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NATIONAL BIOETHICS ADVISORY COMMISSION

HUMAN SUBJECTS SUBCOMMITTEE

Salon 3
Crystal Gateway Marriott Hotel
1700 Jefferson Davis Highway
Arlington, Virginia

Thursday,
January 8, 1998

Gilmour
164 pp.

The meeting was convened, pursuant to recess,
at 8:10 a.m., DR. JAMES CHILDRESS, Subcommittee Chair,
presiding.

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DIANE SCOTT-JONES, Ph.D.
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ALSO PRESENT:

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Executive Director

MS. HENRIETTA HYATT-KNORR
Deputy Executive Director

MS. RACHEL LEVINSON
Office of Science Policy

MR. JONATHAN MORENO
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I N D E X

	<u>PAGE</u>
WELCOME	
James Childress, Ph.D.	5
RESEARCH WITH DECISIONALLY IMPAIRED SUBJECTS: DRAFT REPORT	
Discussion: Jonathan Moreno, Ph.D.	17
REGULATORY UNDERSTANDING OF MINIMAL RISK	
Discussion: Gary Ellis, Ph.D.	51
DISCUSSION CONTINUES ON RESEARCH WITH DECISIONALLY IMPAIRED SUBJECTS: DRAFT REPORT	
Jonathan Moreno, Ph.D.	86
STATEMENTS BY THE PUBLIC	
Dr. John Cavanaugh-O'Keefe American Bioethics Advisory Committee	117
Dr. David Shore National Institute of Mental Health	121
UPDATE ON MARYLAND ATTORNEY GENERAL'S WORKING GROUP	
Jack Schwartz, Esq.	128
UPDATE ON REPORT ON THE SURVEY OF FEDERAL AGENCIES	
Bill Freeman, M.D.	137
FUTURE COMMISSION RESEARCH ACTIVITIES	149
CONCLUSIONS	160
ADJOURNMENT	163

P R O C E E D I N G S

WELCOME

1
2
3 CHAIR CHILDRESS: Welcome to the subcommittee
4 meeting, the Subcommittee on Human Subjects Research.
5 We had a very productive day yesterday, with a lot of
6 important questions arising about the fine draft report
7 that we've been working with and an indication of a
8 number of areas that we need to do further reflection,
9 in particular clarifying some of the concerns
10 surrounding the category of more than minimal risk,
11 non-potentially beneficial research, where much of our
12 discussion focused.

13 You've seen the agenda for today. The first
14 activity will be looking at the draft report and we
15 will start with the discussion we had yesterday,
16 looking at the recommendations and seeing where we want
17 to go with those.

18 Then at 8:50 we'll spend some time with Gary
19 Ellis, looking at the discussion of minimal risk, the
20 different understandings of minimal risk, since
21 obviously how we understand minimal risks will -- what
22 these recommendations actually mean. That will come in
23 during the course of our discussion of the draft

1 report.

2 Then at the very end of our discussion of the
3 draft report we will talk about next steps, things we
4 need to do to bring this in to something closer to a
5 final version.

6 Also, as part of next steps we need to think
7 about whether we want to meet in L.A. Apparently the
8 Genetics Subcommittee is going to meet in L.A. I don't
9 have strong feelings about whether we meet or not. We
10 may just want to see where we stand at that point and
11 then make a decision about whether to meet.

12 Then we'll have a discussion with Jack
13 Schwartz, who has appeared before us a couple of times
14 before, on the Maryland Attorney General's Working
15 Group involving draft recommendations from that group
16 on decisionally impaired research subjects. And Bill
17 Freeman will give us an update on the survey of Federal
18 agencies.

19 We'll talk after statements by the public.
20 Let me just mention that it would be helpful if members
21 of the public would indicate if they would like to
22 testify at that point so we'll have some idea of how
23 much time will be required. So you can just sign up at

1 the back and indicate to a member of the staff that you
2 would like to testify at that point.

3 Then we'll discuss future Commission research
4 activities and building on the report of Eric Cassell's
5 committee, and then draw some conclusions.

6 Adjournment would be no later than 12:30. I
7 guess I'll probably be surprised if we run until 12:30,
8 although we obviously have a lot of important work to
9 do, particularly on research with decisionally impaired
10 subjects.

11 Any other points to get out before we get down
12 to work? Harriet, do you have any?

13 MS. HYATT-KNORR: Not right now, no.

14 CHAIR CHILDRESS: Okay.

15 MR. CAPRON: Two questions. The first, is
16 whether we need to have some discussion this morning on
17 the question of the Federal office issue that we heard
18 about yesterday, and that the Commission as a whole had
19 a discussion on. We do not have -- document yet.

20 CHAIR CHILDRESS: Right. She hopes to have
21 that by the end of the month, if I recall correctly.

22 MR. CAPRON: Maybe it's premature, but I did
23 have a slight sense that we were all frustrated that we

1 got the issues out. There seems to remain a great deal
2 of consensus, but we need to make the determination of
3 which is the level we want to recommend.

4 CHAIR CHILDRESS: Well, let me raise the
5 question this way, Alex. I think many of us, I
6 suppose, are in a transition period of moving more
7 toward whole Commission work, away from subcommittee
8 work.

9 I think one of the frustrating things about
10 the previous meeting was that we had such a fine
11 discussion with John Fletcher and Charles McCarthy on
12 this particular topic, a discussion that actually would
13 have been very beneficial to the group as a whole. You
14 did a fine job yesterday of giving the background for
15 that and summarizing it.

16 So I don't know. It would certainly be
17 possible to spend a few minutes talking about some
18 quick responses, but it seems to me that would be a
19 discussion that would be very useful for the Commission
20 as a whole to have.

21 MR. CAPRON: I agree with that. I'd like to
22 know how we're going to have a document that will bring
23 together the contact review that we had. I mean, it

1 seems to me that in some way, most logically, this is a
2 chapter of our Federal agency's report.

3 I mean, it is a much more substantive
4 conclusion to that report than simply reporting on
5 restraints and weaknesses of the responses in different
6 agencies. This is taking that picture and saying the
7 conclusion to be drawn is a little different than
8 simply tinkering.

9 CHAIR CHILDRESS: Right.

10 MR. CAPRON: I entirely agree. I wasn't
11 really trying to say that we needed discussion here
12 now, I just wanted to get some sense of how this fits
13 into your time table.

14 I think as far as the subcommittees, I mean,
15 my hope is that the subcommittees are history and when
16 we talk about meeting on these topics from now on we're
17 talking about all of the --

18 CHAIR CHILDRESS: Good. No. I quite agree
19 with you. I guess the current plan, and we'll talk
20 about this a little more when Bill Freeman reports,
21 would be to finish the report in the area of genetics
22 on tissue samples and to finish the report on
23 decisionally impaired research subjects, and then to

1 finish the report on the Federal agency. So that would
2 give some sense of the timing. As I understand it,
3 that's the time frame.

4 Let me get Eric in and he can really address
5 it better.

6 DR. DUMAS: Well, I see the subcommittee's
7 working on behalf of the whole, so I wouldn't have any
8 objection at all for this subcommittee to make
9 recommendations, specific recommendation, to the body
10 in regard to this issue which I think we can settle and
11 move it off of the agenda. It seems to me that there
12 is a lot of agreement that we need a place to take care
13 of these concerns.

14 So, I feel impatient to get the things we can
15 make decisions on decided. My suggestion would be that
16 we discuss the report, that we make a recommendation to
17 the body as a whole, and that we'll move that part of
18 our business forward.

19 CHAIR CHILDRESS: And I think there is a lot
20 of wisdom in that. The only problem that has come up
21 is that it is often difficult, and we saw this in the
22 discussion yesterday, to recapture the kinds of
23 arguments, and particularly some of the powerful

1 elements attached to them, in the context of the larger
2 discussion after we've had the subcommittee discussion.

3 In this particular area I think we've lost a
4 lot in not having the whole Commission hear those two
5 reports last time. I think we'd be a lot further
6 along.

7 So the question is whether we want to spend
8 the time doing it today or whether, as I think I like
9 the suggestion that we really talk more about a plan
10 for doing it with the larger Commission. Eric?

11 MR. MESLIN: The only thing that I would add,
12 substantively, is just on the organizational front. It
13 would be very useful for us to have Dr. Gonzales' paper
14 in hand, and we should have that within the next, we
15 hope, week or two.

16 Although that is not identical to the
17 McCarthy-Fletcher proposals, complementary as they may
18 be to each other, that was part of the process of
19 gathering some findings that will inform the
20 Commission.

21 I think it will be entirely possible for staff
22 to put together a document that both summarizes where
23 the debate is and, with input from Commissioners,

1 provides a framework for how to resolve this issue and,
2 as you say, get it off the table.

3 It is a fairly important subject and I think
4 we'd like to hear a bit more from the Commissioners at
5 the appropriate time--this might not be it, unless you
6 feel the need to speak up--as to whether it will join
7 the Federal agency's survey as an appendix or a chapter
8 or whether it will be a stand-alone document that will
9 accompany it.

10 So this is something that we can continue to
11 discuss, but it is a high priority subject because, as
12 you say quite rightly, it is something that we can
13 attend to, having heard a good deal of conversation
14 already.

15 CHAIR CHILDRESS: Rachel, sorry. I hadn't
16 noticed that you were here. Did you have anything you
17 wanted to say at the outset?

18 MS. LEVINSON: No. Just let this continue.

19 CHAIR CHILDRESS: Okay. Any further points
20 about this?

21 MR. CAPRON: Well, not a further point, but
22 I'd like to sort of see where we're going on the
23 conclusion. Could you give us a sense then, would it

1 be reasonable to expect that at the March meeting we
2 would have from staff, or the April meeting we would
3 have from staff, a document drawing on the previous
4 discussion, drawing on yesterday's discussion -- in a
5 way, what I was, in a very rough fashion, trying to do
6 orally was to present what seemed to me to be the
7 elements that would go into that, abstracting them,
8 boiling them down from the excellent papers.

9 If the staff has that material -- I'm with
10 Rhetaugh on this, that it doesn't seem as though it
11 should take up a lot more of our time and we ought to
12 move on.

13 But I think that we're at a point on many
14 topics where moving on means having not the oral
15 agreement, which we seem to have, largely, but really
16 on the table the draft document, and we can sign off on
17 that, even if we saw, well, we're going to hold it for
18 a month or two, or three or four, while it goes into
19 some other document which won't be ready until that
20 time. That's fine. We've gotten through that. I just
21 want to get a sense from you, are we saying March,
22 April?

23 MR. MESLIN: I see no reason why it couldn't

1 be available by the March meeting, with two caveats.
2 One, based on your very helpful overview yesterday, I'd
3 hoped you would be able to provide some substantive
4 input into the writing, either by reflecting on some of
5 the documents or offering some proposed solutions for
6 the Commissioners to debate. I think the point of
7 whether or not there is agreement should go not
8 unchallenged.

9 I think there was certainly agreement that
10 something different ought to occur. There was not
11 agreement as to either the exact location or what the
12 administrative arrangements for putting that office
13 into place would be.

14 I think there it would be fruitful to have
15 some further discussion by the Commission. But I think
16 you're entirely right, it could be done by March with
17 input, not just from you but from Alta Charo, who is
18 not here, and had an interest in providing some
19 commentary.

20 MR. CAPRON: Well, Alta, I should say--and I
21 should have made this more clear--and I did discuss
22 this, and I think I was reflecting her views as well.
23 So let's look at the March meeting.

1 What I would personally urge, and maybe we
2 need a straw vote now and maybe only if that draft is
3 there, you could, as the staff, give us the document
4 then with two concluding sections, one of which says
5 the McCarthy-type version, the other says the Fletcher,
6 then we could have the discussions once we have those
7 before us.

8 I would hope that you would vet the idea with
9 it as widely as you think it's appropriate so that,
10 beyond the thoughts of Fletcher and McCarthy, there may
11 be further refinements, there may be issues that are
12 essential to be addressed that they haven't addressed,
13 et cetera.

14 CHAIR CHILDRESS: Yes. Okay.

15 Rhetaugh, do you feel comfortable with this
16 direction?

17 DR. DUMAS: Oh, yes. I'm flexible.

18 CHAIR CHILDRESS: It sounds as though you want
19 it moving forward.

20 DR. DUMAS: Yes. I just think we take too
21 much time --

22 CHAIR CHILDRESS: We hear you.

23 DR. DUMAS: -- to make decisions around here.

1 But I can't have it my way all the time.

2 CHAIR CHILDRESS: And I'm assuming that you
3 could provide, for example -- I think it would be very
4 helpful if all of us would have a print-out of your --

5 MR. CAPRON: Yes. I can do that.

6 CHAIR CHILDRESS: That would be helpful.
7 Okay.

8 Anything else we need to talk about regarding
9 our agenda?

10 (No response)

11 CHAIR CHILDRESS: Okay. Let's start with the
12 -- well, let's see. One more thing. Let me note that
13 everyone should receive at the table this morning a
14 copy of the 10 or 12 pages provided by Paul Oppenbaum
15 for insertion, with modifications, the two sections of
16 Chapter 1, and we'll come back to those pages in due
17 course today.

18 Was there anything else we needed to --

19 (No response)

20 CHAIR CHILDRESS: All right. Jonathan,
21 anything you'd like to say following yesterday's
22 discussion? We will start with the recommendations,
23 pick up where we left off yesterday, and then move to

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other portions of the draft document.

1 RESEARCH WITH DECISIONALLY IMPAIRED SUBJECTS:

2 DRAFT REPORT

3 Discussion: Led by Jonathan Moreno, Ph.D.

4 DR. MORENO: It seems as though we should
5 start by talking about the status of the Research
6 Advance Directive Concept, either the nomenclature or
7 the substance. It would be very helpful, I think, to
8 start there and resolve that question.

9 CHAIR CHILDRESS: And I'm going to try to get
10 everybody to use microphones.

11 MS. FLYNN: It would be helpful to me, and
12 maybe I'm -- little discussion on substance, I'd like
13 to hear a little bit from Rich and others before we go
14 further. I feel that, yes, the discussion was useful,
15 but I don't think we got a chance to complete it and
16 I'd like to share a little bit more substantively.

17 DR. MORENO: Can I just say one thing about
18 that discussion? I'm not sure that in the discussion a
19 key element of the Research Advance Directive Concept
20 was suitably addressed, namely for people who --
21 actually, Trish has talked about this with me, and I
22 think is reflected in the text.

23 For people who are anticipating a period of

1 incapacity, who've already experienced it, these truly
2 would be advance directives. I'm not sure that that
3 concept was fully appreciated in the discussion
4 yesterday.

5 So that even if, in other respects, the
6 concept of an advance directive for this kind of
7 research proves not to be importantly different from
8 informed consent, garden-variety informed consent, at
9 least in that kind of situation it would seem to be
10 useful.

11 CHAIR CHILDRESS: Good point.

12 Trisha?

13 PROFESSOR BACKLAR: Yes. That is -- it's
14 terribly hard for me to hear people speak, I must say,
15 even when they're speaking into the mike. And it may
16 be my advanced age, but I urge all of you to speak
17 clearly as possible.

18 MR. CAPRON: Because this is an airplane
19 hanger and there seems to be some loud noise coming.

20 PROFESSOR BACKLAR: It gets distorted. Yes.
21 It's really horrible. Now that I've said that, let me
22 put it aside.

23 Yes. Exactly and precisely as you said,

1 Jonathan. These are people who have experienced, and
2 may experience again, periods of an inability to do
3 decision making, periods of incapacity. So what the
4 advance concept is planning for those periods where
5 they may not be able to make decisions about their
6 involvement in the research -- so it is not a misnomer,
7 for that particular group, to call it an advance
8 directive.

9 In that same way, it's no different from an
10 advanced directive for psychiatric treatment, so that
11 there are certain things that will fall into place
12 should that capacity for decision making be lacking.

13 I don't think I need to spell out the rest of
14 it, because what we tried to build into it were
15 protections inasmuch as there would be a top decision
16 maker, there would be an outside provider who was not
17 connected to the research, and that provider did not
18 need to be a physician, it could be a case worker, et
19 cetera.

20 CHAIR CHILDRESS: I think it's very important
21 because it clarifies what this is about, but also
22 limits it. I think that the -- limitation group of
23 subjects to whom it would apply is also very important.

1 PROFESSOR BACKLAR: And because there was this
2 -- it is also important to understand that what was
3 intended in this process of planning was that during
4 the consent process that takes place in any research
5 protocol, one hopes, is the appointment of the -- the
6 proxy should be involved for somebody who is in that
7 situation where they may lose their capacity. So if
8 the proxy doesn't come in later, in other words, people
9 are -- the proxy is educated at the same time and
10 learning about it along with the person, the subject.

11 DR. MORENO: And it's worth knowing that the
12 current, much maligned chart on page 150, for the
13 category of greater than minimal, non-beneficial
14 research, the current framework calls for having --
15 whether there's informed consent or an advance
16 directive, calls for having the necessary involvement
17 of a legally authorized representative, as well as the
18 health professional monitor, which would go to Trish's
19 wish to ensure the involvement of such an other person
20 in the process.

21 PROFESSOR BACKLAR: And there seemed to be
22 some confusion yesterday, and I'm not certain it is in
23 the document, Jonathan, as you've written it--I tried

1 to find it last night, but I'm afraid my eyes were
2 closing--about whether or not that surrogate could be a
3 family member.

4 DR. MORENO: Absolutely.

5 PROFESSOR BACKLAR: I is my intention that it
6 absolutely could be.

7 DR. MORENO: Yes.

8 PROFESSOR BACKLAR: It didn't have to be, but
9 it certainly could be.

10 DR. MORENO: Could be. And I had tried to
11 work Number 4 on page 145 in such a way that would
12 invite the local jurisdictions to develop their
13 legislation for regulations in such a way that there
14 could, indeed, be a default mechanism. That's what
15 people wanted yesterday.

16 PROFESSOR BACKLAR: I also would like to say
17 one thing that I don't think was clarified yesterday.
18 There was a lot of discussion about people didn't think
19 -- advance directives. I wasn't seeing it as a matter
20 of choice, that if you had a subject who could lose
21 their capacity for decision making, it would be built
22 into the process of consent.

23 So it wasn't, oh, you won't have -- if you're

1 not going to have consent to a research protocol, then
2 you might not have an advance -- whatever we're going
3 to call it, you might not have this particular
4 operation.

5 DR. MORENO: Well, the incentive is -- if you
6 look at the chart. For greater than minimal, non-
7 beneficial research, largely, is the language I'm using
8 to describe that kind of study. You have to either get
9 the informed consent of the subject, which is
10 presumably proximate within a matter of hours or days
11 of initiation.

12 CHAIR CHILDRESS: A couple or three of us are
13 having problems hearing you. I'm not sure it's the
14 microphone.

15 DR. MORENO: Let me try again.

16 MR. MESLIN: And speak a little more slowly,
17 if you would, Jonathan.

18 DR. MORENO: For greater than minimal, non-
19 beneficial research, I would be -- as the current
20 framework is written, the investigator would have to
21 get either the informed consent of the subject, which
22 is presumably pretty much proximate to the initiation
23 of the study itself, the matter of hours, but at the

1 most a few days, or an advance directive authorizing
2 this kind of research.

3 Now, we can argue about what this kind of
4 research means. I'm not sure the research sorts itself
5 into actual kinds a la Aristotle, but, nevertheless,
6 it's a way to get started in this discussion. So the
7 pressure on the investigator is precisely of the kind
8 that Trish has just described for this category of this
9 research.

10 That would not be the case for potentially
11 beneficial research in which you would get either the
12 informed consent of the subject if the certain
13 situation is right, or we get the advance directive, or
14 permission of the legally authorized representative,
15 which could be, again, the family member.

16 But when there is a greater than minimal
17 amount of risk and it's not beneficial, this framework
18 would encourage the investigator to get either informed
19 consent or, alternatively, the advance directive.

20 PROFESSOR BACKLAR: Again, this, of course,
21 brings us back to something we need to talk about and
22 which we are maybe talking about, because I find it
23 very confusing not to know what we are meaning when we

1 talk about these breakdowns, more, thus, and so on and
2 so forth, because intuitively I want to say that there
3 are a group of people which -- and I think we'll get
4 back to this, that almost anything that you're going to
5 do -- research with a particular group of people, that
6 you may want to have certain protections in place.

7 CHAIR CHILDRESS: Let me just point out that
8 this draft also, for those of you who have memorized
9 it, as with the previous draft, on page 146 it tries to
10 deal with the minimal risk definition problem by using
11 examples and actually suggests that those examples
12 might even be written into regulation.

13 PROFESSOR BACKLAR: I couldn't hear you.

14 CHAIR CHILDRESS: Okay. This draft, as in the
15 previous draft, tries to deal with the question of the
16 definitional problem for risk by using examples that
17 might even be written into regulation.

18 Now, one could go further and do as the
19 Canadians have done recently and stipulate that there
20 is perhaps a different scale that is appropriate for
21 people who are lacking capacity with respect to what
22 counts as risk. So one could even add that kind of
23 statement to make the point clearer. Thanks to Eric

1 Meslin, for providing me with that document.

2 PROFESSOR BACKLAR: But again, I want to say
3 that I'm hoping that the discussions we have with Gary
4 Ellis is going to sprint us forward in being able to
5 make this --

6 CHAIR CHILDRESS: So we'll come back to the
7 minimal risk part. I have Alex -- just a moment.
8 Laurie, does this help get under way the kind of
9 discussion -- I think it's helped clarify some of the
10 issues and I think one of the critical things you have
11 to decide is basically whether we pay too high a price
12 in terms of research if we have restrictive conditions
13 of this sort, and that was the debate between Zeke and
14 Alex yesterday.

15 MS. FLYNN: Yes, I think it is helpful and it
16 reinforces my concern that I expressed yesterday, that
17 we are, indeed, I think unwittingly, erecting too great
18 a barrier to research that I think is a modest increase
19 over minimal risk and is, in fact, quite essential at
20 this point in terms of basic neuroscience.

21 CHAIR CHILDRESS: Trish, did you want to get a
22 response in?

23 DR. SCOTT-JONES: I just wanted to say that I

1 don't think that there's -- that when you have
2 vulnerables on any subject, that one must be very
3 concerned about their protection. The costs may be
4 very small in comparison to the kinds of costs that go
5 into research anyway.

6 MS. FLYNN: My concern, and I certainly agree,
7 was actual limitation and whether, in fact, this
8 current structure would essentially obviate much of the
9 research that is now going on.

10 CHAIR CHILDRESS: Did you want to address
11 this --

12 DR. SCOTT-JONES: I wanted to ask Laurie to
13 just say a little bit more about the point that she
14 just made, because I think it's important at this stage
15 because we want to come to some sort of consensus to
16 really hear what each of the commissioners is saying.

17 Laurie, I was just wondering if you could be
18 more specific. Do you think it means that there would
19 be additional costs, there would be too much time taken
20 up with the consent process, or what specifically would
21 you see as the obstruction to the research process?

22 MS. FLYNN: I guess I would want to recommend
23 that we hear from some who are directly involved in

1 administering or conducting research, because I'm not
2 one of those people. But it seems to me that the large
3 number of studies that are now under way that represent
4 a minor increment over minimal risk needs to be
5 analyzed.

6 I guess my concern has been that we've looked
7 at this in terms of, how do we try to stop certain
8 kinds of research or how do we try to limit certain
9 kinds of research.

10 My focus has always been on, how do we extend,
11 expand, and improve both the informed consent process
12 itself, which I think we don't have nearly enough
13 attention to here, how do we educate IRBs and engage
14 the community of interest in the work of the IRB so
15 that the design of the studies, including the
16 protections and consent procedure, can be strengthened?

17 This appears to me to be moving to a kind of
18 narrower approach of, some research is okay and some
19 research is not. I'm not comfortable that we know
20 enough about that research and about the vulnerability
21 of that population in any particular study to make
22 those kinds of final judgments.

23 CHAIR CHILDRESS: I guess one question would

1 be, and this came up yesterday, what additional
2 information we would want from whom to help think about
3 this matter. Jonathan, then I'll get Alex's response.

4 DR. MORENO: I think this is an empirical
5 question. How much research is going on that involves
6 a minor -- right now that could not be done under the
7 conditions described in this proposal? I think that is
8 a very important question. I'm not sure anybody really
9 knows, Jim, with a high degree of reliability the
10 answer to that question, but it's one that we might
11 well want close to the OPRR.

12 CHAIR CHILDRESS: Alex.

13 MR. CAPRON: I endorse that view, but I wanted
14 to address something else, if it's all right.

15 CHAIR CHILDRESS: I'm sorry.

16 MR. CAPRON: We're sort of having two
17 discussions. You're talking about advance directives,
18 then we're talking about what seemed to me to be a very
19 fundamental point that arose in the meeting yesterday,
20 which is, if we had made the categories too simple we'd
21 collapse too much in. We need to unpack some of that
22 so that we don't protect people out of the opportunity
23 to benefit from new science.

1 I'm very concerned that we figure out how to
2 go about this, because I don't think it is just a
3 matter in this case of hearing from OPRR. I think it
4 is probably a matter of hearing from, on the one hand,
5 researchers, and on the other, some who have observed
6 the abuses of research.

7 Among the researchers, also, to find out
8 whether there are colleagues who say, well, it's true,
9 you could do the research that way, but you would also
10 do the research this way with a group that has the
11 ability to provide consent.

12 To me, the hardest case that Laurie raised
13 was, if there were fundamental scientific questions
14 that would only be answerable in subjects who,
15 throughout their life, had a permanent incapacity to
16 provide consent and where you were automatically
17 putting in a surrogate, and if some of that research
18 fell within our more than minimal risk category, it
19 would never be doable because we see some requirement
20 for the individual to consent.

21 What I wanted to do, however, was come back to
22 the discussion that Trish was having a moment ago
23 because the one thing that did come out yesterday in

1 our discussion with the larger Commission, and I feel
2 that in that discussion I was a proponent of, more or
3 less, what we had here about the advance directives.

4 But I realized that in the discussion we may
5 have been using the terms in different ways. There is
6 the circumstance which is, I think, and correct me if
7 I'm wrong, Trish, the one which you seem to have in
8 mind most of the time when we're talking about this is
9 the person who not only has fluctuating capacity so
10 that they have some experience with their illness and
11 they have periods when they are quite able to
12 participate in their decisions, but for whom it is
13 possible to specify with a good deal of accuracy what
14 the research protocols would likely be that they are
15 being asked to participate in.

16 And it's just a matter that, we won't do this
17 research on you while you're in the state that you're
18 in when you're able to consent, the time we need the
19 study, whether it's a physiological study or whatever,
20 metabolic study, or a study of a medication, or
21 whatever, is at the point where you have manifestations
22 of your illness that would not make you able to
23 consent.

1 That seems to me to be captured by avoiding
2 the phrase "advance directive" simply by some notion of
3 prospective consent. That is to say, you are actually
4 going through a consent process the way you would if
5 you were going to have an intervention tomorrow, but
6 the understanding is that this intervention will not
7 occur for weeks or months, or it is even possible
8 never, in your case.

9 If you never went back down in that part of
10 the cycle of your illness, you would never be a
11 suitable subject. That is just a hypothetical. That
12 is not very problematic, it seems to me. We could
13 address that with some phrase about prospective
14 consent.

15 Now, when you can join that with durable
16 powers of attorney for health care, which are not just
17 about end-of-life care, you can have a situation in
18 which the person is able, under the law in most states,
19 to also appoint an agent at that time, and one would
20 hope that right from the beginning from that point the
21 agent is involved with the researcher in learning about
22 the research and being really prepared, with the
23 subject, to take on that role of the on-the-spot

1 decision maker.

2 The harder cases are the ones which I thought
3 were also encompassed in looking at the materials here
4 on pages 121-125 or so, or 127 or so, I wasn't at all
5 clear whether we now were saying this or not.

6 I thought we were also thinking about
7 something which really comes closer to me to being an
8 advance directive because of its generality for
9 patients who are sliding toward a state where they
10 won't be able to make decisions, the dementia patients,
11 in particular, but whose course is not so advanced that
12 you can't engage them in discussion, but they're clear
13 enough about the fact that they know that's where
14 things are going and they may have a number of years of
15 life there where the question would be -- at least one
16 question one could ask is, are you willing when you are
17 in that state to be involved in a study which wouldn't
18 be for your immediate benefit, which would have no
19 potential for benefit for you, and would have some
20 increment over just minimal risk of the type that is
21 more or less part of daily life.

22 For that, some phrase about advance directive
23 is certainly suitable. But I couldn't tell, Trish,

1 whether you, in the exchange with Zeke, were actually
2 saying, well, no, I'm not thinking about advance
3 directives for that group.

4 And I obviously don't know what the rest of
5 the commissioners say. It seems to me that there
6 really still is a difference, and my sense was that you
7 had two categories of potential subjects, those who
8 have told you, I'm willing to have this happen, and
9 those who haven't told you this. Now, this is relevant
10 to the pages we have in front of us because--I think
11 it's on page 123--there's some suggestion of -- the top
12 of 123.

13 For instance, "Research Advance Directives
14 might only be valid when the research presents some
15 prospect of patient benefit and strict time limits
16 could be imposed that require the renewal of a living
17 will."

18 Then there's a reference to the option of the
19 appointment of the legal representative, which is
20 really the discussion of the next section here, so it's
21 kind of out of place.

22 I would like us to highlight at some point
23 here, if we're in agreement, that the advance

1 directives has the ability to play this useful role of
2 separating people who are willing to say now, I will
3 take greater risk for something that won't benefit me,
4 from those who aren't willing to make that commitment.

5 I disagree with Zeke on the notion that if you
6 took a poll among this category of people and you had
7 80 percent of them saying it would be all right to do
8 this, but only 20 percent of them will sign a
9 directive, that that's an indication that the directive
10 method doesn't work, the same way it doesn't work when
11 we know that the public says they want a certain kind
12 of end-of-life care and they don't get around to
13 filling out advance directives about their end-of-life
14 care.

15 One of the things that I believe is valid
16 about the end-of-life care, and I would certainly say
17 is valid about this, is there's a huge difference
18 between expressing a general opinion and committing
19 yourself that this is a course you're willing to
20 follow, and that barrier of not signing the papers
21 isn't just due to laziness.

22 There are psychological factors that would
23 lead a person to say, if asked generally, well, do you

1 think that's research that ought to be able to go on,
2 yes, will you sign up for it, well, let me think about
3 it, and then they never sign up for it because they
4 actually have a reluctance. They don't want to be the
5 subject of such research.

6 So it seems to me that it's a reasonable
7 sorting process between those people who ought to be
8 made unavailable for such research by the fact that
9 they haven't committed themselves to be available.

10 Now, one final note. All of this is against
11 the context of what used to be the law, and I have not
12 researched this recently, but one of the conundrums for
13 research with children and with those who can't make
14 decisions is, the old view used to be, people in this
15 situation cannot be used for something that doesn't
16 have some prospective benefit for them.

17 You can't be a surrogate decision maker and
18 allow someone to be used. Now, we've said, well, let's
19 make a small exception to that. If there really is no
20 more than minimal risk, isn't this the kind of thing
21 that most people could be presumed to be willing to
22 run? Sort of a consensus grew up, yes, that's all
23 right after all.

1 But when we get beyond that more than minimal
2 risk, it seems to me that we are correct in saying that
3 the old view really ought to be adhered to, which is a
4 surrogate, appointed or otherwise, who can't go around
5 consenting people to something that isn't going to
6 benefit them. I mean, it's the archetype of the
7 exploited person.

8 PROFESSOR BACKLAR: That's right.

9 MR. CAPRON: Maybe we should have a discussion
10 on that, and I have a couple of other points in here,
11 Jonathan, about what we say along those lines.

12 CHAIR CHILDRESS: Let me let Trish respond
13 directly, if I could, Eric, from there.

14 PROFESSOR BACKLAR: I do think that it would
15 be extraordinarily helpful, instead of -- in this more
16 abstract way, and I have -- is to situate a situation
17 in which one would use an advance directive like this,
18 and of course, the infamous now UCLA protocol would be
19 a perfect place for this. I'm not going to repeat what
20 that -- is, because I've done it enough times.

21 So you could use a little scenario. It would
22 work in this. Then you'd start to move it along to
23 these other scenarios. When I responded to Zeke

1 yesterday it was because I had thought it through very
2 carefully in terms of some research protocol like UCLA.
3 As we moved along, for instance, into prospective
4 dementias, Alzheimer's, you need to alternate the model
5 somewhat. It doesn't stay rigidly the same.

6 There has to be some way in which we could
7 describe this not being quite so rigid, at the same
8 time keeping those protections in place. That's why
9 when we discussed about Greg Sachs, who's done quite a
10 lot of work here in this, we could use some of his
11 models. So it isn't just one rigid model.

12 CHAIR CHILDRESS: Absolutely. But I think
13 it's also the case, at least judging from my
14 conversations with you, that you would have no
15 objection to our getting rid of the term "Research
16 Advance Directive" to cover the whole area.

17 PROFESSOR BACKLAR: Absolutely.

18 CHAIR CHILDRESS: I think it is misleading.

19 PROFESSOR BACKLAR: I'm not married to a term,
20 I'm married to a concept.

21 CHAIR CHILDRESS: Well, and I think that the
22 term, though, brings in some other things --
23 association. So we're clear about that. I have no

1 problem with that. We'll try to find some alternative
2 way to do it. That still leaves the question of
3 whether there's something very close to the advance
4 directive in a certain area, and that's what Alex
5 focused on also.

6 PROFESSOR BACKLAR: Right.

7 CHAIR CHILDRESS: That will have to tie in
8 more closely with what actually occurs in some areas.

9 PROFESSOR BACKLAR: And I go back to using the
10 words that I'm very comfortable with, which is
11 anticipatory planning.

12 DR. CASSELL: The whole thing is anticipatory.
13 It seems to me that we're talking about two separate
14 kinds of people. If we could separate them out, we
15 would have an advantage. One has to do with a
16 psychiatric patient who has a disease of fluctuating
17 capacity, and also fluctuating clinical states. That's
18 not at all unusual in medicine, even in patients who
19 have no psychiatric disorder.

20 They sign up at the beginning of a research
21 project and they give consent for the project, and good
22 consent, and discusses what's going to happen in the
23 possible stages of the disease.

1 They have given consent when they have the
2 capacity to give that consent, and I don't see any
3 fundamental difference--I'll come to what I think is
4 one difference in a moment--between other medical
5 states and the psychiatric disorders, in which case the
6 person is not giving prospective consent, they are
7 giving consent and the consent has to specifically
8 cover that time when they might not want it.

9 However, we also know that this group of
10 patients might not just wish -- when they are confused,
11 agitated or extremely upset they might not simply not
12 wish to take part, they might refuse to take part, and
13 they have to be protected in both cases.

14 So we have added in a representative --
15 advance directive or advance consent. It's consent for
16 research. If a patient comes onto a research unit in
17 the agitated state, never has been seen before, that
18 person does not qualify. They can't give consent.
19 They shouldn't be used as a research subject. It
20 hasn't been discussed with them when they are in a
21 state when they could discuss what they think is in
22 their own best interests.

23 I don't think a prospective aspect applies. I

1 think we have to make clear the consent for research,
2 greater than minimal risk, requires a full discussion
3 of what might occur, and so forth and so on, and also
4 the protection which we already had in there.

5 Then we have this other problem where people
6 who become permanently decisionally incapacitated, such
7 as the dementias. They are the group that I can -- I
8 can't think of another group, actually, where permanent
9 incapacity is the issue.

10 There the idea that somebody may say in
11 advance, I would like to be considered a part of
12 research, I think that makes perfect sense also,
13 although they, too, may have to be protected by a
14 representative.

15 But we're not talking about advance
16 directives, really. The name does matter. I think we
17 ought to separate those two groups out clearly,
18 otherwise -- it may be my confusion, that's why I'm
19 saying all this, but otherwise we keep getting around
20 to that problem. As far as this, I agree with Trish,
21 the people like the dementias, they make a statement
22 ahead.

23 Their care-givers, the people who are taking

1 care of them, may discuss it with them just like they
2 discuss any other advanced aspect of their care, which
3 they should assent to and sign to while they still have
4 their capacity.

5 CHAIR CHILDRESS: Let's see if there are a few
6 more comments around this part of the discussion. I
7 know Alex has some others to get in as well. But what
8 we'll do is, after getting more comments around this
9 area we've talked about as advance directives, but with
10 all the important qualifications in language and the
11 situations to which this might apply, once we've done
12 that, then we'll get Gary Ellis on on minimal risk and
13 then we'll come back to some of these.

14 But anything else around this particular set
15 of issues? Arturo?

16 DR. BRITO: I want to respond to something
17 that Alex said. I agree with most of what he said,
18 except at the end, I'm not sure. I might have
19 misunderstood something, and I want you to clarify it,
20 that concerns me a little bit.

21 When we're talking about greater than minimal
22 risk, and I'm interested to hear what Gary Ellis has to
23 say about that to clarify it a little bit for us, but

1 their major research has greater than minimal risk,
2 that do not have obvious or immediate direct benefit to
3 the patient, but may later prove useful for that
4 patient, 10, 20 years down the line because of the
5 findings of that study.

6 What concerns me is that blanket policy that
7 does not permit consent for this type of research, even
8 if it is above greater than minimal risk, it may
9 actually prove to cause more harm in the long run. So
10 I'm not sure.

11 Were you saying that if there is greater than
12 minimal risk that there should be a -- and if there is
13 no direct benefit, it's obvious -- I mean, after all,
14 it is research so sometimes during the research process
15 we find what the benefit can be. So are you saying
16 that your opinion is that there should be no means for
17 being able to consent for someone that can't make their
18 own decisions for that?

19 MR. CAPRON: Well, I think, Arturo, this is
20 the issue that we're all struggling with and, in part,
21 is not an empirical question, as it was being posed
22 yesterday, but it is a question about which information
23 might cause us to refine how we go about it. That is

1 to say, how much research are we talking about, what
2 kinds of things are at issue here? As a general
3 matter, however, I was saying, more or less, what you
4 heard me to say and what you may disagree with.

5 My experience in looking at human
6 experimentation for the last, almost, 30 years is that
7 the history of human experimentation is littered with
8 victims of good intentions on people's part, too much
9 enthusiasm for the value of the knowledge, the
10 knowledge often not really quite as forthcoming, very
11 often not as beneficial to the people it was supposed
12 to benefit, and too much willingness -- the more
13 disabled the subject is, the more different the subject
14 is, to go ahead and do the research and have that
15 thought that there may be some benefit there override a
16 sense that this person is just being used.

17 I mean, I think that there are circumstances,
18 extremely moving circumstances, in which a person with
19 any kind of a disease, mental, physical, whatever,
20 agrees to take on, on behalf of others, risks.

21 Sometimes great advances come and sometimes
22 those are, as the mind run of science is, they don't
23 add at that moment to anything that can be used, but it

1 was still a heroic thing for a person faced with that
2 to do.

3 I think that we degrade that choice when we
4 treat as though they are equally extraordinary gifts
5 from people the use of other people who haven't made
6 that choice and who have not said, faced with this,
7 this is how I want my life to unfold, this is a
8 sacrifice which I am prepared to make.

9 I mean, I think the people who do it, it's a
10 supererogatory thing to do. It's not a required thing.
11 We are not all required to be in science simply because
12 we are, in a large sense, the beneficiaries of past
13 researchers. It's a wonderful impulse. It's a grand
14 thing to do that. It's a terrible thing when you do it
15 under misimpression of what you are doing, but it's a
16 grand thing to do when you do it --

17 DR. BRITO: I want to -- what I heard from the
18 public testimony and from reading historically what has
19 gone awry in research in the past, all the atrocious
20 research endeavors, what I keep hearing over and over
21 is not so much whether or not there's greater than
22 minimal risk, whether or not the type of research
23 necessarily, but the process in which it was done,

1 under deceit, to the person or the person taking care
2 of that person.

3 In other words, I think that maybe if it's not
4 so much we shouldn't be worried so much about -- I
5 mean, of course we should worry about the risk
6 involved, but maybe we should be concentrating a little
7 bit more on the informed consent process and not be
8 worried so much about saying this policy that you can't
9 involve somebody in research -- you could involve
10 somebody that has a valid representative in research if
11 it is clearly explained and it is clearly understood
12 that there may not be a direct benefit to that person.
13 Once again, therapeutic misconception, that's the
14 common problem in research, it is not explained whether
15 or not you're decisionally impaired.

16 MR. CAPRON: Well, I agree with just about
17 everything you've said. I guess I just draw the limit
18 on the authority of the surrogate to make a decision
19 which has not been in some sense also chosen.

20 Now, we're talking about these advance
21 directive sorts of things, we're getting away from the
22 term if we can, but the choice is a generalized choice.
23 It would not, itself, meet the requirements for

1 informed consent but it is some sort -- what I'm
2 looking for is some sort of commitment from that person
3 to say, I'm in Category A rather than Category B.

4 I'm in the category of people who -- I'm
5 willing to make a sacrifice. And without that, I'm not
6 comfortable with the surrogate doing that. It just
7 seems to me -- and I entirely do -- one of the things
8 you've said.

9 For most of what we're talking about, the
10 important issues are avoiding deception, avoiding the
11 therapeutic misconception, and other things where
12 people go into something think that they're doing X
13 when they're really doing Y, because there hasn't been
14 good communication.

15 I entirely agree, and I think Laurie said this
16 before and I agree with her about that. We need more
17 attention to that issue throughout all our research
18 stuff and in our document still. But there's still
19 this residual category.

20 CHAIR CHILDRESS: Okay. We'll get Laurie,
21 then let Alex respond, then we'll turn to Gary Ellis
22 and we'll obviously come back to these issues.

23 MS. FLYNN: This has been very, very helpful,

1 I think, and I think we have identified clearly that
2 box, if you will, in which we have some concern and
3 some difference of view.

4 Just two thoughts. One, I do want to stress
5 again my concern that we may want to look at, because
6 of the issues of those who may really not be able, by
7 virtue of their illness, to ever give fully informed
8 consent or participate in the ways we would like to see
9 strengthened, I would look to surrogacy, particularly
10 in terms of someone who has durable power of attorney
11 or who is a guardian as something to be explored for
12 research that is a minor increase over minimal risk,
13 and this includes a vast array of things like PET
14 scans. These are not intrusive, these are not risky in
15 the sense that many of us may be thinking about. One
16 needs to ask ourselves whether our perception of this
17 and the research enterprise has been unduly skewed by
18 some of the kinds of testimony that we heard.

19 We did indeed hear, and we need to pay close
20 attention to, allegations of abuses in psychiatric or
21 other research. There clearly is a very vulnerable
22 subject population here and there clearly have been
23 significant abuses.

1 But we don't know anything yet about the
2 scope, the scale, the standard that's out there. We
3 really may be over-responding and thereby preventing
4 some important research and the benefits of that
5 research.

6 That's why I think there is an empirical issue
7 here, as well as perhaps the value of looking again at
8 some work I think the Alzheimer's people have done,
9 developing more of a sliding scale, looking at a little
10 bit more of a complex layout that increases the
11 protections and supports for the individuals as the
12 increases in risk advance.

13 So I wonder if we might be helped as we think
14 through this with the different kinds of subject
15 populations and the different degrees of risk, which
16 again, we all need to hear more from Gary about.

17 CHAIR CHILDRESS: Jonathan?

18 DR. MORENO: Could I just point out that the
19 current framework does permit potentially beneficial
20 diagnostic studies to be permitted, or consent, if you
21 will, by a legally authorized representative. PET
22 scans could be beneficial to the subject, insofar as
23 they are a monitoring procedure.

1 MS. FLYNN: Well, I guess one would need to
2 discuss what we mean when we say diagnostic study. If
3 it's diagnostic to the individual --

4 DR. MORENO: Yes.

5 MS. FLYNN: -- that's not the only way in
6 which those studies are valuable. Those studies look
7 at the basic interactions going on in mental disorders
8 and they may or may not directly benefit that
9 individual, but they clearly benefit the advance of
10 knowledge about what goes on with --

11 DR. MORENO: Sure. I've heard them described
12 as also a potential benefit to an individual subject.

13 DR. DUMAS: I don't think there's any research
14 project where anyone knows a priori that it's
15 definitely going to benefit the subject, because you
16 don't know, a priori, what the findings are going to
17 be. So there is no situation in which we can assure
18 people that they are going to be directly benefitted
19 from this research.

20 I think that in the case of people who have
21 difficulty or some impairment in making decisions where
22 there is greater than minimal risk, we have to have
23 appropriate protections.

1 We are disagreeing about what those
2 protections should be, but I worry about using people
3 in that category because of the very reason that we are
4 having to spend this time with this population: they
5 have been exploited. And I want to make sure that we
6 have guidelines that will minimize the possibility of
7 that type of exploitation.

8 Now, we know that it happens and we know it's
9 continuing to happen, even among people who try or who
10 think that they have made provisions to protect. So I
11 don't think that we can be too zealous in our efforts
12 to impose some limits on how human subjects are used,
13 and under what conditions, for research.

14 CHAIR CHILDRESS: Okay. We'll get Trish, and
15 see if Alex wants to say anything in response, then
16 we'll turn to Gary.

17 PROFESSOR BACKLAR: I just want to remind us
18 about the limits of consent and why we're so eager to
19 put protections in place with any population.

20 MR. CAPRON: One further concern, Jonathan,
21 also on page 123, where you talk about one of the other
22 objections to advance directives. Then you go on and
23 say that it may be necessary for the states, if this

1 became part of regulation, to adopt legislation. If
2 what we are talking about is something in the category
3 of a prospective consent, I hope we'll be very clear
4 that, for something of that sort, one really doesn't
5 need --

6 DR. MORENO: Right.

7 MR. CAPRON: Yes. And I think that that
8 doesn't come through here and it sounds as though that
9 would be a problem. I'm going to hold my other
10 comments, because we've been trying to get to Gary for
11 quite a while.

12 CHAIR CHILDRESS: All right. Let me just
13 mention, what Alex is proposing in terms of some
14 detailed alteration, we really need to do this as
15 individuals now, let's say in the next few weeks. This
16 report has been a long time in gestation. We've had
17 discussions surrounding it.

18 There are clearly some other things we need to
19 do in terms of getting additional information, but we
20 also need to be working over this draft very, very
21 carefully, making sure that we get the changes in that
22 we think are important.

23 Jonathan is putting those in bold, so the next

1 time we look at this we can check and see if Alex has
2 proposed something on page 123, that it's been
3 incorporated, and then we can see very quickly, well,
4 wait a minute, we don't like the way that's going.

5 But we really have to do that, otherwise we
6 won't be able to bring this to a close. So this is for
7 future steps or further steps. Let's commit ourselves
8 to doing that over the next two weeks so we can really
9 bring this to closure.

10 DR. CASSELL: Will we see any changes as a
11 result of this meeting before we do that, or will we --

12 CHAIR CHILDRESS: Oh, I think you should --
13 no, no. You see, basically, other than the discussion
14 we've had right here we haven't had a lot of discussion
15 of the text.

16 DR. CASSELL: It seems like -- you're in
17 trouble now.

18 MS. FLYNN: Jim, don't -- tried to incorporate
19 the NIH's group's views. They have not yet been
20 articulated for us, but I think there was some
21 substantial expertise there. A useful review of that
22 material might also enrich our --

23 CHAIR CHILDRESS: Two things. One, is a lot

1 of that has already been incorporated. Arturo, Diane,
2 Trish, I, Jonathan, and Eric, and Henrietta--did I
3 catch everyone there--met for a good while after that
4 conference.

5 Actually, if you go back and look at the bold,
6 particularly in the early parts of this, you will see a
7 lot of that already reflected. So we did a lot of
8 that. However, we will have in a few weeks a fuller
9 statement from that conference, and we'll want to make
10 sure that we've incorporated and attended to what's --

11 Now, the bottom line was, no further
12 regulation. We are apparently going to make some
13 recommendations in the area of regulation. Is it
14 urgent? No. We can hold off.

15 Okay. We are glad to welcome Gary Ellis to
16 help us think about minimal risk. We're always glad to
17 have you help us clarify matters. Thank you for
18 joining us.

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1 REGULATORY UNDERSTANDING OF MINIMAL RISK

2 Discussion: Gary Ellis, Ph.D.

3 DR. ELLIS: Thank you, Mr. Chairman. Good
4 morning.

5 Can I have the slides on, please?

6 I'm going to respond to the question that, you
7 asked me to define and describe the regulatory view of
8 minimal risk. In order to do that, I need to give some
9 background as to when the term applies, who applies the
10 term, and you'll recognize that this is because of the
11 structure of regulation that we have.

12 (Showing of slides.)

13 DR. ELLIS: So the Federal policy for
14 protection of human subjects contains the term minimal
15 risk and it is defined, so it applies to 17 government
16 department and agencies' research portfolios.

17 (Changing of slides.)

18 DR. ELLIS: Similarly, the regulations of the
19 Food and Drug Administration contain the term. It is
20 defined in the exact same way as the Federal policy for
21 protection of human subjects.

22 (Changing of slides.)

23 DR. ELLIS: And so the term minimal risk that

1 I'm going to use and define applies to research funded
2 by any of 17 departments or agencies, regulated by the
3 Food and Drug Administration, or voluntarily pledged to
4 the regulations of the Department of Health and Human
5 Services.

6 (Changing of slides.)

7 DR. ELLIS: There is no mandate that is
8 applied to research not conducted by the aforementioned
9 departments or agencies not regulated by FDA or not
10 pledged to 45 CFR 46. This is very important. You've
11 heard me say this before, you've seen these slides
12 before. You heard Alex describe these yesterday. It's
13 very, very important.

14 (Changing of slides.)

15 DR. ELLIS: Minimal risk means--this is the
16 regulatory definition--that the probability and
17 magnitude of harm or discomfort anticipated in the
18 research are not greater in and of themselves than
19 those ordinarily encountered in daily life, or during
20 the performance of routine physical or psychological
21 examinations or tests. That's the black-and-white
22 definition and it's been more or less unchanged since
23 1981. It was changed in a minor way in 1991.

1 Now, who applies this definition? In general,
2 a quorum of the Institutional Review Board applies this
3 definition. So in any case, that is at least three
4 individuals, which must include a non-scientist.

5 So again, minimal risk is not the judgment of
6 any one individual, ordinarily, it's the judgment of at
7 least three individuals, one of whom must be a non-
8 scientist, by regulation, in the domain of research
9 that I described. Beyond the domain of research that I
10 described, none of this necessarily pertains.

11 Let me stop there and say that I think that in
12 practice the way that minimal risk is applied is, IRB
13 members know it when they see it. I'm not certain that
14 too many IRB members -- well, I shouldn't speculate.

15 We don't know if IRB members could quote this
16 definition, we don't know if they could pull it out on
17 a laminated pocket card, but we are confident that they
18 know minimal risk when they see it. Perhaps they could
19 not explain it in the terms of this definition, but
20 they bring their good sense to the table and they have
21 a feel for what is greater than minimal risk.

22 I'll give you an example so this is less
23 abstract. Let's suppose that you, as IRB members, are

1 considering a protocol that involves lumbar puncture.
2 So you may have a visceral reaction and just determine
3 in your mind that lumbar puncture is greater than
4 minimal risk, or you may ask some questions or seek
5 information, what are the risks of lumbar puncture
6 itself.

7 I think physicians or health care
8 professionals might say, well, there's the risk of
9 infection, there's the risk of nerve damage, there's
10 the risk of headache from upsetting the cerebrospinal
11 fluid, and the extreme risk of paralysis.

12 Others who are physicians may agree or
13 disagree with that list, but that would be a reasonable
14 thought process for an IRB member to go through. Then
15 there is a judgment.

16 So this is a more sophisticated judgment than
17 the first judgment I described, which was a visceral
18 response to everything you know, or think you know,
19 about lumbar puncture.

20 Now, you have specific risks of harm or
21 discomfort attached to the research procedure and you
22 make a judgment as to whether the probability and
23 magnitude of those four specific harms or discomforts

1 are greater than they are in daily life. Let me go
2 forward.

3 (Changing of slides.)

4 DR. ELLIS: On this slide I have not added to,
5 nor subtracted from, the definition of minimal risk,
6 I've just displayed it in a different way so that we
7 can work through what the more sophisticated IRB
8 members or analysts might actually work through.

9 On the left side of the not greater than side,
10 it says, "the probability and magnitude of specific
11 harms or discomforts in the research," so this is not
12 abstract.

13 You are now, as IRB members, considering a
14 specific research protocol and we can know, or at least
15 estimate, what the specific harms or discomforts
16 conveyed by this research might be. Then we can
17 estimate the probability and magnitude of each of those
18 harms or discomforts.

19 Then we would compare, and I'm moving to the
20 right side of the equation, and we ask the question, is
21 the probability and magnitude of these specific harms
22 or discomforts not greater than the probability and
23 magnitude of those specific harms or discomforts in

1 daily life or in routine exams or tests?

2 If you conclude that that probability on the
3 left is not greater than the probability on the right,
4 then you would have something -- a proposed research is
5 not greater than minimal risk.

6 One remaining question on the right side of
7 the equation. It says, "in daily life," and so you may
8 have the question, in the daily life of whom? It's not
9 stated in the regulation. The regulation says just
10 what it says on the slide, "in daily life."

11 Now, I know it's not the daily life of healthy
12 persons, because that trial balloon was floated in the
13 1991 rule making process and the term "healthy persons"
14 was explicitly omitted from the rule. So this, we
15 know.

16 Well, is it the daily life of patients, is it
17 the daily life of people who may be less than healthy?
18 One could proceed under that interpretation but it
19 would lead one to the conclusion that people who are in
20 harm or discomfort, the patients, can actually be
21 subjected to greater harm or discomfort than another
22 ordinary person. And that would be, I submit to you,
23 an unacceptable conclusion.

1 Let me restate that. If you proceed with that
2 interpretation and on the right side of the equation
3 you have the person in extremis, you could do just
4 about anything to that person and you'd come to the
5 algebraic conclusion that this is not greater than
6 minimal risk because the person is in such bad shape
7 anyway. That would not be a positive conclusion for
8 the protection of human subjects and research.

9 So our office prefers to interpret the concept
10 of daily life as meaning the daily life of all people,
11 which includes the research subjects, which includes
12 healthy people, includes people who are less than
13 healthy.

14 So if you proceed in that manner, you would
15 not ever come to the conclusion that you can inflict
16 harms or discomforts on people who are in considerable
17 harm or discomfort because it's no worse than they are
18 anyway, and it would be most protective for human
19 subjects.

20 So to conclude, I just want to restate what
21 others around the table have said before me, using
22 different words. Minimal risk is not moderate risk,
23 it's not intermediate risk, it's not medium risk, it's

1 not midway risk, it's not so-so risk. We take minimal
2 to mean least, smallest, limited, minor. Minimal risk
3 is just what it means, minimal. So this is a narrow
4 category of research that is, as it says, minimal risk.

5 I'll be glad to answer any questions you may
6 have.

7 CHAIR CHILDRESS: Thanks very much, Gary.

8 Trish?

9 PROFESSOR BACKLAR: Thank you, Gary. I'm a
10 little confused. You're saying that this risk is not
11 experienced by healthy people. Are you saying they're
12 ordinary?

13 DR. ELLIS: I'm saying all people, which
14 includes healthy people, less than healthy people,
15 subjects of research. That's what I'm saying.

16 PROFESSOR BACKLAR: All right.

17 DR. ELLIS: I know that it's not the daily
18 life of healthy people. This I know, because that term
19 was explicitly omitted after being floated as a trial
20 balloon in 1981.

21 PROFESSOR BACKLAR: Then would you say, using
22 your example of a lumbar puncture, that this would not
23 be minimal risk, since most of us don't experience this

1 in our day to day lives?

2 DR. ELLIS: I think four out of five people
3 would conclude that lumbar puncture is greater than
4 minimal risk. I think there may be a commissioner or
5 two here who would disagree with that. Perhaps not.

6 PROFESSOR BACKLAR: How would you deal with
7 this then if you're doing research on somebody who, for
8 instance, has schizophrenia and their risks of their
9 everyday life are far greater than yours and mine. So
10 what kind of baseline do you have in mind here, because
11 it's still a little bit fuzzy for me in the way you've
12 described it.

13 I had in mind that it would be ordinary people
14 so that if one were going to describe risk of somebody
15 in a population, for instance, someone who suffers from
16 schizophrenia, right away you would be able to -- the
17 very fact that they're being in research, may be for
18 them riskier than it would be for you.

19 DR. ELLIS: Let me answer twice, first in lay
20 terms and lay language from instinct. I know that I
21 can't come to the conclusion that, because the person
22 has schizophrenia and is in worse shape in some ways
23 than the healthy person, that I could do more to that

1 person or with that person than I would with a healthy
2 person. So I don't think I used any regulatory terms
3 there and I announced I was speaking in lay terms from
4 instinct.

5 Now let me speak as a regulator. If I look at
6 this equation and I say, what is the probability of
7 magnitude of harm or discomfort in the research on the
8 left side of the equation, I suppose I could put the
9 individual with schizophrenia, the prospective subject
10 with schizophrenia, on the left side of the equation
11 and say, well, what's the probability of magnitude of
12 harm or discomfort X, Y or Z for this schizophrenic
13 patient? That's one way to work that person into this
14 equation.

15 But I would avoid putting the individual with
16 schizophrenia on the right side of the equation and
17 saying in the daily life of the schizophrenia, because
18 that could lead me to the conclusion that, in my first
19 statement, I found unacceptable.

20 CHAIR CHILDRESS: Diane?

21 DR. SCOTT-JONES: Gary, I have a question
22 about your reference to the daily life of all people.
23 That sounds as if the point to which you would compare

1 the person who's a prospective research participant is
2 an average, and then you are then referring to healthy
3 persons, aren't you? It seems that in the end the
4 standard is the healthy person. If you're saying all
5 people and then you somehow take an average of all
6 people, that would be a healthy person.

7 DR. ELLIS: If your assumption is that the
8 average person is fully healthy, then I would disagree
9 with your assumption. I think that, if I look at all
10 people, that the probability and magnitude of harm or
11 discomfort X, Y or Z, is real and is measurable in some
12 number of those people. So you and I might be at odds
13 as to whether, with regard to the probability and
14 magnitude of specific harms or discomforts, an average
15 person equals a healthy person.

16 DR. SCOTT-JONES: Well, it seems that the
17 definition is fraught with problems as long as it
18 stands the way it is. Is there the expectation then
19 that the decision rightfully belongs with individual
20 researchers, with specific IRBs? Because it seems that
21 as long as the definition remains this way you will
22 always have instances in which you need to discuss
23 particular cases to decide whether there is minimal

1 risk, a minor increase over it, an increase over it.
2 It seems that there is no way out of the problems that
3 exist with this definition.

4 DR. ELLIS: Let me give some background again
5 on the purpose to which this definition, this term, is
6 used in the regulations. You maybe overestimate the
7 problem or you may be looking to the concept of minimal
8 risk to add a use to the term for which it wasn't
9 intended.

10 The term "minimal risk" is used in the Federal
11 Policy for Protection of Human Subjects, in the common
12 rule, essentially for three purposes. One, as a
13 cleaver to decide what can be reviewed by other than a
14 fully convened IRB. I'm talking about an expedited
15 review process. So that's one important use of the
16 concept of minimal risk.

17 Research that's greater than minimal risk not
18 be found on a list of 10 items must be reviewed by the
19 fully convened IRB. So, as you say, it must be
20 discussed.

21 Minimal risk is also used as a cleaver to
22 decide what research can proceed without consent. And
23 minimal risk is also used as a cleaver to decide when

1 documentation, a consent form, may be omitted. So
2 those are the three principal uses in the common rule.

3 There's another minor use. One element of
4 informed consent says, for research greater than
5 minimal risk, certain information must be conveyed to
6 the subject. But I've described the three main uses of
7 the concept of minimal risk.

8 If you are looking for a cleaver for other
9 purposes, I guess there's two choices. One, is to
10 redefine minimal risk. I don't know that I would
11 advocate that. The other, is to invent some new
12 cleaver to serve your purpose.

13 CHAIR CHILDRESS: Alex.

14 MR. CAPRON: I guess my hope in having you
15 make the presentation today would be that we would get
16 some sense of whether there has developed a kind of a
17 common law of this. That is to say, that in the IRB
18 guidebooks, in IRB educational materials, we have a
19 fairly rich set of examples of the sorts of things that
20 if you were called for your advice and someone said,
21 well, we have a questionnaire for someone to fill out,
22 well, is it a sensitive subject? No, it's not a
23 sensitive subject. Well, that's an example of

1 something that's not --

2 You're going to do a needle prick to get a
3 little blood. Is that? No, that's not. In other
4 words, we're going to do venipuncture. Through the
5 years, all the different kinds of things that are done.
6 Is there any sense of the way in which that term is
7 filled out?

8 I mean, there are many terms that the law
9 uses, the reasonable person and so forth, that remain
10 sort of, each case, a matter of the decision of the
11 jury. There are outer limits where judges will say
12 that something is, on its face, negligent and no
13 reasonable person would have done that.

14 But the term remains elastic. There are other
15 terms which become terms of art where we have, through
16 case law and so forth, a sense of where you could say,
17 well, what does consideration mean here or something.

18 Where are we on this? I guess I was assuming
19 that part of your presentation might be that you could
20 really give us a sense, particularly as it relates to
21 the kind of impaired subjects we're talking about here,
22 where the minimal risk line would likely be drawn,
23 recognizing, as you say, that, strictly speaking, it's

1 a decision of the majority of any IRB. Or it may be,
2 in some cases, the IRB administrator or IRB chair who
3 says, I sign off on this, through expedited review;
4 I'm convinced that it meets the minimal risk.

5 DR. ELLIS: Well, I understand the question.
6 I have no slide. I was going to show a blank slide to
7 illustrate that I have no answer for the question, but
8 that didn't work.

9 (Laughter)

10 MR. CAPRON: Important data showed up on this
11 slide, so I can't do it.

12 DR. ELLIS: Alex is asking for the frequency
13 distribution, where we have arrayed ordinary research
14 procedures that repeat over and over through the years
15 and around the country, a labeling on that frequency
16 distribution of how often an IRB found this to be not
17 greater than minimal risk, or greater.

18 That information was not something that's ever
19 been collected, so there is -- let's call it a
20 folklore. It's not even as formal as the common law.
21 I think that at the extremes there would be 100 percent
22 agreement among IRB members, probably among
23 researchers, among observers, that a needle prick at

1 one end, or something dramatic at the other, is either
2 less than minimal risk or greater. In the middle, IRBs
3 will come to different judgments. On lumbar puncture I
4 thought I could split this group, but nobody spoke up.

5 So the best that we can do as administrators
6 of this large system is to say, well, we're going to
7 put the judgment, under ordinary circumstances, on at
8 least three people who are close to and understand the
9 research site, which means the researchers, the
10 expertise, the prevailing values and ethics of the
11 community. That's as far as we've gone, is just to
12 say, well, we trust that system. That's the best that
13 we can do.

14 Now, why haven't we collected data on that
15 system, is a good question. We heard before that there
16 is a general lack of evaluation of the system. Dr.
17 McKay came before you in January of 1997 and said he'd
18 be back in March 1997 with a results of a 191-question
19 survey, and I for one am still very anxious to see the
20 results of that.

21 MR. CAPRON: Right. This wasn't -- let me be
22 clear. In raising this this way, this was not in the
23 least a statement on my part of reminding us that we

1 have so little data about the system.

2 I actually thought that, through your
3 educational programs and so forth -- I mean, you get --
4 IRBs are not plants that grow in the jungle, they are
5 groups of people who go through processes.

6 Part of those processes, as you suggest, are
7 local processes and then part of them are educational
8 processes. So if you have new members of the IRB you
9 are more likely to want to have them do an educational
10 program so they get their bearings. And I just
11 wondered what the bearings here were. I thought there
12 might be something at that level. There was one other
13 thing, but there's not, so I'm dropping that.

14 There's one other thing that surprised me,
15 what you said, and I may have misunderstood you. When
16 you were looking at the chart that you have up here,
17 you were asking that the -- you were thinking that the
18 IRB would be comparing the magnitude and probability of
19 specific harms or discomforts that arose in the
20 procedure with those same likelihood -- the probability
21 and the magnitude of those same things arising in
22 ordinary life. That surprised me, from just my own
23 experience with IRBs over the years, is the sense that

1 I had always observed what seemed to me to be more of a
2 trade-off.

3 That is to say, well, what's the probability
4 that people fall, break their legs, ski into trees,
5 whatever it is? I think that that's sort of a
6 distribution. And those risks of dying unexpectedly,
7 being injured unexpectedly, and so forth, are the risks
8 of daily life.

9 Now, one may object that, unlike average
10 income, it doesn't make a lot of sense to talk about
11 those as, what is the average person here, because the
12 distribution is so dramatic. It's sort of like average
13 income in a country in which there's a very unequal
14 distribution of income, a lot of very poor people and a
15 few very rich. Is the average income \$20,000 or should
16 we really be drawing on something else?

17 But, I mean, I took that to be some way in
18 which we can say, well, what are the probabilities
19 you're going to have some bad thing happen to you? But
20 not that you would specifically have the same bad
21 things happen to you that you would have from the
22 research.

23 That is to say, what's the probability that

1 you will have a headache or be paralyzed, which are the
2 two major risks of lumbar puncture, but is the kind of
3 discomfort generally or the kind of risks generally
4 there more than what happens to people, on average, in
5 ordinary life?

6 That's what I thought was going on. But you
7 seem to say, no, it's really, you're looking for these
8 specific risks and saying, do those happen to the
9 average person in ordinary life. Did I understand you
10 correctly?

11 DR. ELLIS: You understood me correctly.

12 MR. CAPRON: Is there some regulatory
13 explanation, I mean, some commentary of an official
14 sort that OPRR or others give to tell people that
15 that's how they're supposed to read this?

16 DR. ELLIS: I've shown this slide several
17 times.

18 (Showing slide.)

19 DR. ELLIS: I don't think there's any
20 commentary beyond this. I think what you say,
21 actually, is probably quite true, is that most IRB
22 members, for the right side of the equation, use a more
23 vague or a more grand average of daily life. And I'm

1 not disagreeing with that.

2 In fact, that was the sense of my opening
3 remarks, is that I think most people sort of apply this
4 by instinct and never get to this slide at all. But if
5 we sit down and we try to map out what this black-and-
6 white letter of the regulations say, I think you would
7 actually map it the way that I did.

8 Obviously, I sat down to map it and I came up
9 with that next slide. You may disagree. I think, in
10 practice, most IRB members actually never think that
11 specifically about the risk of harm or discomfort X, Y
12 or Z in daily life.

13 MR. CAPRON: Yes. I mean, the phrase there
14 "harm or discomfort," to me, is different than the
15 phrase "the harms and the discomforts anticipated in
16 this research." Harm and discomfort are like pain and
17 suffering, they are broad categories. But, I mean, I'm
18 not arguing that your interpretation is wrong. Again,
19 you're in an official position to interpret and I'm
20 not.

21 What I'm sort of wondering is, what do we
22 bring in? If we're using that term here, I hate to use
23 the term again, common law, but what sort of received

1 understanding do we bring in here?

2 Yours would be one which I would expect to be
3 a very influential received understanding, particularly
4 if it's been reduced to writing, if it's been used in
5 IRB educational materials and lectures and so forth,
6 it's likely to influence the way our IRBs go about
7 their business.

8 I mean, in my own sense, going back to the
9 Daumel paper, Daumel was -- correct me on that paper; I
10 can't remember. But way back in the time of the
11 National Commission, there was a paper published in the
12 *New England Journal* which looked at research and argued
13 that most research, in fact, does not have greater
14 risks than ordinary life.

15 And they were not just looking at the
16 research, the occurrence of specific incidences of
17 research, and saying, do those things occur. They were
18 looking generally, as I recall the article, at the
19 risks of ordinary life. They had some broad statements
20 about risks of accidents and so forth.

21 I've always understood the term to be derived
22 from that source and to reflect that very, as you say,
23 sort of generalized understanding of what are the risks

1 and discomforts of ordinary life.

2 CHAIR CHILDRESS: Okay. I have Eric, then
3 Arturo.

4 DR. CASSELL: I don't want to tie too much
5 into this, but the definition says, "Ordinarily
6 encountered in daily life -- extraordinary -- of a
7 risk, the population we're talking about now does not
8 have the usual perception of the world around them
9 because they are sick.

10 So our problem is that what we consider to be
11 an ordinary risk, clinical risk, like a physical
12 examination, may be seen by somebody who -- our problem
13 is how to -- outside of them at the same time
14 recognizing -- so we have a minimal risk category, but
15 we also try to protect them --

16 CHAIR CHILDRESS: Gary, did you want to
17 respond?

18 DR. ELLIS: No.

19 CHAIR CHILDRESS: Arturo?

20 DR. BRITO: I've been trying to assist the
21 debate throughout the hearings. I'm one of those
22 people who feels that lumbar puncture is really not
23 much, if at all, minimal risk if it's done in a correct

1 fashion and in the right hands.

2 When you were initially describing the four
3 different risk factors of doing a lumbar puncture I
4 thought your point was going to be that, in ordinary
5 life, your chances of getting an infection are going to
6 be greater than in all the lumbar punctures that have
7 ever been done, in a percentage.

8 Your chances of getting paralyzed are going to
9 be greater than all of the people who have ever been
10 paralyzed secondary to lumbar puncture, even in
11 research -- especially in research protocols. You
12 obviously made the other point.

13 So I'm thinking more of percentages. I'll
14 give you an example of something that is considered
15 minimal risk by most, is venipuncture. They showed in
16 studies that children that have had venipunctures in
17 research protocols, by far, suffer less psychological
18 consequences of having that venipuncture than those
19 that had it in clinical circumstances.

20 So the point there is, in ordinary life,
21 somewhere down the line you're going to get your blood
22 drawn, probably. The research, by doing it in a
23 research protocol, it actually reduces the chance of

1 any harm being done.

2 My point here is, and this is what I was
3 trying to say earlier, that it is so difficult to make
4 a blanket statement or draw the line somewhere of what
5 is minimal and what is moderate. In certain
6 situations, something that appears to be higher than
7 minimal risk may actually be minimal risk.

8 I think I heard Laurie say earlier, somewhere
9 we have to maybe describe a bit more in the sense of
10 gradient and be very careful in not excluding people
11 from research studies that may involve them in what
12 appears to be something that's greater than minimal
13 risk.

14 CHAIR CHILDRESS: Other questions, comments?

15 MR. CAPRON: I don't disagree with that, but I
16 want to underline one thing that the discussion has
17 made clear to me. Which is, if we begin moving away
18 from the standard that we have and the draft as it now
19 is and we start saying, well, when there is only
20 minimal increment to minimal risk, we are adding on a
21 vague notion on top of a notion which, as written here,
22 I think is almost incoherent as it is now being applied
23 and obvious has a utility, and it can be used and is

1 used all the time by IRBs, but it's not a very fixed
2 point.

3 It isn't like average income, the average
4 household income of the United States. What we can say
5 is, that is \$28,272, and a moderate increase over that
6 would be \$2,000 or less. That's moderate.

7 DR. BRITO: As we begin to draw additional
8 categories on something that is as vague as this, we're
9 beginning there -- I would agree with all the comments
10 yesterday when people were saying don't make too many
11 categories, because we're making categories which are
12 like wet spaghetti. I mean, it's just --

13 DR. BRITO: Exactly. So I guess what I'm
14 saying is, let's not make the categories. I think the
15 effort should be more concentrated on the informed
16 consent process and the explanation and communication,
17 et cetera.

18 I think it's impossible to make these
19 categories. I mean, somebody even mentioned PET scans.
20 Well, someone else may say, well, the psychological
21 harm that can come from that is much greater than
22 minimal risk.

23 So there are just so many interpretations you

1 can have from that, whereas somebody else -- you know,
2 I would consider it no big deal for myself, but someone
3 else, particularly somebody who has a psychiatric
4 disorder, may suffer even worse by being put through a
5 PET scan. So the point is, I think we have to be very
6 careful not to categorize it so neatly because I don't
7 think it can be so neatly categorized.

8 CHAIR CHILDRESS: Diane, then Jon.

9 DR. SCOTT-JONES: We have a big problem in
10 getting this report done, because we have a notation on
11 page 143 from Jonathan that we need to decide what
12 we're going to say in this particular report about
13 minimal risk.

14 I think we may have a problem that may be
15 practically unresolvable if we're required to use the
16 definition of minimal risk that's there, because it
17 implies a quantitative judgment, as Eric has just
18 pointed out to us.

19 From what Gary has said, in practice, people
20 make a qualitative judgment. That is, they recognize
21 what minimal risk is, what greater than minimal risk is
22 in an intuitive way, and they're making a qualitative
23 judgment that they couldn't quantify if their lives

1 depended on it.

2 So we're treating this as if we can somehow
3 make a quantitative judgment and talk about increase
4 over minimal risk, a minor increment. Those are all
5 quantitative terms and we are not able to do that.

6 Also, the notion of daily life in that context
7 is absurd, given that Americans' daily lives vary so
8 dramatically, with some people on a daily basis being
9 exposed to enormous risks, ranging from gunshots to
10 being run over by a truck; other people's lives are
11 more sheltered and they're more protected.

12 So we are just being irresponsible if we say,
13 well, it's all Americans' daily lives, when any person
14 knows that some Americans' lives are extraordinarily
15 poor and other Americans' daily lives are wonderfully
16 protected and safe.

17 So I think we have two big problems. One, is
18 we are jumping from qualitative to quantitative
19 judgments, and the other is that we are imagining that
20 Americans have some homogeneous life that is relatively
21 benign or an ideal life when, in fact, that's not the
22 case. We need to do something about this definition.

23 CHAIR CHILDRESS: I don't disagree, but we

1 have to ask what we can do for purposes of this report.
2 To do something with it in the larger sense, in terms
3 of trying to change the common rule or, a much slower
4 process, helping to change the interpretation of this
5 particular category in the common rule, I think we will
6 all be dead before we finish this report.

7 DR. MORENO: Gary, I sometimes wonder what
8 would happen if the definition dropped the first
9 disjunct which is the one that everybody always talks
10 about, namely, those ordinarily encountered in daily
11 life, and only use the second disjunct to the right
12 side of the -- namely, the performance of routine
13 physical or psychological examinations or tests.

14 In other words, part of my question may have
15 to do with what you understand as a regulator to be the
16 nature of the "or." Is that, first of all, an
17 exclusive "or" as logicians say, in other words, it's
18 one or the other but not both, or is it an inclusive
19 "or," "and/or," as we recognize in ordinary English?
20 In either case -- well, if it's the former, then might
21 not IRBs be able to decide which criteria they would
22 like to apply?

23 It seems to me, to take the example of the LP,

1 that lumbar punctures might qualify under the left side
2 of a disjunct, but probably would not qualify under the
3 right side. That is to say, I don't think that lumbar
4 puncture is part of a routine physical examination, at
5 least I don't want to go to a doctor that says it's
6 routine.

7 So then my question is, I guess, several-fold.
8 How much flexibility -- in your view, do IRBs have in
9 deciding which disjunct to apply? Materially, what
10 would be gained or lost if one were to use only the
11 second disjunct?

12 DR. ELLIS: Well, I can answer your question
13 as a matter of reading the plain English. The clause,
14 the "or," to use your words, I think, is exclusive,
15 meaning A or B, it's not an "and," it's an "or."

16 DR. MORENO: Ordinary English is usually taken
17 to be inclusive. So in other words, in order to make
18 it --

19 DR. ELLIS: Let me put it this way. You can
20 have one or the other.

21 DR. MORENO: But not both.

22 DR. ELLIS: You don't need both.

23 DR. SCOTT-JONES: But you could have both.

1 DR. ELLIS: You could.

2 DR. MORENO: In ordinary English, usually to
3 make it exclusive people say either A or B.

4 DR. ELLIS: Yes. I read it as "or," not "and,"
5 because it would say "and" if it was intended to be
6 "and."

7 DR. MORENO: Well, it would say "and/or."

8 DR. ELLIS: But it doesn't say "and/or," it
9 says "or."

10 DR. MORENO: So you consider it to be
11 exclusive.

12 DR. ELLIS: Let me go back to my first point.
13 I think that minimal risk and greater than minimal risk
14 is what a majority of the quorum of the IRB finds to be
15 greater than minimal risk.

16 MR. CAPRON: Why isn't the IRB administering
17 -- excuse me. Into the microphone. If you're
18 dealing with expedited review, isn't that usually
19 something that the chair signs off on? I don't --

20 DR. ELLIS: If you're dealing with expedited
21 review, yes.

22 MR. CAPRON: Well, that is, in my good sense,
23 the major use of it. Yes, if it was occasionally used

1 to avoid the documentation for consent, you're doing a
2 face to face interview with people in public places
3 and you don't make them sign a consent form. Why?
4 Because you're asking them questions which are not
5 risky to them. Occasionally you do that research
6 without any consent at all because you're doing
7 observational studies. The major use is expedited
8 review.

9 DR. ELLIS: I think you're correct.

10 MR. CAPRON: And that can be done because the
11 chair signs off, it wasn't more than minimal risk. I
12 sign off and I approve it for the IRB. So you don't
13 need a majority. You could have a single physician,
14 the chair of the committee, looks at the lumbar
15 puncture and says, this is not more than minimal risk.

16 DR. ELLIS: No, that's incorrect because
17 lumbar puncture isn't on the list of 10 categories for
18 expedited --

19 Let me go back to the main point, that the
20 IRB, in its wisdom, under certain circumstances a
21 single member of the IRB, as Alex points out, for
22 certain procedures that are listed determines what is
23 greater than minimal risk.

1 Now, those individuals do that with reference
2 to this stated standard and I don't think, in practice,
3 that there's the level of dissection of this stated
4 standard that we've just gone through around the table,
5 in all honesty.

6 So if you are interested, for a certain
7 population of prospective research subjects in creating
8 a cleaver, is the word I've used, to decide what
9 research can proceed, what research can proceed under
10 certain circumstances, you may wish to create some new
11 term, some new definition for that term that serves
12 that purpose because the purpose of this term, as Alex
13 has described, is mostly to determine what can go
14 forward for expedited review secondarily, tertiarily,
15 when consent can be omitted, when documentation of
16 consent can be omitted for research that is covered by
17 the Federal departments, policy, regulated by the FDA
18 or voluntarily pledged. So you still have the issue of
19 research beyond that.

20 CHAIR CHILDRESS: Are there any other
21 comments? I know Trish is waiting to get in.

22 PROFESSOR BACKLAR: Well, the problem is, I
23 see that we can't seem to get away from this, indeed,

1 rather relative concept, the way it's dealt with. It's
2 an interesting idea, Jonathan, that you brought up
3 about, which side of the "or."

4 If you went to the physical exam, would that
5 be for a healthy person or would it be -- in the same
6 box? I think the real problem is that average person
7 as opposed to the healthy person.

8 If you had a healthy person, would that give
9 us a clearer baseline through which we could then go
10 into, depending on the population that you're dealing
11 with, that somebody, for instance, again, with
12 schizophrenia maybe having a PET scan might be more
13 difficult than it would be for me to have a PET scan.

14 CHAIR CHILDRESS: Rhetaugh?

15 DR. DUMAS: I think our dilemma lies in the
16 tendency to be too specific or to try to go to a higher
17 level of specificity than is possible in situations
18 such as the ones that we're discussing.

19 It might be that what we need to do is to
20 think in terms of parameters and general principles.
21 I've said this before. There are some things that must
22 necessarily be left to the judgment of the people who
23 are making that decision, and the best that we can do

1 is to give them some guidelines for making the
2 decision, not to make the decision for them. Now,
3 that's one of the points.

4 The other has to do with the same kind of
5 thing about the report. I don't think that we are
6 going to come to agreement on all aspects of the
7 content of the report, but I think we do need to agree
8 on the basic points that we want the report to reveal.

9 If we could do that, the most important points
10 that we want to make in that report, we could come to a
11 decision on that, then we would have to leave it to the
12 writer to convey that. I don't think that we could get
13 all mixed up in the context of this because we'll never
14 finish it.

15 CHAIR CHILDRESS: Any last comments for Gary?

16 MR. CAPRON: I'm sympathetic with the point
17 that Rhetaugh just made. This is really one of the
18 fulcrum issues of this entire report because, and I
19 sense there is a division, a division which may be
20 dramatic in the sense that we may have an 8-10 vote on
21 the Commission, one way or the other, as to whether or
22 not it makes sense to say, because of the value of the
23 research process and the potential findings from

1 research, we want to allow research to go ahead without
2 the consent of the individual, with someone else's
3 consent--I mean, we are still talking about other
4 protections; there would be an IRB reviewing it, there
5 would be some surrogate decision maker--which involves
6 more than minimal risk. So it then becomes important
7 that we have some sense of what we're talking about
8 there.

9 DR. BRITO: But parameters determined by whom?

10 DR. ELLIS: Well, it is going to be determined
11 by the IRB. But there are limits to what IRBs can
12 determine, and there may be -- I'll put it this way.

13 If we discover there is not a common
14 understanding that within the context of this report we
15 should go into some detail, and the writing we'll leave
16 to others, Rhetaugh, I agree, but we should have a
17 discussion of the kinds of things that we believe that
18 term to mean when we use it here, otherwise we haven't
19 said anything.

20 DR. SCOTT-JONES: Could I very strongly agree
21 with what Alex just said? I think we have to decide,
22 even if it's no more than saying that these are
23 problematic, but this is how we're using the term. I

1 believe we have to have some statement in this report
2 or what we have said is going to be meaningless.

3 I think a definition that is left wide open
4 allows for the possibility of mischief when that
5 definition is used in the real world and people are
6 trying to get a research project under way and stay on
7 schedule.

8 I think we have to aim for as much clarity and
9 agreement as we can muster among ourselves. I think
10 this is critical. We cannot just use language to avoid
11 the problem of deciding what we need to say.

12 PROFESSOR BACKLAR: Right. We have to have
13 some kind of baseline that is understood.

14 DR. DUMAS: But you can't exhaust all the
15 possibilities that would fall under that category.

16 DR. SCOTT-JONES: Right. I agree.

17 CHAIR CHILDRESS: Jonathan, then we're going
18 to move to a break.

19 DR. MORENO: At the risk of repeating myself,
20 this draft attempts to deal with this problem by
21 establishing some examples of minimal risk and greater
22 than minimal risk interventions--not research,
23 interventions--for these kinds of populations.

1 The language is on page 146. It's Number 6.
2 We can tweak that for a while as a group, or
3 individually, if you like. There is discussion around
4 pages 90, 91, 92 on this issue. So it doesn't seem to
5 me that there is no basis for this discussion in the
6 current draft.

7 CHAIR CHILDRESS: And what I would urge is
8 that we all look very, very carefully at this and, not
9 that we'll have a chance to do it thoroughly today, but
10 decide exactly how we want to proceed. It may well be
11 that we'll look carefully at this, and a couple of
12 people who have paid a lot of attention to the debate
13 about minimal risk, for example, Alex and anyone else
14 who would like to join in, might propose additional
15 language for our consideration.

16 Bette gets the last comment and we'll take a
17 break.

18 MS. KRAMER: I hate to take the last comment,
19 but I thought it might be helpful to the committee to
20 hear from somebody who is listening to the discussion
21 for the first time.

22 As I've listened to you, and having read the
23 report just recently for the first time, I think that

1 the reality is that what you're talking about, just
2 plain and simple, does not permit an objective
3 measurement.

4 Therefore, it really becomes a question of
5 trust and, you know, how paranoid do you really want to
6 be? I think if you believe it's appropriate to be
7 totally paranoid, then you just don't allow any
8 research at all to go forward where you can't get a
9 true informed consent from the potential subject, and
10 otherwise I think you have to rely on the nature and
11 the character of the narrative.

12 And, as I said, having read the report for the
13 first time, looking at it fresh as opposed to having
14 reworked it and reworked it, and listening to
15 discussions, I really want to compliment you all on it.
16 I think it's beautifully written. I think it expresses
17 great sensitivity. I think it's a document that, in
18 general, the Commission can really be proud of.

19 CHAIR CHILDRESS: Okay. Thank you, Gary, for
20 joining us. We appreciate your help. Okay.

21 Let's take a 15-minute break and resume.

22 (Whereupon, at 10:00 a.m., the meeting was
23 recessed.)

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AFTER RECESS

(10:17 a.m.)

DISCUSSION CONTINUES ON RESEARCH WITH DECISIONALLY
IMPAIRED SUBJECTS: DRAFT REPORT

CHAIR CHILDRESS: Okay. Let's get started
again. Okay. Jonathan wants to say something.

DR. MORENO: Just very briefly. I just spoke
a few minutes ago to a relevant section of the report
that speaks to attempting to array examples of minimal
and greater than minimal risk, is not on pages in the
90s, it's in the 70s. It starts on page 73 and goes on
for about 8 or 10 pages.

CHAIR CHILDRESS: Let's pick up our discussion
and see if there's anything else you want to say about
minimal risk. We've noted that the problems, the
difficulties, in defining it and specifying it. What I
would urge people to do, since this does play a crucial
role in the document as you have it, is actually to
look over those pages very, very carefully and let's do
some e-mail exchanges.

I mean, let's really now pick up along the
lines of the cloning report, movement toward modifying

1 this in a way that can get us to a final draft. Those
2 who feel particularly strongly about things, let's come
3 forward with proposed language and let's move it.

4 Now, connected with that, I see Laurie and
5 Jonathan had a conversation over the break about
6 interpretation of benefit. We do concentrate on the
7 risk side in our discussions, but obviously the benefit
8 side is also important, where we are talking about the
9 probability and magnitude of benefit parallel to the
10 probability and magnitude of harm or discomfort.

11 So let's have a few comments about that since
12 I think their discussion, as I understood it, was
13 potentially instructive, potentially beneficial to our
14 group. Laurie or Jonathan?

15 MS. FLYNN: Well, the comment that I made was,
16 I continue to have real reservations about the
17 structure that was laid out here in terms of greater
18 than minimal risk with no potential benefit, in part,
19 because my understanding of the concept of potential
20 benefit is pretty direct, pretty immediate, and pretty
21 readily and likely to happen for the individual who is
22 the subject of research. That's what I thought our
23 text was saying and that's my understanding of

1 potential direct therapeutic benefit.

2 Jonathan, I think, has a view that is
3 different and appears to feel that the definition may
4 be somewhat more elastic and more broadly applied in
5 the real world than the way I'm seeing it.

6 I think it's useful for us to understand, how
7 is that term defined, what is meant by potential
8 benefit to the patient? I think we really had no
9 conversation, no inputs from the research community or
10 others, as to how that term of art is used when IRBs
11 make decisions.

12 CHAIR CHILDRESS: Okay.

13 DR. MORENO: Laurie has expressed, in essence,
14 what I said to her during the break. Namely that,
15 without endorsing this view, my experience as an IRB
16 member is that the notion of potentiality is, indeed,
17 quite elastic and that investigators are given a
18 relatively large amount of leeway in identifying what
19 could conceivably be of benefit to the subject,
20 including even simply a closer monitoring of the
21 subject.

22 In the experience with the early HIV studies,
23 for example, this was a very common point that was made

1 by investigators, that potentiality of benefit for
2 subjects could include simply getting better health
3 care. That gives rise to other issues about access to
4 health care and so forth, but we're putting those aside
5 for a moment.

6 So what I was saying to Laurie was that,
7 perhaps in practice, more kinds of studies can be
8 captured by the concept of potential benefit than one
9 might at first think or one might think is
10 philosophically ideal.

11 CHAIR CHILDRESS: Jonathan, since I don't have
12 the document fully memorized at this point, I can't
13 remember how well we do it in the document.

14 DR. MORENO: Probably not as well as we ought
15 to do, because the document does try to walk the
16 straight and narrow philosophical line that potential
17 benefit ought to be -- a relatively compelling case
18 ought to be made for potential benefit for the subject.
19 But what I was saying was that, in practice, the way
20 this washes out in the real world is that there is more
21 breadth given to the concept than is done in the
22 textbooks.

23 CHAIR CHILDRESS: Could you take as a task to

1 elaborate in appropriate places on that and we'll have
2 further discussion on it.

3 Other points to be made? Let me, before we --
4 two other things should be mentioned about minimal
5 risk. One, is the FDA has a statement on minimal risk
6 and that sheet will be provided and circulated. So it
7 will be sent to the NBAC office and then will be
8 circulated to us.

9 Then, second, but we won't pick this up until
10 Alex comes back in, there's also a research project
11 under way at NBAC in looking at the literature of
12 trials involving decision impaired subjects to
13 determine, here again with the uncertainties about
14 definition, those that involve more than minimal risk,
15 and then with an effort to look at some of the consent
16 forms related to those research projects. So we'll
17 want to say more about that, and both those points are
18 connected with minimal risk.

19 DR. CASSELL: On the issue of benefits
20 yesterday when we were having that argument back and
21 forth, there is a benefit to people to be treated as
22 though they were normal persons, to be allowed to do
23 what normal persons do. To be altruistic. One of the

1 things that normal persons do is to be altruistic, and
2 that that is a benefit.

3 However, I do not want you to think that I
4 think that's a benefit under the terms usually meant by
5 benefit versus risk. The benefits we mean are direct,
6 usually therapeutic benefits, not the benefits of
7 belonging to humankind.

8 DR. MORENO: No. But what we're -- and what
9 concerned Laurie was not the notion of directness, but
10 the notion of potentiality. That is the issue that was
11 of great concern to Laurie, and how the likelihood of
12 benefits that might accrue to being in a study -- if
13 there's 100 percent likelihood of feeling altruistic, I
14 suppose, though I agree with you, that's not what I
15 would, as a professor of medical ethics, consider to be
16 a direct benefit of being in a study.

17 What Laurie was concerned about was the
18 likelihood that this diagnostic test or this
19 therapeutic intervention that was being examined would
20 be of direct benefit to me as a subject.

21 CHAIR CHILDRESS: I thought it went beyond
22 that, that this might well produce something that would
23 be of benefit to me as a subject and not simply limited

1 to -- if we go the direction you're going in, Jonathan,
2 it seems to me then that brings it much more clearly
3 under what we would ordinarily think about using as
4 traditional language, that we've gone beyond the
5 therapeutic trials.

6 But I would take it that Laurie is looking at
7 the review that, even in what we tend to think about as
8 non-therapeutic trials, a possibility of developing
9 something that would be beneficial should be included
10 on the benefits side. Laurie, am I misunderstanding?

11 DR. MORENO: That's an accurate description of
12 her thinking, just to be clear. What I was saying was
13 that in the real world my experience is that much of
14 what you and I sitting around an academic seminar table
15 might think of as non-therapeutic is often construed as
16 having benefit, not just the psychological benefits,
17 but being observed by good doctors and nurses as part
18 of the study might accrue to your well-being -- your
19 medical well-being.

20 MS. FLYNN: Again, I was focusing on many of
21 the kinds of basic neuroscience studies that are not
22 intended or designed to provide immediate therapeutic
23 benefit that are looking at the underlying etiology and

1 process of disorder. There's no immediate likelihood
2 that my clinical condition, if I am a subject, is going
3 to be enhanced. So I would agree with all of these
4 discussions through the very narrow definition of
5 benefit.

6 DR. MORENO: By the way, also in the real
7 world I'm sure you've all seen on consent forms --
8 often one sees a consent form as a statement. One of
9 the benefits to you for being in this study is being
10 more closely monitored, having your condition more
11 closely monitored. Many people would consider that to
12 be a potential benefit.

13 CHAIR CHILDRESS: As we approach this and
14 think about the revision of the document, one has to
15 worry about excessive elasticity at this point.

16 Diane, then Trish.

17 DR. DUMAS: But knowing about that elasticity
18 just increases my resolve that people for whom the risk
19 is conceived to be greater than minimal should not be
20 included in research projects. There's another point
21 here, too. That is --

22 DR. MORENO: Just to be clear, you mean,
23 should not be included in research projects without

1 their consent or --

2 DR. DUMAS: Without their consent.

3 DR. MORENO: -- without some analogous
4 process.

5 DR. DUMAS: Without their consent.

6 DR. MORENO: Would you permit legally
7 authorized representatives to make --

8 DR. DUMAS: Yes. There would be exceptions.
9 Yes, of course. But I think a general rule --

10 DR. MORENO: Because that's the framework
11 right now.

12 DR. DUMAS: The general rule is that people
13 should be informed about the research. We should make
14 every effort to make sure that they understand what
15 they're consenting to in that process. Now, if there
16 is some reason why that can't be obtained through the
17 regular process, then the conditions under which there
18 would be exceptions should be defined.

19 But there is also a mention in the document
20 about benefits accruing not only to that individual,
21 but to the population. I don't know whether we want to
22 deal with that or not. If the benefit is to the
23 population for which the person belongs, are we

1 interpreting that to be a benefit to the individual? I
2 think that distinction needs to be made.

3 DR. MORENO: I think we're quite clear that
4 that is not considered to be a benefit to the
5 individual.

6 DR. DUMAS: As long as we're talking about
7 potential or likelihood, I'm comfortable. I don't
8 think we can promise anything more.

9 CHAIR CHILDRESS: Diane, then Trish.

10 DR. SCOTT-JONES: I was just trying to look in
11 the draft, Jonathan, to look back and review where you
12 talked about benefit and what it means. I am just
13 trying to see how far we're going to go with this
14 notion of quantitative judgments because we're sort of
15 suggesting somehow that you balance the benefits
16 against the risk and that you have some favorable ratio
17 of benefits to risks.

18 I don't know if we want to do more in that
19 regard than we've already done, and I'm not sure that
20 that was the point of the comment that maybe there are
21 more benefits than we've acknowledged in most research
22 projects.

23 Is that the point, so that somehow the

1 benefits side will have more points on it in relation
2 to the risk side; is that the thrust of the comments?

3 CHAIR CHILDRESS: Well, first of all, we've
4 just not looked at the benefits side. If we're going
5 to include the benefit/risk ratio in the determination
6 we at least need to say something about it.

7 But, second, there was also a question
8 about --

9 DR. SCOTT-JONES: There's quite a lot of it.

10 CHAIR CHILDRESS: That is in our discussion.

11 DR. DUMAS: Oh. Okay.

12 CHAIR CHILDRESS: Our discussion is focused
13 only on the risk part. Then there's the question about
14 whether it can be defined narrowly or broadly.

15 But I think -- either risk or benefit, it
16 can't be purely quantitative because there is the
17 qualitative element that enters in in even defining
18 something as a harm or discomfort, et cetera. So it's
19 going to be much more complicated, even if there is a
20 quantitative sign.

21 CHAIR CHILDRESS: Trish, then Rhetaugh. I'm
22 sorry. Diane, first. Sorry.

23 DR. SCOTT-JONES: I was just going to say,

1 here is already at least acknowledgement of persons
2 saying that there are indirect benefits, such as
3 diversion from routine, the opportunity to meet with
4 other people, to feel useful and helpful, greater
5 access provided to professional care and support. I
6 think we've done a lot already to acknowledge these.

7 CHAIR CHILDRESS: Well, the point was, not in
8 our discussion.

9 DR. SCOTT-JONES: Oh. Okay.

10 CHAIR CHILDRESS: Our discussion here. What
11 we need to do is identify, since we don't have a lot of
12 time, areas that we want to go back and now look at the
13 report and make sure that the report does what we want
14 it to do, and then Alex and Eric can just come in.

15 Then really take a Dali-like approach to this,
16 namely, over and through e-mail and faxes over the next
17 several weeks, really push forward areas where we want
18 to make the kind of revisions so that we can come up
19 with a draft that we can really go through very
20 carefully and see whether that reflects what we, as a
21 subcommittee and as a Commission, want to hold.

22 I have Trish, and then Rhetaugh.

23 PROFESSOR BACKLAR: I want to back up -- very

1 important when we go to this. We know there's
2 potential benefits, just as we know there's risk of
3 harm. There is that balance going on there. I also
4 want to reiterate the subjective aspects of these
5 personal benefits are hard to quantify. The other
6 thing which I really actually believe we have in the
7 report, that some of these benefits which Laurie is
8 alluding to come about because the actual care for many
9 of these people is inadequate.

10 Some people come into these protocols in order
11 to get something they just don't get outside, just like
12 people do who have AIDS. There are all kinds of
13 research protocols going on with different diseases
14 where this occurs.

15 CHAIR CHILDRESS: We'll take Rhetaugh's
16 comment, then we'll turn to the issue I raised about
17 the research project on minimal risk research that the
18 NBAC staff is conducting.

19 DR. DUMAS: What I'd like to do is share with
20 the group what I've said to some individuals, and that
21 is that we need to give greater attention to issues of
22 the characteristics or the constellation of IRBs
23 because you can't quantify the factors that are

1 important to consider.

2 Ultimately, the people who sit on the IRBs
3 will have to make judgments. We need to think very
4 carefully about, as best we can, how those boards
5 should be constellated to get the kind of judgments
6 that we believe that they need to make.

7 CHAIR CHILDRESS: Alex, if you'll make your
8 comment, we want to then talk about the research.

9 MR. CAPRON: Yes. I want to follow up
10 directly on what Rhetaugh just said, because I was just
11 having a conversation with Gary Ellis and I think it
12 would be useful for Jonathan to take a look at the
13 language about the special composition IRBs when
14 they're dealing with research having to do with
15 prisoners because, as Rhetaugh has emphasized,
16 particularly when we're dealing with these vague
17 standards, membership is going to be important.

18 Without having to get into the whole subject
19 of how adequate IRBs overall are and what their
20 composition is and their education, certainly an
21 emphasis on a membership that would have a
22 representative of the relevant patient populations that
23 would be perhaps more heavily balanced towards lay

1 people and outsiders rather than fellow researchers and
2 physicians, or physician researchers -- for this, would
3 be a way of giving us some comfort that the process
4 beyond the consent issue, which is so difficult for us,
5 is adequate to the particular needs of this population
6 where we have a history.

7 I want to just put on the table something.
8 After our last meeting, I was sent a consent form for
9 one of the studies of people who testified. I thought
10 the testimony had been very interesting in emphasizing
11 the quality of the consent process, and so forth.

12 The consent form didn't come up to that
13 standard. I wrote the investigator asking for some
14 clarification because I was afraid I was
15 misunderstanding what was represented in the form.

16 The staff is now engaged in the project of
17 looking at studies in this area that seek to involve
18 more than minimal risk and where there are questions
19 about the subjects being exposed to risk without real
20 consent, and so forth.

21 We'll be following up to try to get some more
22 consent forms to see whether they could usefully
23 address that aspect of the issue, because I agree with

1 what many people have said about the importance of
2 consent here.

3 We all recognize that the consent form is not
4 equivalent to the consent, but certainly a consent form
5 which itself has problems is not likely to be well
6 remedied by aspects of many undefined -- about that. I
7 mean, that's what the UCLA people said. Well, yes, the
8 form was no good, but we had a conversation in which
9 all this came out.

10 I think that the concern about the membership
11 of the IRB is one way of addressing that because I
12 think the more disinterested IRB would have looked at
13 the form that I saw and said, wait a second, what does
14 this mean, why are we saying this, is this accurate, is
15 this conveying what's really at issue here? So perhaps
16 we can address it and perhaps you could get some ideas
17 from other areas of the regulations that already
18 specify special make-up.

19 DR. MORENO: Could I just -- I want to make
20 sure that I have good guidance right now from committee
21 members. Alex, are you suggesting that I should draft
22 further recommendations to the effect that not only the
23 discretionary authority that the IRB now has to add

1 consultants and other members for specific studies
2 involving vulnerable or special populations, but that
3 those ought to be required for certain kinds of
4 studies?

5 MR. CAPRON: Yes.

6 DR. MORENO: Okay. I just want to predict
7 that people will raise questions about the impact of
8 that requirement on the capacity of institutions to do
9 studies with these populations. I can hear some folks
10 whispering in my ear, perhaps not in this room, that
11 the analogy to prison studies would constitute a
12 significant drag on the ability to do research with
13 these populations. Now, as a draftsman I'm only
14 pointing this out to you. I'm trying to anticipate an
15 issue that this will --

16 MR. CAPRON: All protections of human subjects
17 are a drag on the ability to do research.

18 DR. MORENO: Yes. But when we're talking
19 about prison research we're talking about a relatively
20 high threshold, as you know better than I. That is,
21 again, something that this body needs to consider. I'd
22 be happy to draft the language --

23 MR. CAPRON: Why don't you draft something and

1 we'll consider it when we have a draft.

2 DR. MORENO: Okay.

3 MS. FLYNN: Let me just ask a question,
4 because I feel very strongly about this. And I
5 appreciate very much your comments, Rhetaugh and Alex.

6 My organization several years ago drafted a
7 policy that specifically requests guidance to IRBs who
8 do review a great deal of psychiatric research, that
9 they have as members of the IRB no fewer than two
10 representatives of the subject population and that IRBs
11 who do not routinely review this research have an
12 affirmative obligation to bring on as consultants not
13 only experts who are physicians and researchers, but
14 those who represent the community who are the subject
15 population. I guess I'm not clear what the burden is.

16 DR. MORENO: That language that you just used
17 doesn't vary greatly at all from what is currently at
18 the discretion of the IRB. What I heard Alex
19 suggesting was that something along these lines, some
20 proportion of the IRB, not only membership, but a
21 further question is, should they actually be present
22 for the discussion of that study. Very often these
23 folks, as we all know, don't show up.

1 By these folks, I mean, community members have
2 a hard time attending, very often. So it's not only a
3 matter of having them as members on a piece of paper,
4 but also having them actually sign off on the study.

5 MS. FLYNN: Yes. Yes. Yes. Absolutely.

6 DR. MORENO: Okay. That helps me.

7 DR. DUMAS: I feel very strongly that our best
8 bet for getting change is through the IRB. If people
9 in our communities don't show up at IRBs, we need to
10 understand why. In some communities they do and they
11 are very active. It's not comfortable for the
12 scientists.

13 Most often, the groups have more scientists
14 than other members. So if you've got one community
15 member and they feel overwhelmed at not having a voice,
16 I can see why they don't come. But we need to change
17 that.

18 Well, I don't think I need to say anything
19 more about that because the assumption in the past has
20 been that the IRB is a scientific evaluative committee
21 so it should be comprised of people who are involved in
22 research and who have a commitment to the development
23 of science.

1 I think that that is only partially true, that
2 it should also include people who have some interest in
3 the general welfare of those who are being involved in
4 this process.

5 CHAIR CHILDRESS: Okay. Let me Eric to come
6 in. Alex has to leave shortly, right? Would you like
7 to comment on the research project?

8 MR. MESLIN: Sure. I'll just be brief about
9 this and tell you where we are. A couple of stand-back
10 are with us now and we can benefit from any input that
11 the commissioners have.

12 Following the last meeting when Alex had
13 expressed some interest in staff pursuing this we
14 engaged in a number of search strategies, inductive
15 search strategies, designed to identify those projects
16 published in the peer review literature that seemed to
17 meet this generalized concern of studies that involved
18 greater than minimal risk for which not only the
19 consent form or consent process might be an interesting
20 indicator of whether or not protection was adequate,
21 but also more substantively whether or not the research
22 design itself raised any particular ethical questions.

23 So what we are now in the process of doing--

1 and it's a very intermediate process, there's nothing
2 to present to you today--is we've identified probably
3 several hundred abstracts that seem to meet this
4 general threshold of concern.

5 We would love to hear maybe a bit more comment
6 from commissioners as to what they would really like to
7 see, because the next step in this process is to
8 contact the investigators, identified obviously by
9 authorship on the papers, and ask whether they wouldn't
10 be prepared to share with us a copy of both protocol
11 and consent form. This will serve a couple of, I
12 think, very useful purposes.

13 One, since this isn't an investigation into
14 unethical practices but merely an effort to understand
15 what the nature of this research activity is, it would,
16 I think, meet our public obligation at the very least,
17 but it would meet, I think, the more substantive
18 obligation to understand just what is going on.

19 Now, we realize that the publication of a
20 study is not identical with our ability to understand
21 all of the nuances of what goes on in the preparation
22 of a protocol and how consent forms in the process
23 might be carried out.

1 At this point, that is what our strategy is
2 and we would hope to be able to complete a summative,
3 if not formative, analysis of that within the next few
4 weeks.

5 CHAIR CHILDRESS: Any comments on that?

6 (No response)

7 CHAIR CHILDRESS: One other thing, before Alex
8 leaves, I'd love for us to decide, and that is whether
9 we want to meet in February.

10 MR. CAPRON: Well, I'm not clear from
11 yesterday's discussion we didn't come away with the
12 impression that, if we're dealing with a topic in Los
13 Angeles the next meeting, we ought to all be dealing
14 with that.

15 So if the Tissues Report is in a position
16 where it ought to be discussed, I would hope we don't
17 have Tissues or Genetic Subcommittee meetings in which
18 the rest of us would then come in and be presented
19 again with something which would require, for Genetic
20 Subcommittee people, to go over that ground again and
21 either feel frustrated that we're all so naive and
22 unsophisticated or that they've gone off in a direction
23 which others are not happy with.

1 Likewise, I would hope we don't go much
2 further on this report. We had some good feedback from
3 the other commissioners yesterday and it helped to make
4 clear for us areas where the report needs to be worked
5 on. But from now on in, aren't we thinking that we're
6 going to be meeting as a committee of the Commission
7 instead as of a couple of subcommittees?

8 If so, Eric, Jim, I mean, it's really a matter
9 of saying, how much are we going to have from our
10 various work products that are ready for further
11 discussion to be mailed out two weeks from now, which
12 is really what you're talking about if you're going to
13 have a useful discussion.

14 So part of the agenda may be this report and
15 part of the agenda may be the Tissues Report, and the
16 Federal Agencies Report, and whatever.

17 CHAIR CHILDRESS: I'm quite open on this. I
18 understood from the discussion that evolved that the
19 Genetics Subcommittee felt the need to meet in February
20 to move their report.

21 MR. CAPRON: I'm just saying, we shouldn't let
22 them meet by themselves.

23 PROFESSOR BACKLAR: Right. I second that.

1 MR. MESLIN: Sounds like we're going to L.A.
2 in February. You will be hounded for your calendar
3 availability, since we are currently trying to secure
4 two dates in February. The two dates being either
5 February 5, 6 or 6, 7, and not everyone has responded
6 to that yet.

7 It would be very helpful, since the Genetics
8 Subcommittee knows what it will be able to get
9 accomplished within the next couple of weeks, i.e.,
10 within the next two weeks so that documents can be
11 circulated in more than sufficient time for all
12 commissioners to receive and think about them, it is
13 not an entirely revised Stored Tissue Report, it is
14 some specific aspects of that report that will be
15 required for a focused discussion.

16 It would be very helpful if this subcommittee
17 could also make the same kind of request of staff, or
18 of Jonathan with us, for what it specifically wants to
19 have on the agenda for the February meeting.

20 CHAIR CHILDRESS: Could I throw out some
21 possibilities?

22 MR. MESLIN: Please.

23 CHAIR CHILDRESS: One, is we've had some

1 things identified that we need to work through. Some
2 of those having to do with minimal risk and benefit,
3 for instance, can be -- the addition of -- materials
4 that we've not talked about.

5 Basically I would say our discussion with the
6 whole Commission did not talk about the report. We
7 only focused on a couple of recommendations. So I'm
8 not at all concerned about not having something to do.
9 I think we could have a very profitable discussion with
10 the whole Commission about this report.

11 That, at least, is my sense. I don't know
12 what others feel. We should really go through it and
13 think it through, with the changes that will be made
14 also. But not that we have to have made every single
15 change we think would be important at this point.

16 DR. CASSELL: And in these two weeks we'll be
17 doing back and forth. The two weeks before our
18 document has to be produced we'll be going back and
19 forth on e-mail.

20 CHAIR CHILDRESS: I should hope so, if people
21 are willing to commit to that. I think we could have a
22 document that would be just a step or two short. But
23 we have to obviously get the whole Commission's

1 agreement on certain kinds of things, and some of that
2 will come in February.

3 DR. MORENO: I just need to be clear, Jim, on
4 what we can do and what I can humanly do in the next
5 two weeks. Is your theory that the whole Commission
6 will be working from the current draft?

7 CHAIR CHILDRESS: The current draft as
8 modified, which would include any material -- any
9 changes we can make in the discussion of minimal risk,
10 et cetera -- the recommendations based on the
11 discussion yesterday and today, doing the kinds of --
12 making the kinds of changes that we're committing
13 ourselves to working on over the next several days and
14 exchanging on e-mail.

15 DR. MORENO: I can certainly make some headway
16 in modifying the current draft. I am a little
17 concerned, though, that there will be confusion if I
18 make -- some of the modifications are substantive,
19 quite substantive, and that the full committee will
20 then be at a disadvantage in not being able to keep
21 straight which is --

22 MR. CAPRON: Do a cover memo. Just do a --

23 DR. MORENO: Yes. What I've done, and so

1 forth.

2 MR. CAPRON: Read these pages for that, and
3 this is new material and very -- and we're all --
4 discussing it for the first time.

5 DR. SCOTT-JONES: Could I add to that that
6 Jonathan already did some of that by noting points,
7 like on page 143 and 144, issues we would need to
8 discuss, things that are not in the draft.

9 I think doing that type of thing, and also
10 bolding the additions so we would know the things that
11 had already been done in response to previous concerns.
12 I think all those kinds of things helped us to be able
13 to --

14 CHAIR CHILDRESS: I agree. And we are going
15 to have to have a discussion with the whole Commission
16 on this document. I should note that the outside
17 critics have had less to say about--and internal
18 critics--about the first several chapters. It's really
19 only at the end where most of the problems have come,
20 but we need to think about how all the things
21 integrate. So I think we really need to have that
22 study -- having that with these modifications in
23 February, if that would be suitable for --

1 PROFESSOR BACKLAR: I think the Genetics
2 Committee is going to be very interested and very
3 involved in the discussion -- same issues.

4 DR. SCOTT-JONES: I think, in addition to the
5 cover memo, Jonathan, or I guess any one of us, perhaps
6 you, Jim, could lay out for the whole Commission what
7 these issues are -- in addition to their having them
8 pointed out in the actual draft, because I think the
9 discussion might be more productive now if it's really
10 focused and not so wide-ranging.

11 CHAIR CHILDRESS: I agree. Jonathan, Eric and
12 I will take the lead on that, but we'll circulate
13 materials to you to review, that is, what we are going
14 to propose along these lines.

15 DR. CASSELL: Just for clarification -- not
16 making any changes in the hard copy before -- e-mail --

17 CHAIR CHILDRESS: We need to set a closing
18 date for this. Let's look at the calendar and see
19 exactly when NBAC needs to send out --

20 MR. MESLIN: May I make a suggestion, at the
21 risk of helping Jonathan organize his work schedule.
22 You all have his draft from today. I don't know
23 whether everyone has given Jonathan any comments,

1 written or otherwise, based on that text. If you are
2 intending to do so, please do that as soon as possible.

3 If you are also going to be providing
4 additional materials based on the sort of homework
5 assignments that seem to be coming out, please do that
6 within the next week, i.e., within seven days.

7 DR. CASSELL: We are using as our baseline
8 draft of December 22, 1997.

9 MR. MESLIN: Correct.

10 DR. CASSELL: Unchanged, at least until that
11 week is past.

12 MR. MESLIN: Correct. It would be staff's
13 hope --

14 DR. CASSELL: The baseline draft is this draft
15 until seven more days.

16 MR. MESLIN: Yes. Right. And it would be
17 staff's hope that two weeks prior to the full
18 Commission meeting, or sometime in the week of -- I'm
19 just guessing here --

20 DR. CASSELL: The 19th. I believe the 19th.

21 MR. MESLIN: Thank you. The 19th of January.
22 We will be sending out the briefing books or have the
23 briefing books being prepared with these revised

1 materials, giving the full Commission at least, and
2 hopefully, two weeks with directions for how to make
3 their way through the materials, cover memos, et
4 cetera, for what needs to be focused on.

5 I mean, I'm pleased to say that with some of
6 our additional staffing now that's something that we
7 can do much more efficiently, and that you will come to
8 the Los Angeles meeting prepared to discuss those items
9 identified in that cover memo. The full Commission
10 will receive all materials from this point forward.

11 Is that what seems reasonable?

12 CHAIR CHILDRESS: Any dissent to that?

13 (No response)

14 MR. MESLIN: This is a good time to talk about
15 the dates.

16 CHAIR CHILDRESS: Okay.

17 MS. HYATT-KNORR: The only other issue I would
18 like to raise is a very simple one, namely, which date
19 would you like to pick. The 5th and 6th would be
20 Thursday/Friday, the 6th and 7th would be
21 Friday/Saturday. We have all agreed on the 6th
22 already, the question is just, which day would you like
23 to add at one end or the other for yourselves.

1 DR. CASSELL: Would we have to start first
2 thing in the morning on Thursday if we started on the
3 5th?

4 CHAIR CHILDRESS: Could we start early
5 afternoon? I think that would be helpful for --

6 DR. CASSELL: We can travel out. You want to
7 use the Thursday to get out there anyway. It's just a
8 question of getting an earlier flight.

9 DR. SCOTT-JONES: I can't. I'd have to do it
10 Friday and Saturday. I teach on Thursday.

11 CHAIR CHILDRESS: Friday and Saturday.

12 MS. HYATT-KNORR: Thursday and Friday.

13 PROFESSOR BACKLAR: It doesn't matter to me
14 either way.

15 DR. CASSELL: Thursday/Friday.

16 MR. MESLIN: What we will likely have to do,
17 is we will have to take one final poll with the rest of
18 the Genetics Subcommittee members as well, and we'll
19 have to make a decision that allows everyone to
20 obviously be there on the 6th, which will end up being
21 a full day. Some will be able to come for the half
22 day, which may turn out to be the way we do this,
23 either on the 5th or on the 7th.

1 So I hope you will appreciate that as we're
2 moving into this new arrangement towards full
3 Commission meetings with everyone participating, that
4 every effort will be made to attend as much of the
5 meeting as possible.

6 We realize that this is difficult, and we're
7 making these dates on the fly with previously existing
8 commitments for your day jobs already in place.
9 Hopefully by February forward, we will be able to
10 schedule the rest of the Commission meetings along the
11 lines that we had discussed in the planning bucket
12 yesterday. So no one should take it personally if your
13 preferred dates are not the dates that the Commission
14 will be meeting in Los Angeles.

15 CHAIR CHILDRESS: But it sounds as though
16 everyone can make the date that had been previously
17 scheduled, and that's very important. Okay.

18 Any other discussion of what we need to do on
19 the report, because it's almost 11:00.

20 (No response)

21 CHAIR CHILDRESS: We do have two people who
22 have indicated that they would like to offer public
23 testimony. If anyone else is interested in doing so,

1 if you would indicate to a member of the staff.

2 Jack Schwartz and Bill Freeman, could you wait
3 until after the public testimony? We only have two
4 people who are planning to testify, we can go ahead and
5 do that since we planned to do that at 11:00, if that
6 will be all right. Okay.

7 First, is there anything else we need to say
8 about how we're going to proceed on the draft report?
9 I think we may have covered everything we need to. But
10 let's plan to be active and revive the e-mail exchange
11 program and move very quickly on this. All right.

12 I know some are having to leave, Alex in
13 particular. Let me just thank everyone at this point
14 for being here and for a productive day and a half.

15 The first person presenting in public
16 testimony is Mr. John Cavanaugh-O'Keefe, who needs no
17 further introduction. He is with the American
18 Bioethics Advisory Committee.

19 And you know there's a five-minute rule, I'm
20 sure.

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STATEMENTS BY THE PUBLIC

Statement by: Dr. John Cavanaugh-O'Keefe

American Bioethics Advisory Committee

DR. CAVANAUGH-O'KEEFE: Got it. Yes. Thank
you very much, Doctor. I wanted to issue an
invitation, with a quick preamble.

1 I was very much intrigued by Dr. Rhetaugh
2 Dumas' question yesterday, or challenge to the
3 Commission, why is it that it's so difficult? What are
4 the underlying issues? As we look at protection of
5 human subjects, is there something that's not on the
6 table?

7 Why is it that this, which appears to be
8 simple, in fact, becomes radically complicated very
9 quickly? It did seem to me that at least one of the
10 underlying issues is the issue that Ms. Kramer
11 mentioned this morning, and that's the question of
12 trust or lack of trust.

13 What came to mind for me was the issue of
14 spina bifida research. During the second World War,
15 spina bifida nearly disappeared in Great Britain, but
16 for the next 50 years researchers looked for the
17 genetic predisposition for it.

18 Almost all, 99 percent of research on spina
19 bifida from World War II until about two years ago, was
20 a complete, total waste of time. Nearly everybody who
21 was born with spina bifida, or 90 percent, after World
22 War II need not have been born with that condition.

23 If anybody had looked at what happened 50

1 years ago, what they would have found is that it can't
2 be a genetic predisposition if it disappeared during a
3 war.

4 What happened in Britain? It was only fairly
5 recently that people looked at that and realized that,
6 during the war, the British were on rationing and were
7 eating government-made bread which had Vitamin A added.
8 That need not have waited 50 years.

9 I think that it is fair for people to be
10 extremely angry at a research establishment which, for
11 50 years, ignored a cure that was staring them in the
12 face. So I think that the question of trust is the
13 underlying issue that Dr. Dumas was looking for.

14 Responding in a tiny way to that, I wanted to
15 issue an invitation. That is that on January 23 there
16 is a Pro-Life college group from the midwest that will
17 be sponsoring a protest in front of the offices of the
18 National Bioethics Advisory Commission dealing with the
19 issue of human cloning.

20 They've invited me to come speak there, and I
21 said that I would. But I would also really urge that
22 anybody from the Commission who would like to come out
23 and talk with these folks, I'd really urge you to come

1 out and do so. I think that they would make room for
2 you on the program, if you wished to do that.

3 But whether you want to speak or just listen,
4 I'd really urge you to respond in some kind of way.

5 Doctor, thank you very much.

6 CHAIR CHILDRESS: Are there any questions,
7 comments?

8 (No response)

9 CHAIR CHILDRESS: Just a question for
10 clarification. The focus of the protest would be the
11 report or --

12 DR. CAVANAUGH-O'KEEFE: The issue of human
13 cloning, responding, I think, to the NBAC's Human
14 Cloning Report.

15 CHAIR CHILDRESS: And you say that's going to
16 be held --

17 DR. CAVANAUGH-O'KEEFE: That will be January
18 23. It's in conjunction with the Rowe v. Wade protest
19 of January 22. This will be the next day.

20 CHAIR CHILDRESS: Any questions on this?

21 (No response)

22 CHAIR CHILDRESS: All right. Thank you very
23 much.

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And Dr. David Shore of the National Institute
of Mental Health.

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STATEMENTS BY THE PUBLIC

3

Statement of: Dr. David Shore

4

National Institute of Mental Health

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DR. SHORE: Good morning. I'm here

6

representing the NIMH, taking the place of Rex Calgary,

7

who has moved on to try and serve as a liaison between

8

the clinical research community and the private sector,

9

perhaps moving from a difficult job to an impossible

10

one. We shall see.

11

I just wanted to make four brief comments, and

12

I'll try to stay within the five minutes. First of

13

all, I wanted to let you know that the intramural

14

research program at NIMH has finished their

15

investigation of some of the allegations that were

16

presented to this group previously and that we have, as

17

you call it, a penultimate draft that we have delivered

18

to Dr. Childress conveying a number of action items.

19

If there are questions about those as you look at them,

20

please let us know and we will try and clarify any of

21

those issues.

22

The second point I wanted to mention was that,

23

as you heard, December 2nd and 3rd of this year we did

1 have a trans-NIH panel meet to discuss some of these
2 same clinically relevant issues in research involving
3 those with questionable capacity, uncertain capacity.
4 We've certainly gone back and forth on the title
5 several times as well.

6 This panel report is in draft at present. It
7 is circulating to members of the NIH community and
8 should go out to members of the panel this coming week.
9 We would hope to have it available for you by the end
10 of this month.

11 I can tell you that it will focus on guidance
12 for IRBs, the idea that there are already provisions in
13 Federal regulations that permit additional safeguards
14 for certain populations in situations in which there
15 might be increased risk, and we are going to try to
16 make some clear recommendations as to how IRBs might
17 best take advantage of those additional safeguards.

18 So if I can just say that perhaps we're not so
19 much anti-legislation or anti-new regulation as we
20 would like to take advantage of some of the safeguards
21 and protections that currently exist and may be perhaps
22 under-appreciated by some of the local IRBs.

23 The third point, is that we did have some

1 concerns with the November 1997 draft. We greatly
2 appreciate your sharing that document with us and
3 allowing our staff to take a look and make comments.

4 You all now have copies of the critiques of
5 some NIMH staff about that and, in particular, our
6 concerns that the very scholarly imbalanced text be
7 reflected in the specific recommendations.

8 Unfortunately, these days generally executive
9 summaries and recommendations are read at the expense
10 of thoughtful and deliberative text.

11 Finally, I just want to echo the concerns of
12 some of the members of the Commission, that you
13 continue to get input from experts on clinical
14 research, in particular involving those who have done
15 research involving individuals with psychiatric or
16 neurological impairments to inform the NBAC about some
17 of the clinical disorders and some of the nuances of
18 clinical research.

19 CHAIR CHILDRESS: All right. Thank you.

20 Are there any questions or comments?

21 (No response)

22 CHAIR CHILDRESS: Let me just ask one, if I
23 could. Incidentally, regarding the response to the

1 allegations, that will be sent to all Commission
2 members by the NBAC office next week, or this week, I
3 guess. Tomorrow. Today or tomorrow.

4 But regarding the other draft which members of
5 the subcommittee, at least, had a chance to see, I
6 guess one question was whether, since a
7 misunderstanding came up in the meeting yesterday about
8 whether what we were proposing in the recommendations
9 would apply to more than minimal risk research or
10 whether it was only to more than minimal risk research
11 or also to minimal risk research, it seemed to me that
12 the response from the National Institute of Mental
13 Health actually thought that we were making this apply
14 to minimal risk research too, so some of the things
15 that would be excluded from your interpretation,
16 actually, would not be from ours. I apologize, because
17 there unclarities in the document on that point.

18 DR. SHORE: Right. At the end of the document
19 that you drafted, and of course that's the November '97
20 version to which we had access, it did appear to, in
21 effect, prohibit even minimal risk research on those
22 with questionable capacity to consent in a case in
23 which it was non-therapeutic or no direct benefit,

1 depending on which term you use.

2 We believe that there are certain
3 circumstances in which greater than minimal risk
4 research might be justified without direct benefit, but
5 we are certainly willing to concede that in such
6 situations additional safeguards should probably be
7 employed.

8 I expect that we will advise IRBs as to
9 additional steps, perhaps independent monitors, that
10 might be used to assure that input from the family,
11 from independent clinicians, et cetera, is used to best
12 advantage.

13 But our major concern was that the version
14 that we saw did not appear to make the distinction
15 between even minimal risk research, asking a few
16 questions of an individual or taking a tube of blood
17 and would appear to outlaw such studies which have been
18 so useful in finding the genetics of Alzheimer's
19 disease, for instance.

20 CHAIR CHILDRESS: And that has been clarified.
21 The revised draft that we're working with also
22 incorporates the input of several subcommittee members
23 who had the opportunity to attend the conference in

1 early December, a very beneficial conference. It was,
2 indeed, for all of us.

3 I guess one question would be whether you'd
4 mind if we go ahead and work with the draft of the
5 recommendations that are coming out from that meeting
6 because, as you've heard our schedule, we are trying to
7 move forward, if you think it would be appropriate for
8 us to go ahead and least use that for our reference at
9 this point, would be helpful.

10 DR. SHORE: Perhaps we can compromise on what
11 I may call our penultimate draft, and I can make a
12 promise to try and get that to you, say, two weeks
13 before you meet.

14 I don't feel completely comfortable, of
15 course, in sharing with you a document that has not
16 been vetted by the members of the panel, but, as you
17 may know, I'm not the most patient individual myself so
18 it is my desire to get this in final form as soon as
19 possible and get it to you immediately thereafter for
20 penultimate form.

21 CHAIR CHILDRESS: Anything else?

22 DR. BRITO: It would be helpful to have a
23 specific example of what you mentioned, that there are

1 greater than minimal risk research has been useful in
2 the past, something that's been done. So if we could
3 have specific, concrete examples of that, that would be
4 really helpful.

5 DR. SHORE: I mean, I would just say things
6 like PET scans in suicidal adolescents, spinal taps.

7 DR. BRITO: But the references and the
8 publication. Appreciate it.

9 CHAIR CHILDRESS: Thank you.

10 Does anyone else wish to offer public
11 testimony?

12 (No response)

13 CHAIR CHILDRESS: All right.

14 Let me then turn to Jack Schwartz. Thank you,
15 Jack, for bearing with us in the modification of the
16 schedule. Jack will provide an update on the Maryland
17 Attorney General's Working Group. You have seen
18 several drafts from this working group over the last
19 year, and we're glad to have Jack offer an update.

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UPDATE ON MARYLAND ATTORNEY GENERAL'S WORKING GROUP

By Jack Schwartz, Esq.

MR. SCHWARTZ: Thank you. I'll summarize the current status and identify some current issues pending before our group. My summary of those issues will make it plain, I think, the areas in which we need your help.

The Maryland Working Group has been about its task for more than two years. Our objective was to

1 come up with a draft statute on research involving
2 decisionally impaired people that could actually be
3 enacted by the Maryland legislature.

4 That last qualification is an important one.
5 I daresay that many members of the Maryland legislature
6 have never even heard the word "bioethics" but they
7 know a bioethics controversy when they see one and they
8 know how to avoid it.

9 So for legislation of this kind to have a
10 realistic chance of enactment, it must arrive at the
11 legislature with a fair degree of consensus. If the
12 hearing on the bill turns into an ethical debate, the
13 bill will simply disappear without a trace.

14 A consensus is not achievable without
15 something that resembles a public conversation. So we
16 have been at pains to try to have public reaction to
17 our thinking as we go along through the medium of now
18 three reports that we issued soliciting public
19 comments. The last two of these three included draft
20 statutory language that people could react to. The
21 more you ask people to give you comments, the more they
22 do.

23 So a satisfying aspect of this process is

1 that, at least in the last go-round, some people
2 participated, reacted, who didn't have an a priori
3 interest in the subject, people who had no particular
4 organizational identification, leaders of religious
5 groups in Maryland, advocates for the homeless.

6 Their overall reaction was twofold. To think
7 that the essentially unregulated status quo about
8 research involving decisionally impaired subjects was
9 unsatisfactory, but that the proposal then on the
10 table, the August '97 version of our document, fell
11 short in a number of respects. I'll summarize those in
12 a moment.

13 But the upshot, from my perspective, is that,
14 given the current reaction to our draft that's on the
15 table, given the prospect that you all will serve as
16 the cavalry coming over the hill to save us in some
17 respects, that it was not ready for introduction in the
18 session of the Maryland legislature that begins next
19 week.

20 Hence, we will not offer a proposal in the '98
21 session of the legislature, which is a three-month
22 session. Essentially, if we were going to do it we
23 would have had to have done it by now. That is to say,

1 have a draft that was essentially ready, talk to key
2 member of the legislature. None of that has happened
3 because we're not ready yet.

4 So we will have the opportunity to be guided
5 by the Commission's report as we continue this process.
6 I anticipate that we'll have another draft out by
7 middle of spring, again, soliciting public comment.
8 Our goal method was to try and share our thinking as we
9 went along. That's been fruitful, and I commend that
10 strategy to you.

11 Let me try and summarize in general terms the
12 reaction that commentators had to the proposal that's now
13 on the table, our proposal.

14 The first, was to be nervous about something
15 that we did not include in the document that we left
16 out, and that is the issue of capacity assessment. The
17 current Maryland draft simply takes as a premise that
18 the individuals who are the potential research subjects
19 are decisionally incapacitated and regulates from
20 there.

21 Well, there was much focus on the lack of
22 discussion or lack of provision in the bill for a
23 process of capacity assessment, so we are wrangling

1 with that. Our sense, of course, is that despite the
2 excellent scholarship in this field, Dr. Applebaum's
3 and others', that there is no broad agreement within
4 the field on the methodology for capacity assessment.

5 Hence, I think it is likely that our next
6 proposal will simply impose an obligation on
7 researchers where the research subjects have a
8 condition that raises a red flag, if you will, about
9 capacity to describe what method they are planning to
10 use to assess capacity and charge the IRB with
11 reviewing that recommendation or that proposal by the
12 investigator.

13 Hence, there will be no command and control
14 state regulation, but instead the obligation on the
15 part of the investigator and IRB to address the issue.

16 The commentators were wary of things that we had
17 included in the measure, not only things that we had
18 left out. There was considerable concern over a topic
19 that you all have addressed this morning, and that is
20 Research Advance Directives and the circumstances under
21 which those ought to be given the legal security of a
22 statute.

23 An interesting aspect of concern was, what is

1 to prevent investigators from potentially turning these
2 into blank checks, to essentially solicit the signing
3 of a research advance directive upon admission to a
4 facility, worry that if the provisions on advance
5 directives were too open-ended, that it might invite
6 abuse of that kind.

7 A second aspect of concern was over capacity,
8 assessing capacity to executive an advance directive.
9 There seemed to be general recognition of the truism
10 that people may have differing capacities for differing
11 decisions and, therefore, the fact that an individual
12 might not be capable of giving informed consent to
13 research participation did not necessarily imply that
14 the individual lacked the capacity to execute an
15 advance directive.

16 Those are different decisions, depending on
17 what the advance directive is, of course. I'm speaking
18 now of proxy-type advance directives designating a
19 substitute or surrogate decision maker.

20 Yet, there were worries that at least the --
21 in situations where an investigator had determined that
22 a potential research subject lacked the capacity to
23 give informed consent and yet then solicited an advance

1 directive, was a worrisome phenomenon and, hence, ought
2 to be addressed through some provision calling for, at
3 least in those circumstances, an assessment of capacity
4 to execute the advance directive, a separate issue than
5 capacity to give informed consent.

6 There was worry over elements of our proposal
7 that essentially borrowed Federal concepts. We had
8 understood our own role from the outset as being unable
9 to fix problems that arose from the common rule itself.

10 So, insofar as there are difficulties, as
11 there plainly are, with the definition or concept of
12 risk, as reflected in the Federal or in the common
13 rule, we imported those difficulties into our proposal
14 because we simply borrowed the definition of minimal
15 risk and erected categories of risk based on that sandy
16 foundation.

17 But we didn't think that we could, in
18 Maryland, do anything useful by way of addressing a
19 problem that is a fundamental one, as you've
20 identified, and that has national import, and we have
21 been criticized for that.

22 How can you, people say, invest substitute
23 decision makers with authority in particular categories

1 of risk when, to borrow Professor Capron's phrase, the
2 categories are bounded by pieces of spaghetti.

3 There isn't any satisfactory answer that we
4 can give to that, except this was sort of the given for
5 us. So to the extent that the Commission is able to
6 help inform our understanding of risk and, hence, of
7 the categories of decision making authority that can be
8 built on risk, we would be most grateful.

9 Another issue that will engage us at our next
10 meeting in, I think, early February has to do with what
11 limitations, if any, state law ought to place on
12 participation by decisionally impaired subjects in
13 placebo-controlled studies.

14 The concern is over circumstances in which
15 there is standard therapy and yet individuals with
16 decisional incapacity are enrolled in placebo-
17 controlled studies so that they are removed--one arm of
18 the study--from their standard therapy and given
19 placebo.

20 As usual, we lack data in knowing how often
21 this occurs, but the commentators were worried that the
22 proposal, as currently framed, would allow that because
23 it really doesn't address very much about placebo, or

1 the control aspects of a randomized clinical trial. So
2 that's another matter on our particular table.

3 So those are what we are grappling with. Any
4 aid from you all would be deeply appreciated. We will
5 be having a set of discussions within the working group
6 over February and March.

7 I would imagine by late March, early April we
8 ought to be in a position to again share our thinking
9 with you and the public through the publication of
10 another report.

11 The idea would be to be in a position by
12 summer to have completed our work and identify
13 consensus, if there is one, and then go about the
14 business of trying to develop legislative support for
15 the proposal.

16 CHAIR CHILDRESS: Thank you. Thank you very
17 much, Jack.

18 Are there any questions or comments?

19 (No response)

20 CHAIR CHILDRESS: Well, thank you very much.

21 MR. SCHWARTZ: Thank you.

22 CHAIR CHILDRESS: We appreciate your sharing
23 with us.

1 Bill Freeman. I saw him a moment ago. Oh,
2 he's on the telephone now. The latest word, is that
3 right, Bill?

4 DR. FREEMAN: Not quite.

5 CHAIR CHILDRESS: Bill, we're grateful to you
6 for updating us on the report.

7 Let me just mention, for those who may not
8 have been here when we talked before, the plan is to
9 complete the report from the Genetics Subcommittee and
10 the Commission as a whole on tissue samples and the one
11 on decisionally impaired research subjects, and then to
12 complete the one on the Federal Agency Report, perhaps
13 in conjunction with recommendations about Federal
14 oversight. So this will be the third report released.
15 The data collection is still in process, but almost
16 done. So Bill is going to update us about that.

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UPDATE ON REPORT ON THE SURVEY OF FEDERAL AGENCIES

By: Bill Freeman, M.D.

DR. FREEMAN: Becoming the third report has given us room, time, to do more things that we need and want to do. We are greater than 90 percent at Phase I. That was a structural survey of every agency that has signed on, including some agencies that did not sign on that we found are doing research.

We're greater than 70 percent at Phase II. That's a smaller number, looking at a range of various kinds or sizes, et cetera, of IRBs in those agencies that have them or in the mechanisms for grants and contracts, what are the procedures to make sure that grants are contracts are -- on these institutions that have the protections in place. You've seen in the past

1 the general, broad conclusions. They remain.

2 We continue the process, and I want to
3 emphasize this, that every agency has reviewed our
4 draft--or at least has been given an opportunity to
5 review our draft; we can't make them do it--for the
6 facts at the time of the survey and gotten back to us.

7 They have that opportunity, and we will come
8 to an agreement about what those facts are before the
9 first draft about that agency gets to you. That review
10 also includes any other modifications or suggestions
11 they have.

12 So if, for instance, there was a rumor that
13 some agencies thought, well, maybe they didn't present
14 themselves, didn't take it seriously when they
15 interviewed them. There's plenty of opportunity to set
16 the record straight. This is an iterative process,
17 really, as long as it takes, and also for additional
18 suggestions.

19 Those suggestions, by the way, are coming in.
20 We asked for those initially and I think it would be
21 very helpful about how to implement the regulations.

22 One of the things that was suggested a couple
23 of meetings ago has been modified a bit. We aim,

1 before the completion of the report, to have at one of
2 the NBAC meetings -- invite Federal agency officials to
3 come and talk about their suggestions about how to
4 improve the implementation process of these
5 regulations.

6 They will also, of course, be able to make
7 generic statements about our generic suggestions. We
8 will not, we hope, get into defending or attacking any
9 given agency. That's not the purpose of our report, or
10 the purpose of that meeting, for that matter.

11 Finally, staff have developed also over the
12 holidays, given it was difficult to meet with people,
13 possible general implications--and we're still in the
14 process of this--for adoption or non-adoption of
15 innovations by agencies. It's from the political
16 science and sociologic literature. This may complement
17 the papers by McCarthy, Fletcher and Gonzales about,
18 they're primarily on location in the Federal Government
19 for Federal oversight.

20 This would be more, what are the functions or
21 the processes that should be included in this entity,
22 whatever it is and wherever it is, to maximize the
23 innovation -- the acceptance -- excuse me, the adoption

1 of these regulations that we have found have not been
2 adopted 100 percent throughout the Federal Government.

3 Of course, you'll be getting plenty of a
4 chance to look at that in a draft. But we have found
5 some information that I think has turned out to be
6 very, at least at our first glance, very helpful.

7 CHAIR CHILDRESS: Well, thanks very much,
8 Bill, and other members of staff who have been working
9 on this project over many months.

10 Are there any questions or comments for Bill?

11 (No response)

12 CHAIR CHILDRESS: Okay. Bill, thanks very
13 much, again, and to the staff working on this.

14 I had got a note to ask Jonathan Moreno to say
15 something about the TD case, and Jonathan came up to
16 say that Jack Schwartz was the person to ask about the
17 TD case.

18 Jack, if you wouldn't mind just telling us
19 where matter stand as that has evolved.

20 MR. SCHWARTZ: Sure. Just a little recap on
21 that. The TD case involved a challenge to the legality
22 of regulations that had been issued by the Office of
23 Mental Health in New York governing research

1 participation by decisionally incapacitated people in
2 mental health research.

3 The original decision, the trial court
4 decision, had invalidated the regulations on a rather
5 narrow ground, namely that the regulations were not
6 properly issued by the mental health office, but rather
7 were within the authority of the New York Health
8 Commissioner; not exactly a technicality, but a
9 relatively narrow ground.

10 When the case came to the intermediate
11 appellate court in New York, that court agreed about
12 this who has the authority question, but then went on
13 to suggest that there were significant constitutional
14 problems with the regulations.

15 This intermediate appellate court decision
16 suggested that there were constitutional reasons why
17 individuals with decisional impairment could not be
18 involved in non-beneficial research that posed greater
19 than minimal risk, some extensive discussion in that
20 opinion of constitutional and common law issues.

21 The matter was brought to the New York Court
22 of Appeals, which is New York's highest court. In a
23 decision about three or so weeks ago, that court in

1 essence vacated throughout the portions of the
2 intermediate court decision that had dealt with the
3 more interesting issues, the constitutional and common
4 law issues.

5 So the state of the matter is that the only
6 thing that this case now stands for, it's the
7 incredible shrinking case. It now stands for the
8 narrow proposition that it was one official rather than
9 another in New York State that has the authority to do
10 these regulations, and the discussion of constitutional
11 issues is now tossed out.

12 So what happens next? The New York Health
13 Commissioner presumably will do regulations. There's a
14 task force at work in New York to provide advice to the
15 health commissioner.

16 Once those regulations are newly issued, then
17 presumably the plaintiffs in the case, if they are
18 dissatisfied with the new regulations, can start their
19 challenge over again, again alleging the constitutional
20 problems that they perceived before. But we are years,
21 presumably, away from an authoritative decision on that
22 matter.

23 CHAIR CHILDRESS: Any questions about that?

1 (No response)

2 CHAIR CHILDRESS: Thanks very much.

3 DR. MORENO: And I'd just say, as a member of
4 that -- task force, we're waiting to see what you guys
5 have to say about this too, as are the good people in
6 Maryland.

7 DR. CASSELL: There's a kind of circularity in
8 the Maryland and New York task force and NBAC.

9 CHAIR CHILDRESS: And it all comes back to
10 you, Jon.

11 We have scheduled a brief discussion of future
12 Commission research activities. I wonder if Eric could
13 lead us on that. We won't spend a lot of time on this,
14 but notice the number of topics that were identified
15 that have to do with research. So let's see if there's
16 any feedback on that.

17 DR. CASSELL: I cannot be the only person who
18 has a certain feeling of both déjà vu and frustration
19 in this discussion as we go around and around on
20 subjects that were impossible to solve the last time
21 around, and here we are again. Only we have done one
22 significant thing, there is no question about it. We
23 have added a surrogate. We have added a friend. That

1 is no small matter.

2 On the other hand, it seems to me that one of
3 the things we always end up on, is we come back to the
4 IRB. We're going to let the IRB do this and the IRB do
5 that. Yet we all know, almost everybody who for any
6 length of time has served on IRBs, and some of us have
7 even chaired them for prolonged periods and we know
8 their difficulties, that IRB members have variable
9 knowledge of what they are actually doing and we know
10 that there is even in some cases questions of good
11 faith in IRBs, depending on where they are, and so
12 forth.

13 The point is, I cannot see how we can avoid
14 the subject of research on IRBs toward -- toward a
15 change in the IRB method. Now, having said that, I
16 think it's a matter of discussion, what, in fact, does
17 that mean. I think Eric already has some things going
18 and we might have a discussion here, a brief
19 discussion, to go home with.

20 Well, what does that all mean; what do we want
21 to do as a Commission? If we leave this subject and
22 don't do something to change this, I think we would
23 have been remiss. We had a dinner meeting last night

1 that came to much the same conclusion.

2 Eric?

3 MR. MESLIN: Well, at the risk of belaboring
4 the discussion, there was full Commission discussion on
5 this subject yesterday. One of the decisions the group
6 seemed to come to was that there was a general
7 consensus that all of those topics were extremely
8 interesting and relevant.

9 It might be useful if you were to pick up Dr.
10 Cassell's challenge of identifying the top two or three
11 that you thought were most urgently pressing, and I
12 think Arturo mentioned this yesterday as well, that we
13 can do and that we can do well.

14 Several of these have come up, including the
15 IRB study, the study of international clinical trials.
16 It may be useful for you just to ruminate once more
17 about where you see the importance for the full
18 Commission going forward, because we will revise this
19 planning bucket document and recirculate it.

20 Harold's wish yesterday before leaving was
21 that we would pick this up at the next meeting of the
22 full Commission, so don't feel constrained by a
23 decision to come to closure today.

1 DR. CASSELL: Then there's the other subject
2 which is mentioned, and we have documents on, is it
3 comes out of the paper on the capacity consent in
4 neurobiological research, the Berg and Applebaum paper.
5 My own direct investigative experience -- this paper is
6 a sea of misunderstandings and poor definitions. The
7 word judgment -- we're talking about people making a
8 judgment.

9 What people mean by a "judgment" is not at all
10 clear through this. Repeatedly, everybody's experience
11 is that people given consent forms frequently do not
12 understand the content of their consent form, never
13 mind remember it.

14 That's already a different issue. But they do
15 not understand the content of the consent form,
16 medically ill as well as psychiatrically ill patients.
17 Yet, we continue to do the same kind of thing as we did
18 before.

19 So I don't really know what the answer is. I
20 would hate to leave this meeting feeling, well, okay,
21 what you have to do, is every Commission has to sing
22 the song and dance the dance, then wait for the next
23 Commission to have some bright idea about what to do to

1 solve it.

2 But I actually think if we start with where we
3 are going and continue research into the nature of the
4 thing called consent, that we will have made a
5 contribution, if it clarifies how we believe people
6 should give consent to research and what safeguards we
7 have for that consent.

8 I have a side feeling that we are going to
9 have to figure out what community means in this
10 relationship and we haven't figured that out yet
11 either. The fact that we haven't figured out all these
12 things doesn't bother me in the slightest, if we pick
13 them up. If we don't, then it's --

14 CHAIR CHILDRESS: And we do have a paper, a
15 contract paper on community that will be circulated in
16 the next few weeks after some minor revisions.

17 PROFESSOR BACKLAR: It's interesting that in
18 the remarks on the November draft, that NIMH seemed
19 very much at sea and misunderstood our references to
20 community -- show that we --

21 CHAIR CHILDRESS: Bill?

22 DR. FREEMAN: I'm sorry. I didn't hear that
23 well where I was. Is there a concern about people

1 being at sea about the community; was that the
2 statement?

3 CHAIR CHILDRESS: That in the response from
4 the National Institute of Mental Health to our November
5 document, there were some expressions of concern about
6 our invocation of community and how we were going to
7 use that.

8 DR. FREEMAN: CDC -- not in the mental health
9 field, as far as I know, but CDC has just come out with
10 a not-very-thick book about the role of community in
11 research, which is some of the best that I have seen,
12 and includes the Mohawk of Tanawaga in Montreal and
13 their involvement in research, and others.

14 I ought to be able to get copies for the
15 entire Commission. There will be some perceptions from
16 the point of view of community people and researchers
17 who have worked with them about what that relationship
18 can look like.

19 CHAIR CHILDRESS: Can you get that to us
20 fairly quickly?

21 DR. FREEMAN: Hope to get it probably within a
22 week.

23 CHAIR CHILDRESS: Good. That would be

1 helpful.

2 Bette?

3 MS. KRAMER: This is a question of process. I
4 was wondering if it would be possible for the staff to
5 do some research into the existence of some good
6 material on issues like consent, such as what Bill
7 refers to about community, because even in as a
8 preliminary move we can make reference to those
9 materials in our reports, and I think that that would
10 be an addition.

11 MR. MESLIN: Are you asking about research
12 that's been done and the concept of community
13 consultation and whether it's been affected?

14 MS. KRAMER: Yes. But no consent.

15 MR. MESLIN: Consent as a broad --

16 MS. KRAMER: Consent forms. The process of
17 consenting to research.

18 MR. MESLIN: We can certainly discuss that,
19 sure. Let's do that outside.

20 MS. KRAMER: All right.

21 CHAIR CHILDRESS: Okay.

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FUTURE COMMISSION RESEARCH ACTIVITIES

CHAIR CHILDRESS: Other points to be made about future research and Commission research activities. I guess one possibility would be whether we want to recommend, in terms of the list that Eric's committee provided, and that the Commission went through, whether we want to make any recommendations about priority.

I don't recall that we actually set any priorities. There are some things that have a kind of immediacy about them that you noted in your report and in your discussion. But are there any comments that you would like to make about that, since I assume that the Ad Hoc Committee may well be providing further

1 guidance.

2 DR. CASSELL: It was our hope that people
3 would reflect on -- well, let me divide it up again.
4 We had two categories. We had an immediate set of
5 problems and we discussed those, then we had these
6 larger issues, the limits of clinical medicine and
7 ownership of body is two examples of them, that people
8 have to sort of chew around and decide, is this a
9 subject for us.

10 It's easy to see that the report acts as
11 though this Commission will go on beyond its present
12 allotted time, and it's like time will be extended
13 because of what we've already discussed.

14 The immediate needs will carry us to 1999
15 without -- but it is our hope that people would pick
16 up, particularly, Alta Charo's, what does it mean to
17 say? I mean, we take it for granted that people are
18 giving a consent to have something done to their body.
19 That implies a certain kind of relationship to the body
20 and -- spelled out what that relationship is. That
21 would be an interesting subject.

22 Certainly we can't even come near reproductive
23 technology, I would think, without beginning to

1 clarify, what is the woman's relationship to her body
2 and to what it does, because those are issues that bear
3 directly on reproductive technology.

4 The limits of clinical medicine issue is also
5 -- it's a question that we keep coming up against here
6 but we bounce back, and that's the question of
7 progress. Is scientific progress an unlimited good?
8 As Alex pointed out, quoting -- it's a limited good.

9 There are greater goods. I have a colleague
10 at the head of the table once who reminded me that
11 saving lives was not the highest good, that there were
12 greater goods than that. I think freedom was one at
13 the time. These are issues that I think we have to
14 consider for the future to determine our work and set
15 us on a course that commissions have not yet started.

16 CHAIR CHILDRESS: So this is viewed as a
17 process then.

18 DR. CASSELL: Yes.

19 CHAIR CHILDRESS: The question is whether we
20 have anything we want to suggest at this point, or
21 simply, as Eric has noted, reflect on this, since the
22 question of priorities would be addressed at subsequent
23 Commission meetings.

1 Anything you'd like to add?

2 DR. BRITO: My general feeling, talking to
3 different people in the Commission, is that the IRB
4 problems -- I think almost everyone that I've talked to
5 agrees that that's probably -- they agreed with your
6 comments yesterday about that being a very important
7 issue, and I think we should proceed with that -- start
8 to proceed with that at some point in the future.

9 The only problem with that, that's such a big
10 topic that it will take time. In the meantime, that
11 could be our big topic to cover. We could refer to the
12 more focused topics and pick a few to also do in
13 between.

14 CHAIR CHILDRESS: -- it seems to me that we
15 should have at the February meeting an update from the
16 two groups currently studying IRBs and begin to plot
17 with staff sort of what's the better move and what
18 might be done. So I think that's an important thing we
19 could recommend to the Commission as a whole, depending
20 on what comes in.

21 DR. BRITO: And the topic of limitations of
22 clinical medicine, et cetera, even though it's
23 something I'm very interested in, I'm not sure how much

1 that deviates from what our goal is to protect
2 substantive research. I don't know. I'm just tossing
3 that out.

4 DR. CASSELL: I think everybody should
5 recognize that us education freaks on this Commission
6 know that issues of IRB bring up issues of education
7 and issues of investigator information, and so forth.
8 So for all of us, these are sneaky ways of bringing in
9 the --

10 (Laughter)

11 CHAIR CHILDRESS: Diane?

12 DR. SCOTT-JONES: I would just like to follow
13 that with a comment that I've been reflecting a lot of
14 the references to the IRB today and yesterday, and even
15 though I agree with the general sentiment that there
16 are lots of problems with the IRBs, I think that we
17 can't really consider IRBs without also considering the
18 regulations with which they have to work, the guidance
19 that they're given, which also are problematic.

20 Then on the other end, the researchers who
21 want to move forward their research without delay, who
22 also make demands on the IRB, so in some ways IRBs may
23 be caught in the middle without appropriate guidance,

1 without clearly defined regulations, and then on the
2 other hand being perceived as obstructionist by persons
3 who want their research to move forward without any
4 delays. So I think we need to look at both of those
5 ends at the same time.

6 DR. CASSELL: Let me make it clear, I agree
7 with you entirely in that I would say that it isn't
8 IRBs, per se, it's the process of institutional review.
9 It's the process of institutional review which adds --
10 investigators in the institution with pressures on the
11 --

12 MR. MESLIN: Since it appears that in the
13 report yesterday, which was divided into two
14 components, a set of procedural issues and a set of
15 substantive programmatic issues, has at least been 50
16 percent dealt with. Many of the process issues were
17 addressed yesterday by the full Commission and I think
18 agreed to to a substantial extent.

19 Would it be helpful to the commissioners if,
20 before the full Commission meeting in February, staff
21 would prepare a brief memo summarizing these items in
22 the program and listing, if you will, what the kinds of
23 research projects might arise from those, if you will,

1 topical areas?

2 We could go so far as to offer a provisional
3 priority for you to respond to, or it could simply be
4 in a non-lexical order and give it to you
5 alphabetically.

6 But now that you've dealt with many of the
7 process issues, we'd be pleased to provide that list of
8 the sort of seven, eight, or nine items, with a brief
9 descriptor of what we think you might mean by those
10 topics.

11 DR. CASSELL: I would find that enormously
12 helpful.

13 CHAIR CHILDRESS: Good. I agree.

14 Trish?

15 PROFESSOR BACKLAR: Maybe I missed this,
16 but -- if you would need to talk about putting this
17 report --

18 CHAIR CHILDRESS: Well, my assumption, at
19 least -- I can't remember what we said about it. But
20 my assumption was that we wouldn't do that before the
21 next draft.

22 PROFESSOR BACKLAR: Well, I wasn't thinking
23 that.

1 CHAIR CHILDRESS: Yes. But I think the --
2 agreement to do that. Is that right?

3 DR. BRITO: That's what I thought.

4 CHAIR CHILDRESS: I agree.

5 DR. BRITO: I forget when the conversation
6 takes place sometimes, but we're almost ready -- or 60
7 days before --

8 PROFESSOR BACKLAR: I was talking about --
9 what you suggested -- report.

10 DR. BRITO: For the Web site.

11 CHAIR CHILDRESS: Yes. Maybe I'm wrong, but
12 if there's no objection, I thought we had come to an
13 agreement on that.

14 PROFESSOR BACKLAR: Yes. I'm sorry. Yes.

15 CHAIR CHILDRESS: But if there are any
16 objections to that, I think --

17 Anything else you would like to raise, Bette?

18 MS. KRAMER: Jim, to return to the prior
19 subject, there was one issue that was mentioned some
20 time ago that wasn't captured in the list that Eric
21 presented yesterday. That was the use of genetic tests
22 -- making genetic tests available to the public, in
23 fact, encouraging the public to make use of genetic

1 tests before there is an approved therapy.

2 CHAIR CHILDRESS: Eric, was that considered as
3 a --

4 DR. CASSELL: I didn't hear that. I'm sorry.

5 CHAIR CHILDRESS: Could you repeat that?

6 MS. KRAMER: I mentioned to you last night the
7 use of genetic tests before there's an approved
8 therapy.

9 DR. CASSELL: That was not brought up, but
10 certainly you can raise it now. As I said last night
11 when we discussed that, there was quite a lot of
12 literature about that a number of years ago.

13 There was a consensus at that time about
14 genetic testing which has crumbled away in the
15 intervening years because first more tests have come up
16 and the genetics' star is shining -- the simplistic
17 genetics' star is shining. So it might very well be
18 that we have to revisit that.

19 MS. KRAMER: I have great concern about that
20 because of some of the advertisements, the strong
21 advertising campaigns that are under way by certain
22 institutions urging women, particularly, to get tested
23 for breast cancer, for BRZ-1-2, and these women are

1 going in there assuming that there's something that can
2 be done. I mean, it's a problem. I think we need to
3 consider it.

4 CHAIR CHILDRESS: This may well be, and maybe
5 we can ask staff to include -- other comments that have
6 come out about other things. I would note that the
7 list, actually, of immediate concerns, as well as long-
8 term, that list focuses more on the research side of
9 our dual mission than on the genetic side.

10 The use and management of genetic information
11 is one of our two major concerns. This would seem to
12 me to fit quite appropriately under that, and perhaps
13 would add a bit more of the genetics side to the list
14 of topics to look at over time.

15 DR. CASSELL: Well, now that we have more
16 staff, and really a highly professional staff, that
17 seems to me to be something that could be reproduced as
18 a document, as a contract document, a discussion of
19 genetic testing in its place and so forth, which then,
20 after we have reviewed it, goes out under the NBAC
21 seal.

22 NBAC pointing out the problems of genetic
23 testing, where we do not have to raise it as something

1 to occupy two or three meetings of the Commission. In
2 other words, it's something we ask to be done because
3 we recognize its importance, yet we don't put it on our
4 meeting agenda to occupy us to do it.

5 CHAIR CHILDRESS: Or if we look at it, we'd
6 decide whether it's something we should put on our
7 agenda to look at.

8 DR. CASSELL: Yes.

9 MR. MESLIN: I would only suggest that,
10 procedurally, my sense of how we might want to think of
11 going forward, is once we've produced the list, if you
12 will, the grocery list or wish list of the topics that
13 we think would be appropriate for NBAC to consider, be
14 it within our current mandate or in an infinite
15 mandate, we would then try and prioritize those items
16 in a systematic way.

17 Then following that, you would hopefully be
18 able to rely on each other and staff to offer the best
19 method for proceeding, whether they be a series of
20 contracted papers or working groups that will provide
21 the necessary data for the Commission to start
22 deliberating.

23 There would be nothing that would prevent a

1 paper on this subject, but there would be nothing to
2 prevent a Commission paper on any of the subjects that
3 are currently in that planning bucket.

4 You might also wish to consider, and this will
5 come up probably in the memo that we prepare for you,
6 that there has been an awful lot of work done by the
7 National Human Genome Research Institute and the
8 Department of Energy. A major task force has issued
9 its report. There is an awful lot that has been going
10 on.

11 When Francis Collins, the director of the
12 Genome Institute spoke at the first NBAC meeting, I
13 think he provided an overview of many of those
14 subjects. Staff would probably be delighted to go over
15 that initial listing and flesh out in more detail what
16 those potential topics would be.

17 CHAIR CHILDRESS: Are there other points that
18 you would like to make as we move closer to
19 adjournment.

20 (No response)

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CONCLUSIONS

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CHAIR CHILDRESS: It says Conclusions. I

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don't really think I need to offer any. We have talked

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about what we need to do to prepare the report on the

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decisionally impaired subjects, or whatever title we

14

come up with.

15

I guess that might actually be an appropriate

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thing to close with, is any other thoughts about what

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direction we might go in terms of categories to use or

18

a category to use toward the report, since questions

19

emerged about research subjects with questionable

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capacity, as well as questions that emerged about every

21

other category.

22

You may not have any thoughts today, but this

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is something we obviously need to think about, since it

1 does raise issues for a variety of issues. These terms
2 apply various things for different individuals, and we
3 do need to be aware of how they might be perceived.

4 DR. CASSELL: I thought that that was a safe
5 -- impairment of decision making capacity was a -- but
6 it isn't, is it?

7 CHAIR CHILDRESS: I think questions have been
8 raised.

9 PROFESSOR BACKLAR: I think it's interesting
10 to look at Paul Applebaum's -- and we might want to
11 take clues from that. Not to copy it, necessarily,
12 just the nature of disorders that affect decision
13 making ability. I'm not certain exactly how one
14 affects the disorders that affect decision making
15 ability -- some way of visualizing this.

16 DR. CASSELL: All I -- decisionally
17 challenged.

18 DR. SCOTT-JONES: Jim.

19 CHAIR CHILDRESS: Yes.

20 DR. SCOTT-JONES: What was the deadline we
21 gave ourselves for responding to the draft of this
22 paper?

23 CHAIR CHILDRESS: One week.

1 DR. MORENO: One week.

2 CHAIR CHILDRESS: We said one week. But would
3 you like to try to sneak in 10 days? One week. All
4 right.

5 DR. MORENO: One week.

6 CHAIR CHILDRESS: One week.

7 One last thing. Eric reminds me that there
8 has been some discussion about getting a paper that
9 looks at the various kinds of assumptions in trying to
10 determine incompetence, incapacity, or lack of
11 capacity, the kinds of measurements that Paul Applebaum
12 and others have developed. There's been some
13 discussion that Alex, Trish, Eric and I have been
14 involved with about a possible paper in that direction.

15 Any thoughts about that? This is one other
16 contract paper that could be useful to us, and perhaps
17 could be, if not available in -- couldn't be available
18 in full form by the time we need, but we might be able
19 to get a possible contractor to talk with us about the
20 kinds of issues that are involved in measurement in
21 some type of capacity. Is that an area where we'd like
22 to have some kind of report on this in February?

23 DR. BRITO: That would be useful. I wouldn't

1 be surprised if what we come up with is -- well, we
2 know that there's a lack of standardization, and it may
3 actually open up another area where -- go ahead. Were
4 you going to say something?

5 DR. CASSELL: It's a can of worms.

6 DR. BRITO: It's a can of worms. But it would
7 be useful just to find that out.

8 CHAIR CHILDRESS: I was intrigued by the
9 Maryland approach, which was at least through the --
10 people to investigators to indicate how they're going
11 about determining this, and that's obviously one kind
12 of procedural way to go. But it may be useful for us
13 to look at some of the issues involved, so we will try
14 to do that.

15 Any last points that people would like to
16 make?

17 (No response)

18 CHAIR CHILDRESS: Well, I thank you for your
19 forbearance. I thank the others who were here for
20 their contributions. We really appreciate the work of
21 staff. We thank you very much for all that you've done
22 to make this period of two days very successful. Thank
23 you. Thanks, everyone.

1 (Whereupon, at 11:56 a.m., the meeting was
2 concluded.)
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18 C E R T I F I C A T E

19 This is to certify that the foregoing
20 proceedings of a meeting of the National Bioethics
21 Advisory Commission, Human Subjects Subcommittee,
22 held on January 8, 1998, were transcribed as herein
23 appears, and this is the original of transcript

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thereof.

WILLIAM J. MOFFITT
Official Court Reporter