it going to be a social measure of use? You know, how -- what is it that we are trying to assess?

In the discussions it seems to me is that we want there to be respect for this special type of research and we want people to be respectful. Well, but what does that mean? In what regard is that respect? I do not know the answer to those questions. I think that we have to -- if we are going to -- and I think we should set this thing up that we have to answer those questions.

DR. SHAPIRO: Bernie, then Eric, then Steve.

DR. LO: If we are thinking about this in the
context of NIH funding I think we should keep in mind some of the parameters by which grants are reviewed and awarded so that, first of all, there is a built in lag time between the time of submission to peer review and award so that it is possible it seems to me in that setting to design this process so we may not need to add on additional time.

Secondly, it seems to me the -- I would be willing to defer to the NIH peer review process for the scientific merit. Now Dave will have to address whether that is misfounded trust or not but my sense is it is going to be pretty rigorous and things that are funded even with a projected increase in funding are going to be pretty meritorious and have gone through a pretty strict peer review process. So I think -- I am not sure that needs to be duplicated because I think that is one of the things that the study sections do well.

And I think depending on where you want to insert this level of review, I mean one thing is to say that when you submit an application it gets reviewed at the onset on two different tracks. One for scientific merit and one to this -- whatever we are going to call it
-- to make sure that issues of respect and confidentiality are taken into account. That it seems to me need not add any extra time but it would create a lot of work for this panel depending on how many grants come in.

On the other hand, if you wait until you get grants above a certain score, you have fewer things to be reviewed but on the other hand then you have a built in time lag. I would actually -- if -- I do not have a feel for how many proposals are going to be coming in here.

I think there is a merit -- there is a benefit to having everything funded and submitted because you want to give some feedback to those investigators as to whether what they are doing sort of is in the ball park in terms of ethics and policy but that it seems to me could be a very big order and you may be overwhelming this committee at the onset.

DR. SHAPIRO: Eric?

DR. CASSELL: I think in some ways this -- the function of this committee is different than it is in other kinds of research but it is not different from what is coming. Sensitive research like this using human
embryos and human tissues -- moving human tissues -- is
going to be coming down the line and not -- this
committee or commission, whatever it is, is going to take
some time to figure out what its function really is.

For example, the idea of talking about
respect rather than the classic way of consent and so
forth, that is not so easy to figure out what that is.
It is also -- if you say there are social issues to be
resolved, it is not clear what they are in the beginning
so that the working through of this is like the very
early days of IRB's.

In the very early days of IRB's the mandate,
you know, was a consent form and not much more than the
consent form. That is what you did, is you looked at the
consent form. But gradually it worked to understand that
the IRB had a larger function than that.

DR. SHAPIRO: Steve?

MR. HOLTZMAN: Let me contradict myself. I am inclined to say before we jump to a national committee
what we ought to do is say what are the different issues
we wish to be addressed and why and that will -- may lead
us to the "hmm."
So that -- you know, one model is for the creation of ES cells, which involves embryo research. You can imagine one kind of regulatory structure. That is effectively what the U.K. has. Or you can imagine an advisory board that puts out guidelines, all right, that would track on the kinds of guidelines we have for the donation of fetal -- fetuses for materials. But once those guidelines are out, it does not necessarily need review. That is distinct from the quality of the research to use the ES cells where if it is a grant application it will be scientifically reviewed. In that sense you will not have a local review in play.

So that is a very different kind of model and if you think back on the RAC most of it tended to focus on the gene therapy aspects of the RAC. The RAC was initially started to review all DNA protocols because there were concerns about safety.

Once that was established as relatively safe they delegated to a local IBC -- it is called local Institutional Biosafety Committee -- to take over that role. All right. And then the gene therapy protocols, once those were established as safe, effectively went
Eric is articulating a very different kind of perspective. Here is my contradiction. He was basically saying -- and it then goes beyond ES cells -- we are moving into a new era of research with live human tissues. And ought we create some sort of national body to think through all of those issues? Because sitting here on its face I think of the kind of paradigm experiments with ES cells -- forget this transplant stuff.

People are going to want to look for the factors that are affecting differentiation. And if we are going to erect a RAC-like body that reviews each one of those protocols but in the meanwhile I can walk down the street and get fetal tissue and look to isolate those factors, and I do not have to go through that, I am not sure why exactly we did that.

DR. SHAPIRO: Diane?

DR. SCOTT-JONES: I am thinking through what everyone has said about the advantages of having a national body and not having a local body. It seems to me that most universities would want to have within the
university an IRB-like body that would review that research in addition to having a national body.

It seems that universities would not want to relinquish all of that to a national body without having something first at the university level. So it seems to me that there would -- it would be important to have some sort of local review in addition to a national review and it is customary for proposals to go through a review within the university typically prior to being submitted for federal funding, although not always. So it seems to me it would be hard to bypass some sort of local university review for work of this kind.

DR. SHAPIRO: Other comments?

Prof. Capron: Steve, I agree with your description but I want to point out that you truncated 25 years of history in a couple of sentences. And while the issues are not exactly the same, a process in which a national group helps to make sure that everybody is off on the right foot differentiates those things that are problematic from those that are not. It delegates -- it basically says as long as you are doing X, Y, Z, we do
not have to see it any more after all because we have
confidence that the local IBC in that case is doing a
good job.

Yes, in the first couple of years that may
mean a few protocols are held up a little while because
you cannot operate as quickly as the study sections
operate or whatever. But remember part of what we are
talking about here is a process that will have consent
issues and we may have a national body that looks at a
consent form that comes from a very good university, as
the RAC not infrequently did, and said this consent form
really does not do a good job even though it passed local
review, here is what it ought to do.

Now what I would hope is that it could,
through its point to consider type mechanism, basically
say make sure you have dealt with these things and we are
not going to start fine tuning the language of every
consent form but make sure that it addresses these
considerations. Make sure that if we have recommended
that there is a sequence, all the discussion we had about
the word "after" in the process of when you give consent
to the use of the excess embryos, that that is all done
in an appropriate way.

If that message gets through very quickly then the national body is mostly sitting around for the big remaining issue, Harold, and that is the question are we ready to now say that the research in other fields has advanced or the need has advanced in some way, and enough to say there is a reason to allow somatic cell nuclear transfer creation of cell line, embryonic cell lines, et cetera.

And it seems to me that that is the point at which you really need the national body because you want this to have a lot of visibility and if the group has been doing its job it has been staying informed. There are several years when human gene therapy was up for issue that no one was ready to do it but the RAC met regularly and, in effect, educated itself and all those meetings were public, educated the public or the relevant sectors of the public as to what the issues were and how they might be resolved. That was a very valuable process.

When the first real protocol came in there was a real framework for discussing it and I think that a
group like this can become somewhat expert in an
institutional sense. That is valuable and I would like
to see us recommend it and I would give explanation of
that sort as commentary as to why it is useful.

DR. SHAPIRO: Larry?

DR. MIKE: I think a national review body
could do all of these things but it could quickly
delegate the review of the uses and simply just sort of
follow along with the peer review mechanism.

And then keying into that since the NIH must
be interested in the fruits of that research and how
relevant that is, that is another tie in, so that this
review body could concentrate in the beginning about the
derivation part of the research process. And then once
those kinds of things are settled then they can become
more an overview about the state of the art of the stem
cell research and then what might be done in terms of
opening it up later on if the fruits seem to warrant it.

So it seems like you can put all this in one
body and then they can do all of these functions not --
maybe not all by themselves but by relationships with an
existing body.
DR. SHAPIRO: Other comments?

Steve?

MR. HOLTZMAN: I did not mean to truncate 25 years of history but I think that is the profundity of what Eric was saying, is that you could create such a body and give it this broader charge of a consideration of the use of human tissue, live human tissues. It naturally leads itself there it seems to me.

You do not -- maybe I am very influenced by the fact that I am perfectly convinced that within two years people -- investigators will be able to order ES cells from catalogues. So if you are thinking about a national review body reviewing every protocol that involves every ES cell it is -- it is very different than the kind of a vision, I think, that Eric is articulating that there are a slew of issues coming into view.

DR. SHAPIRO: Well, this is exactly the issue that I am concerned with, with respect to -- since we are all in the business of contradicting ourselves here, what I am about to say, I think, has a number of internal contradictions but let me blurt them out in any case.

The -- on the one hand if we separate in one
way or another the derivation and use, which makes a lot of sense in a lot of ways because I think the use is going to be very common place and will overwhelm very quickly any committee. It does not matter how big, small, how much staff they have and so on. So it seems to me not reasonable that some national group would have to deal with -- they may want to keep track of or otherwise issue some guidelines with respect to or -- but not actually deal with protocols that -- protocol by protocol on use. If it -- so that part seems quite clear to me just as a practical matter.

Then there comes the issue, well, all right, if you separate use and derivation, given the public/private differences that we have regarding who has to do what in the current time, there is going to be an enormous incentive to have all the derivation done in the private sector, which can ignore all of this anyhow, and those people in the public sector will just be buying, whether it is out of a catalogue or some other way, they will buying it into their research projects and, therefore, the use -- the derivation, which is, if anything, is the most sensitive part of all this, will
not receive any public oversight if I understand this thing correctly.

MR. HOLTZMAN: But if you get the sort of distinctions that this commission seems to be recommending, all right, for example, federal funding for the use if and only those -- the cells came from excess embryos, you will then have a commercial practice, all right, which forces the labeling of these things in order to be able to satisfy that to meet the market.

DR. SHAPIRO: Right. I am not denying that. I think that is absolutely right. I mean, I agree with that as a prediction. All I am saying is that the use -- the derivation will take place primarily in the private sector under a scheme like that. The way I see it, for one thing it avoids all the difficulties.

It is not that hard -- it will not be that hard to do before very long and it may or may not be legal. That is fine. But that there will be no oversight on the issue which appears to be the most sensitive of the issues. Maybe that is fine but that is -- I just do not -- I am not quite satisfied yet that I know how to deal with that or I know how to recommend a
structure which I would find satisfactory as we step out on this issue.

MR. HOLTZMAN: But again if you imagine this committee or this commission or the kinds of recommendations that we are having effectively moving towards, which says federal funding would be allowed for the creation of these things provided the following conditions are met.

DR. SHAPIRO: Correct.

MR. HOLTZMAN: All right. And then you say that federal funding of the use of cells is allowed provided the cells were derived in the following manner -- then the commercial sector will follow all the same rules so that it can sell to those federally funded researchers.

DR. SHAPIRO: I want to think that through. Maybe you are right but I want to --

DR. COX: But I hear Harold's problem being that, yes, the federally funded creation will be regulated but not the private creation and that is the rub.

DR. SHAPIRO: I think what Steve is
recommending -- I am sorry to interrupt, David -- or
suggesting is that if the federal regulations are written
in such a way that you can only use them if they have
been derived or in a certain fashion that that is the way
people will derive them because they want to sell them to
you or want to have a little commercial market. I want
to think that -- I want to think through what that means.

DR. COX: Harold, I heard him say that. The
question is how do you know that that is the case.

So actually, Steve, why don't you put a coda
on that then so that -- I mean, because there are
professional standards in some ways, right. Or industry
standards. So how are industry standards enforced then?
I mean, how do people know that that is actually how it
was done?

DR. SHAPIRO: So, I guess -- you mean rather
than just write it down as if it were done?

DR. COX: Yes.

DR. SHAPIRO: I see. Well, let's put aside
the audit issue for a moment. That is how would we know
the people are doing what they say they are doing. Let's
just suppose that people say -- you know, report honestly
what they are doing. That means the regulations we would have to write or suggest here would be that federal funding is available for the derivation, that is you can buy these things, only under the following conditions: That is that these were derived from these sources and treated in this and that way, whatever you might want to write down.

MR. HOLTZMAN: Again, we are going down a logic path that says with respect to the federal funding question there is no moral space between derivation and use. We are going to say that with respect to derivation, right, these are the only licit sources if it is conducted in the following way, and the use will be federally funded if and only if the cells that we are using came from that.

That in itself does not make any reference to who made those cells. Right? What I am suggesting is once you have got that in place by implication anyone who wants to provide the cells for the federally funded user of the cells is going to have to meet those conditions in order to be able to provide them to that marketplace.

All right. Now, David, to your question,
what is -- the second order and it is mislabeling and
everything else.

DR. SHAPIRO: The FDA would have jurisdiction
over the production.

MR. HOLTZMAN: No. FDA only has jurisdiction
only if you are going back into someone with them.

DR. MESLIN: We think that if the paper that
is in the briefing book from Robert Brady is read maybe
there will be some further insight on that issue. I do
not think it is settled, Steve. You might want to look
at page 25 of Bob Brady's paper.

DR. SHAPIRO: Bernie?

DR. LO: It seems to me that what this
commitee is going to be doing will change over time and,
you know, I do not think we are going to be able to
specify the sort of guidelines Steve was talking about
that would be mandatory for federally funded research. I
mean, the sort of conditions under which you could
produce a stem cell supply and hope that it will be
carried over in the private sector.

So it seems to me that at the onset this
commission would probably try and draw up a set of
criteria which would meet the criteria that Steve was
talking about and that would be useful. And I think what
we need to do is think out whether with good intentions
we may be setting up a sort of procedure that actually
may make things worse.

I mean, I heard what you were saying, Harold,
that we actually may create incentives to drive the
production of cell lines away from the public sector back
in the private sector because this sort of oversight is
viewed as sort of cumbersome or whatever.

I think that is partly an empirical question.
I mean, it has to do it seems to me with how many -- what
the market is for these cell lines to be used in
federally funded research, and is it large enough that
companies will take the trouble to manufacture a product
that meets certain specifications.

DR. SHAPIRO: I agree.

DR. LO: But I guess it just seems to me that
it would be good to have some body that in an ongoing way
would be able to look at all these issues and sort of
address them as they came up over time rather than to
sort of have to create a new body each time that this
came up.

DR. SHAPIRO: If I understand the comments that we made here, it is that the general sense is that we should look towards the establishment of a national body, that that body ought to have considerable leeway in deciding what it should take on itself and what it wants to delegate to local IRB's, and how much long-term issues it wishes to address versus short-term issues and sort of give that body the job of what we are trying to struggle here with. And give it a public disclosure function that is either meet in public or otherwise have a public disclosure function as a way of building the kind of confidence -- and yet giving them as much flexibility as possible since we are really just speculating on the issues that could come up. They may come up in a somewhat different and surprising form.

We do not really know how many protocols there are going to be. There might be tens of thousands. There might be ten so I just do not know myself but there will be lots, I think. So just judging by the frenetic activity to get ready for it, it would be a guess that people expect lots.
So perhaps what we will try to do is develop a recommendation that establishes a national body that yet leaves it considerable authority to decide what to delegate and what to keep but gives it a public disclosure function and a so-called registry function of some type, and we will just have to work it out in some detail.

Allowing them, though -- the way I am thinking about it now -- allowing them to decide whether it wants use of the local level or some other way of dividing the work. But our objective is to get some high level oversight plus transparency in what it is they are doing and what it is they are thinking, and how it is they are handling the situation, and dividing up the work between themselves.

Is that sort of on the right road? I do not mean to be detailed about this.

DR. LO: No, absolutely. And I think then the other thing we need to do is type that to what I take with the comments last Friday that even those who had strong moral objections to this type of work wanted -- if this was going to happen despite their objections there
to be a very sort of strong and visible oversight process.

It seems to me it is a way of our showing --
acknowledging the concerns that opponents of this type of
research have and that we take it serious enough that we
want to create a body that we would give both flexibility
and power to make sure that things do not slip through
the cracks later in the next couple of years.

DR. SHAPIRO: Thank you.

Other comments or questions?
I am sorry, Diane. I apologize.

DR. SCOTT-JONES: I like what you were saying
about the national body having a high level of oversight,
being transparent, having the flexibility to delegate,
but I think it would be good if there would be a way to
have the active involvement at the local level so that
IRB's from the very beginning become actively involved
and even though they would need to defer to the national
body that there be some review at that level just so we
would promote the idea that ultimately researchers need
to have moral agency in what they do and that we are not
somehow trying to take away from the researcher and from
their own institution this important need to consider
these ethical issues.

So I would prefer if there could be worked
into the plan some first level at the university and I
think universities would want that.

DR. SHAPIRO: The more I think of it, the
more it becomes clear to me that just the capacity to
handle this requires important functions at the local
level and so I do not think there is any way to avoid
that. If the committee -- we will have to find some way
to state that so that a committee does not imagine it can
just take it all itself even if it wishes to, that this
is -- at least they would have our view this would not be
an appropriate thing.

Bernie?

DR. LO: I mean, I agree with Diane, in
particular, because it seems to me we are eventually
evisaging that a national body would delegate off to
local bodies a lot of the sort of more routine oversight.
I think we need to be very flexible as to what that local
oversight would look like because I have very grave
concerns about IRB's as currently constituted being
appropriate to do this. I think we need to be more
creative.

DR. SHAPIRO: Bette?

MS. KRAMER: I would like to incorporate in
an obligation on the part of the body not -- I do not
think just disclosure is sufficient but an obligation to
provide an educational arm for the public.

DR. SHAPIRO: I think we can certainly
recommend that. A lot will depend on just -- there are
small but important issues like where is it going to be
located and who is going to appoint its members, what its
budget will be, but I agree that would be a very valuable
function.

All right. I think that we perhaps talked
about that enough for one day. We might, in fact, have
exhausted ourselves from talking about anything sensibly
any longer.

Are there any -- tomorrow morning will
primarily be our visitors. Looking at people's schedules
we are unlikely to go as late as 12:00. I have already
said I, myself, have to leave early. I think I have to
leave around 10:30. But the visitors are coming first
thing in the morning and they really should be quite interesting. I think they are looking forward to the discussion and I hope we will carry that out and then just continue with the meeting as long as possible.

Bernie?

DR. LO: Do you want to start at 8:00 rather than 8:30?

DR. SHAPIRO: I am quite happy to start -- I do not know when our visitors are coming.

DR. MESLIN: At 9:00.

DR. SHAPIRO: They are coming at 9:00.

DR. HANNA: Dr. Shapiro has a flight that gets in at 8:00 so as soon as he gets here we can start with him but he probably will not get here until 8:30 or 8:45.

DR. SHAPIRO: Why don't we -- is 8:00 sort of -- I mean, it is 9:00 o'clock for those of you on the East Coast time and Bernie has, of course, already volunteered to -- why don't we -- does anybody object to starting at 8:00 and we will see what issues there are and then we will just wait so that we will try to get as much done early in the morning.
MR. HOLTZMAN: Anyone who wants to talk about HBM we could start at 7:00.

(Laughter.)

MS. KRAMER: (Not at microphone).

DR. SHAPIRO: It is difficult for me to say since I -- I expect we will adjourn somewhere --

DR. BRITO: (Not at microphone.)

DR. SHAPIRO: We will see if we get back to if we get some time to spend on it tonight or not. That is what I just do not know. If not, we will do --

DR. BACKLAR: (Not at microphone.)

DR. SHAPIRO: We are meeting at 8:00. Now I have to say every other time I have called a meeting at 8:00 I have been sitting here alone at 8:00 o'clock but that is okay. We will get started at 8:20. It is better than 9:00. It will be 20 minutes delay no matter what we do but I will be here at 8:00.

DR. BACKLAR: Some of us are still from the West Coast. 8:00 o'clock is still not 8:00 o'clock for us.

DR. SHAPIRO: It is 6:00 o'clock. The suggestion came from the West Coast so I thought Bernie
spoke for everybody on the West Coast.

Okay. Thank you all very much.

(Whereupon, the proceedings were concluded at 4:53 p.m.)

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