

National Bioethics Advisory Commission

19th Meeting

February 5, 1998

1:43 p.m.

Los Angeles, CA

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- 1:30 p.m. Welcome, Overview of Agenda
Harold T. Shapiro, Ph.D.
- 1:35 p.m. Executive Director's Report
- 1:45 p.m. Future Commission Research Activities
Eric J. Cassell, M.D., and Commissioners
- 2:15 p.m. Capacity Assessment Instruments
Elyn Saks, J.D., University of Southern California, and Commissioners
- 2:45 p.m. Break
- 3:00 p.m. Public Testimony
- 3:50 p.m. Federal Oversight of Research Involving Human Subjects
R. Alta Charo, J.D., and Commissioners
- 4:15 p.m. Tissue Samples Report: Analysis of Professional Society Requirements
- 4:50 p.m. Next Steps
Harold T. Shapiro, Ph.D.
- 5:00 p.m. Adjournment

DR. SHAPIRO: Good afternoon, colleagues on the right and the left.

1 Think about that the way you want to. You like being on the right, Eric?

2 DR. MESLIN: He likes to think right, not necessarily on the right.

3 DR. SHAPIRO: Maybe I can change my position so you can be on the
4 left, over there. All right, I'd like to call the meeting to order, and let me spend a few
5 moments just talking about our agenda over the next day and a half. There are some
6 members of the Commission who will be arriving during the afternoon, depending on
7 their flight arrangements and so on. But I think the agenda is long enough that we have
8 to proceed.

9 If you look at the agenda for this afternoon, after a few words from Eric
10 we'll deal with our future agenda. We all have a memo on that from Eric—which is in
11 our books—and that discussion will proceed after hearing from Eric. And then Elyn
12 Saks, who is sitting on my left over here, will be here to present to us on capacity
13 assessment instruments. Thank you very much for being here; we're very grateful for
14 your taking the time. We'll then take a relatively short break and we'll have public
15 testimony. We have quite a few people who have signed up for public testimony—quite
16 a few meaning five, although some come in pairs, so it could be more than five people.
17 We'll try to start the public testimony no later than 3:00. Just out of deference for those
18 who've come to give testimony. We'll then pick up an item that we had scheduled at our
19 last meeting in Washington but didn't quite get to—having to do with the process of
20 changing regulations—and Rachel will lead that discussion. We'll then go on to continue
21 our discussion that began last time, or the last two times, dealing with federal oversight
22 of research involving human subjects. Alta will lead that discussion. We've had some
23 material on that, we've had some guests on that; the last couple of meetings had some
24 experts report to us. We have a number of different propositions to consider and that'll
25 be an important discussion. The item that's currently scheduled at 4:10—the Staff
26 Analysis of Published Research—we're going to take that off the agenda. We really
27 don't have a discussion item there. It'll come up tomorrow as appropriate when we deal
28 with that general overall subject, but it doesn't seem to me that it's a necessary part of
29 our business this afternoon. And then we'll go through some analysis of professional
30 society positions on the tissue sampling area, and we all have that information put
31 together by staff and we'll see if we understand that. That'll be quite important as
32 background for our more general discussion tomorrow on that issue. And I really want
33 to thank the staff for putting that material together. I found it really very helpful. And
34 we'll conclude the afternoon with whatever miscellaneous issues seem to be appropriate
35 to comment on at that time.

36 So to begin, let me turn to Eric.

1 DR. MESLIN: Just very briefly, welcome everyone, to Los Angeles and
2 to the Omni. I want to make a couple of brief housekeeping remarks from the staff's
3 perspective. We're in the process now of transitioning to a logistics contractor who will
4 help us not only in our travel arrangements but also in putting together meeting agendas
5 and the like. The briefing book you received is sort of a first effort to try to make what is
6 often an awful lot of information more simple and accessible to you. Comments that you
7 have about the books would be greatly appreciated. I want to thank Pat Norris for
8 working so hard to put together this briefing book. You'll find that it has a number of
9 tabs that correspond to the items, and we hope that those tabs are at least reasonably
10 accessible to you. Obviously there are items underneath the tabs and we'll try to direct
11 you to them in the event that they're hard to find.

12 I want to identify one item in particular under Tab B, which is the Annual
13 Report for the Commission. This is a report in which Kathi Hanna had a major role in
14 providing some draft guidance. Staff has continued this effort and we now have what we
15 hope is a final Annual Report for 1996-97. We're hoping that you will find this to be a
16 noncontroversial document. It really says only what our accomplishments are, and in that
17 spirit we would greatly appreciate your giving us any comments you can within the next
18 week, seven days from today. We would then like to begin publishing it and making it
19 widely available. In that same spirit of "widely available," I know that many of the
20 Commissioners are aware, but for the public citizens attending, on the 28th of January
21 we were able to launch the revised and updated NBAC website, located at
22 www.bioethics.gov.

23 DR. SHAPIRO: I might add, sir, it has very attractive pictures of the
24 Commissioners on that website.

25 DR. MESLIN: I feel like I'm in court here. Rob Tanner, one of our staff
26 members, has handed me the absolute, up-to-the-minute number of visits to the website:
27 As of the 28th of January, we've had 1,732 visits to that website with approximately 65
28 dedicated comments. There is a comment section at the website, which NBAC staff will
29 answer. Many people send their requests for publications there, so please tell your
30 friends about that website. It is constantly being updated and revised. It is our hope that
31 all of the transcripts for all of the meetings will be available on that website; that all of
32 our reports will be available on that website; and that contents of the briefing books that
33 are relevant—agendas, tabular forms and the like—will also be available. We made the
34 decision to put the website up sooner so that it would be useful; and please bear with us
35 if you're hoping to get the transcript from many meetings ago and it's not quite
36 available. We're doing our best to get that done. The only other item from the staff is to
37 mention that we are starting to wrap up our staff complement, and we are pleased that
38 Melissa Goldstein who, although she isn't here with us today, has joined the NBAC staff

1 as a consultant. She is a Yale-trained lawyer who is currently a Greenwald Fellow at
2 Johns Hopkins University. And you will note Melissa's imprint on some of the
3 documents in the briefing book. There will be some other announcements of "staffing
4 up" at the appropriate time. We are also pleased that we have attracted a contract paper
5 from a Professor Alan Buchanan, currently of the University of Wisconsin and soon of
6 the University of Arizona. More on that later, but many of you are aware that Professor
7 Buchanan has an extensive history and involvement in bioethics activities in this country.
8 He is providing a very useful paper for the stored tissue report.

9 And I suppose the last item in this five-minute overview is to thank the
10 Commissioners who were following the last Commission meeting, who were very
11 generous in their time in being able to respond to numerous press requests from both the
12 print and visual media in response to stories about cloning. We are able to—I
13 think—meet all of the press requests and many of you around the table were very
14 generous in your time and very eloquent in your presentations, and I think you helped
15 the public understand what the Commission said when it issued its report last year.

16 Those are the only items, Mr. Chair, except for the pleasure to tell you
17 that we are set for our next five meetings, and I think you will all join me in breathing a
18 great sigh of relief that the meetings have been finalized and the dates are in your briefing
19 books. We will be meeting March in Washington, DC; May in Cleveland; July in
20 Portland; September in the Washington, DC area; and November in Miami. For those
21 who are interested in those dates, they are available outside at the registration desk.

22 DR. SHAPIRO: If I could just say one other word about the awakened
23 interest in cloning ever since the State of the Union speech. Many scientific societies and
24 other groups from Washington are rushing ahead to try to get positions established on
25 this issue. Many of them not necessarily take off from but at least build around our own
26 set of recommendations. The astonishing thing is they may normally send me copies of
27 what they're proposing. And I would say that 50 percent of the cases have had to call
28 back up and correct just the way they read the document, let alone whether they thought
29 their position was right or wrong. But there is a lot of interest, and I would say that the
30 Congress—various senators and so on—is receiving at the other end of these memos
31 that people are drafting on this issue. So I'm sure we'll hear more about that as time
32 goes on.

33 All right, let's go on to our ... any questions for Eric? On the meeting or
34 any other aspects? Let's go on to the Future Commission Research Activities. There is a
35 memo from the staff, Eric, outlining some of the discussions that have taken place, and
36 this is staff's view of the summary of those discussions we had last time. So let me turn
37 to Eric to see if he feels they've captured the kind of main issues that he and his

1 colleagues had wanted to advance regarding our future agendas. Eric?

2 DR. CASSELL: We indeed do have a revved-up staff, and in numbers
3 and energy. And this discussion about our proposed future projects takes advantage of
4 that. Eric Meslin and I had conversations about this during the past couple of weeks.
5 One of the things I should say is that as we go through this, this is an action discussion.
6 We should be able to nearly finalize what it is we want to do. However, we should also
7 realize that staff can be asked to prepare detailed plans about how we would accomplish
8 things, in what order, what we have to do, and what our timing would be and so forth.
9 So we ought to come out of this with some idea of what we actually are going to do and
10 then get feedback on that. You're seeing what you saw the last time we discussed this, in
11 essence. There are some things that seemed more immediate than others. The ethical and
12 legal issues in research supported and conducted in other countries is really quite
13 pressing. I don't know about the rest of you but I got a letter from the *Journal of Black*
14 *Higher Education* asking for some discussion about it, and I told them it would be a
15 great idea if they attended the meetings where it was discussed. And I think we ought to
16 come up early with that one. The same thing is true of Institutional Review Boards.
17 We've committed ourselves already to a discussion of them and in the Moreno Report,
18 which I think is excellent, we talk about them constantly; it's now time to come down to
19 what we think they ought to do and what changes ought to be made. The issue of
20 genetic discrimination and privacy is part of our mandate, and that's there.

21 Now, the ownership of the body, if Alta could say a word about it, it was
22 her proposal and I'm not sure we have captured what you meant by that. Could you...

23 MS. CHARO: In the course of the discussions about the use of tissues, it
24 occurred to me that there really is not a well-developed and coherent set of rules in law.
25 And I couldn't speak to ethics but I suspect in ethics about how it is that we regard
26 personal control in every aspect of one's own body, both the tissues while they're still
27 incorporated into your body, and particularly once excised. There are very different and
28 conflicting rules about the ownership of tissues once excised. Sometimes they're treated
29 as if it were your regular, ordinary, toaster-oven kind of property; other times it's treated
30 as a nonproperty item that doesn't have any kind of property rules attached to it; other
31 times it's considered to be your essential self because of the information it contains. And
32 when one takes a close look at it—it happens that I supervised a master's law thesis on
33 this topic—one finds that the absence of a coherent, legal regime is part of what leads to
34 confusion about who gets to do what with which. It's part of a deeper set of issues about
35 personal control and personal autonomy that reach into things as varied as self-
36 mutilation, suicide, the disposition of corpses, archaeological and ethicological work on
37 the long-dead, and community ownership in particular among people like Native
38 Americans. And in the more immediate sense, the legal background has so far been

1 undiscussed of the stored tissue problem, and whether or not there is any degree of
2 residual control that belongs to the people who were the sources for that tissue. Since it
3 comes up in so many different contexts, it occurred to me that it might be worth taking a
4 look at it as a topic on its own.

5 DR. CASSELL: And, Eric, I think this would be one in which sort of
6 sketching out just exactly how would we go about this would be a very good idea.
7 There's a lot of background. We would need a lot of background input from other
8 people and papers about the issue of relationship to the body—not just ownership, but
9 relationship to the body.

10 DR. SHAPIRO: Could I ask a question? It may have come up as your
11 student and you did work in this area. I understand exactly the issues you're raising
12 regarding ownership and you had some e-mail on that subject also. In that
13 literature—review and/or analyses that were done—are there laws that consider this
14 “gift” as opposed to “property”? That is, a gift of property as opposed to just your
15 property you sort of hang on to?

16 MS. CHARO: You mean your tissue?

17 DR. SHAPIRO: Yes, that's right.

18 MS. CHARO: It depends on the context. There are times when the tissue
19 of your body—let's focus just on excised tissue—once separated from the rest of your
20 body—is sometimes considered your personal property that you've now abandoned,
21 which would be typical of things like excreta. Other times it is considered a gift, and
22 that's a classic formulation of the notion of what happens in blood, although we backed
23 away from that when we needed to call blood-giving a service rather than delivery of a
24 gift for product liability purposes, lest the blood banks wind up strictly liable for
25 transmission of HIV. This is a good example, by the way, of the kind of ridiculous levels
26 of complication we get into. Other times, it's considered neither a gift nor personal nor
27 abandoned property. An example would be corpses, in which your continued control
28 over disposition through indications is in your will but your kin's control leaves it with
29 no particular status—which is exactly why we don't understand what to do with the
30 burial remains. So the usual lawyer's answer, Harold, is “it depends.”

31 DR. SHAPIRO: Okay, thank you. Eric.

32 DR. CASSELL: That also underscores what an interesting topic it is and
33 how pervasive its reach is. We have next a *Belmont Report* revisited which, as laid out
34 here, is really a scholarly effort to rethink the process. And I think we're ... that's Larry

1 (teleconferencing in). Yes, okay, Larry, wonderful, wonderful. I'm not too sure how you
2 make it louder so that Larry can hear. Anyway, I think we saw the *Belmont Report*
3 revisited as a scholarly effort to rethink these older concepts that went into the first
4 Commission's report. And I think we're committed to that, so that should go ahead. Eric
5 Meslin and I talked about the issue of education. Bette Kramer is also very interested in
6 the issue, and the question is, is it really a separate topic in which we have hearings and
7 we go at what we mean by education and so forth? Or should we make it a part of every
8 one of the other topics, such as when we're talking about genetic discrimination and so
9 forth, what is being done to educate people about the problem; and for Institutional
10 Review Boards, what is being done to educate members of Institutional Review Boards?
11 As Eric Meslin and I have left it now, we have made it a part of every other rather than a
12 separate topic. And I think that may get our work accomplished and also save some
13 meeting time.

14 Informed consent is another one. It's really related to the topics we are
15 discussing now. It's certainly important enough to revisit, and it speaks for itself.

16 Compensation for research-related injuries is a topic that comes up again
17 and again, and I think we're just going to have to have some discussion about whether
18 we want to pick that up or not.

19 Experimental medicine is an issue, particularly now. A great deal is done
20 that does not come under the rubric of research and yet there's inadequate protection of
21 the people who participate. They see it as therapy; it may not be therapy, really; it may
22 be somebody doing a piece of research. But I do not think that we would have to devote
23 a lot of time to that.

24 And then we discussed the last couple of times the right to health care
25 and reproductive technologies as both difficult topics and very time-consuming, so we
26 had them listed this way because we think that at the present time they shouldn't occupy
27 the center of our agenda, though all of you may vote that that's exactly where the action
28 is and that's what we should do.

29 That leads us to the summary that Eric Meslin has here: ethical and legal
30 issues in research in other countries, genetic discrimination, privacy and confidentiality,
31 Institutional Review Boards, ownership of the body, the *Belmont Report* revisited—with
32 education specifically a part of every one of those topics—and reports. We would prefer
33 if you would just give us your input so we know just exactly what we are going to do.

34 DR. SHAPIRO: Okay. Jim, then Trish.

1 DR. CHILDRESS: Thanks very much, Eric and Committee, both Erics
2 and the Committee. I think this is exceedingly helpful to have a good, clear sense of what
3 we think to this point we are committed to and how we might revise this over time,
4 revisiting it at each meeting. I very much agree with the topics in the order and let me
5 just take the first three in that order. But let me say a word about Institutional Review
6 Boards because we've discussed this several times, agreeing that this is a central matter
7 for us, and yet we've also indicated that we need to have access to the reports that are
8 under way: the report from the Office of the Inspector General and the McKay Report.
9 Over the last few days I have talked to the parties involved in both of those, and it looks
10 as though we'll have access to the material by March. So by March we should have the
11 McKay material. I've seen a draft of some of the materials presented out of the data at
12 the December meeting of Primer, and I think that the data will be very interesting and
13 helpful to us. That should be available by March.

14 DR. MESLIN: Is that 1998?

15 DR. CHILDRESS: 1998, yes. Although now that you've raised it, I'm
16 not sure I was as clear in my conversation I should have been. Thank you.

17 DR. MESLIN: I learned a long time ago as a forecaster that you don't
18 forecast an event and a date together. One or the other is your best bet.

19 DR. SHAPIRO: Good to know that.

20 DR. CHILDRESS: We have heard about that particular study several
21 times. But the other one we've not heard as much about recently and I was somewhat
22 surprised, actually, to find that its scope has expanded considerably, and that now,
23 instead of just one report there will actually be four, and they're available now in
24 working draft from going to the FDA and NIH and OPRR. We should be able to get
25 those in March as well.

26 Let me just mention what will be covered there. One will be the
27 challenges in oversight for already-approved research protocols. Promising approaches
28 emerging in the research oversight on the part of IRBs will be the second one. Third is
29 an examination of independent IRBs—how many there are, how they're functioning, and
30 what their workload is; and then finally a wrap-up report with recommendations. I don't
31 now have a sense of direction to each of those; this is just simply an indication of what
32 they're covering. But again, we should have that material in March because the Office of
33 the Inspector General would very much like to have him back in the loop and have this
34 material be useful. So I think this is very encouraging for our own work on IRBs.

1 DR. SHAPIRO: Thank you. Patricia?

2 MS. BACKLAR: I don't know if everybody knows that the NIH has an
3 RFA of a T-15 type on education, as Eric is nodding his head. But I think it's important
4 that the Commissioners see that RFA and get some idea of the scope that would be
5 involved. This would be educating researchers and IRBs; it's a little bit vague in the
6 RFA, but it would be a big help to us if this was going to happen. And it's quite a large
7 grant. I think it's between two and three hundred thousand a year for about three years,
8 going out to various institutions throughout the country. Have I described it adequately,
9 Eric, or do you want to add something?

10 DR. MESLIN: Yes. The only thing is that a T-15 refers to one of the
11 NIH granting mechanisms, which is a training grant, and this is designed as an
12 opportunity to develop short courses in research ethics.

13 MS. BACKLAR: But with some kind of method of evaluation, so it could
14 be more than just short courses and using the electronic media as a way of getting this
15 kind of education out to researchers and IRBs.

16 DR. SHAPIRO: Steve?

17 MR. HOLTZMAN: Regarding this subject on education, I was curious
18 how you folks thought about this translating to the level of college courses and graduate
19 courses. I was very impressed with the presentation in San Francisco a year and half ago
20 by the Danish group talking about the development of tools used just for the common
21 person, even for children, and to what extent you were thinking about that, to what
22 extent LC monies, for example, are going into that, and is that something that we ought
23 to be thinking about?

24 DR. CASSELL: Well, one of the reasons in my own view of it is that it's
25 reasonable to put it as part of other subject is that clarifying just those points, what do
26 we mean by it? Do we mean that the level of education about science and science-related
27 matters—of which ethics is one—should be at all levels of education in the United
28 States, or do we mean more specifically that we want to see IRB be? That idea, what
29 exactly do we mean by it, I think, is one of the things that ought to shake out as we go
30 through these other subjects and talk about it as part of the other subjects. Myself, I also
31 mean education stretching down to younger grades.

32 DR. SHAPIRO: It was a Danish group that discussed their material last
33 June over a year ago.

1 DR. CHILDRESS: I need to be refreshed on the question of whether the
2 Commissioners received last year, when we were beginning our work, a copy of the
3 report on compensating for researcher injuries. Was that distributed to everyone?

4 DR. SHAPIRO: Yes, I think it was.

5 DR. CHILDRESS: Okay. Because it's not noted in the helpful write-up
6 from the staff here on that topic, and certainly the notion that what we are doing is
7 pushing through on a topic that has received prior study from at least three groups,
8 including the President's Commission, which laid out a very specific plan about how to
9 go about finding out data and assessing the potential effect of having a system of
10 compensation. Obviously an issue of having a system of compensation is that injuries
11 may suddenly start arising that didn't exist before, something akin to the moral hazard
12 problem. And one doesn't want to move in that direction and just create a problem that
13 doesn't exist. But at the same time, as the staff memo notes, we really have no data on
14 the extent of injuries. And it may be that the anecdotal sense that they are few in number
15 is correct or it may simply be that they're below the radar. So it would probably be
16 helpful in the future, if we are going to explore this topic, to have some way of
17 refreshing ourselves on what that earlier report—which in turn summarized the two prior
18 reports—said on the subject.

19 DR. SHAPIRO: Thank you. Other comments? Let me make a general
20 comment. As I look ahead over the next year and a half or so, we really should think
21 about this in the context of what we can get done in that time period as opposed to just
22 listing topics, every one of which is very interesting and topical. It's my own sense that it
23 is a good time regarding new topics, topics we're not yet engaged in. It is a good time to
24 take up this issue described here as an ethical and legal issue: research done abroad
25 supported by the U.S. It's extremely topical, all of you have been reading about it, it's a
26 very interesting issue on which, in my own view at least, adequate analysis is yet to be
27 fully formed, so I think we could have a contribution to make to this analysis. And it
28 seems to me that it's a well-defined problem. We don't know all the answers yet,
29 obviously, but it's a well-defined problem. And something—in the timeframe that we
30 have and with the resources we have—we could incorporate into our overall ethics. But
31 the staff did leave it listed here as—I don't know if it's superiority order or not,
32 Eric—on the last summary and next steps. But I really would be interested specifically in
33 whether other Commissioners agree that this is a topic that is useful for us. It's a new
34 topic, we'd have to mobilize ourselves, staff would of course have to create an agenda
35 for us, and so on. We don't have that worked out. Jim?

36 DR. CHILDRESS: I'd very much agree with the view that this should
37 take first priority. In my comments I just concentrated on Institutional Review Boards in

1 order to lay out the background—the foundation—for approaching that area. I think that
2 this is a topic that is continuing to receive a lot of attention, obviously, growing out of
3 the controversy about the AIDS trials, but also in regard to Dr. Satcher's nomination.
4 And I think it would be—I guess I want to say it a little differently—not only do I think
5 it's important and something that we could do and do very well in a reasonably short
6 period of time, but I think in some ways it would be a failure of moral responsibility for
7 us not to do it. That is to say, with this topic being discussed in this society as it is, for us
8 not to attend to it as quickly as we can in a very responsible way would be a failure on
9 our part.

10 DR. SHAPIRO: How do others feel? Does that seem like people agree?
11 Because if so—and I sense agreement around the table—we would ask the staff by our
12 next meeting to have a proposed action plan for us including resources that we would
13 have to access in order to reach our conclusions. All right, let's...Alta, did you want to
14 add something to that?

15 MS. CHARO: No, never mind.

16 DR. MESLIN: In the spirit of collaboration and recognizing that we start
17 our bimonthly meetings after the March meeting, meaning we're going to be convening
18 again within 30 days, staff would be grateful if you have suggestions of individuals who
19 might be appropriate to come before the Commission and offer their input. I think
20 everyone can come up with a very helpful list—some of you in the room would be
21 helpful testifying—not only of those who can appear before us but who might be
22 appropriate for preparing commissioned papers. So please use the regular e-
23 mail/telephone method for getting those suggestions to us. We will collect them, work
24 with you, and come back with an action plan in March.

25 MR. CAPRON: If we're thinking of getting started on that in March, or
26 the possibility that we might even want to do it then, I think we'd be remiss if we didn't
27 turn right away to Drs. Angel and Varmus to hear from them in person. We saw some of
28 the correspondence and the commentary that came out of that. And right there in
29 Washington, Larry Gosten at Georgetown served as a consultant when he was with the
30 American Society of Law, Medicine, and Ethics to the Council of International
31 Organizations of Medical Sciences for their work. And if we can go to your home
32 country—to a transplanted Britisher—Bernard Dickens took the lead. He's at University
33 of Toronto Law School. All of these are people who could gear up extremely quickly
34 and prepare consultants' reports and also would be able to provide a verbal overview of
35 what that report might deal with. And I do feel the pressure of time. And if the March
36 agenda isn't firmly set, you may find that they're even available on that kind of notice,
37 not waiting until May.

1 DR. SHAPIRO: Those are excellent suggestions. I also thought that it
2 was a thoughtful article in *Science* that bloomed it, which I found to be very carefully
3 thought out. He had his core structure in his head about how to work his way through
4 this problem, which was helpful, and that's another possibility. You don't have to ...
5 can't accommodate everybody all at once. But if there are other suggestions, please let
6 Eric know.

7 MS. CHARO: Rachel, perhaps, may be right person to ask this question
8 of. To what extent does the State Department have an interest in this issue, since they do
9 have a section that deals with international science cooperation. Do they have anybody
10 there who actually focuses at all on this, or are we free to influence?

11 MS. LEVINSON: I'm not sure what to make of your last comment,
12 whether or not you're free of State Department influence.

13 DR. SHAPIRO: I declare myself independent of those things.

14 MS. LEVINSON: But it's primarily an HHS issue because they're the
15 funding agency. So that would be the lead and then there are other aspects having to do
16 with the State Department or ID, but I think you can focus first of all on HHS.

17 DR. CASSELL: Although there are aspects of this that have to do with
18 anthropology and sociology and the issues of cultural imperialism and so forth that came
19 up, particularly after the second World War and which has sort of died down now, the
20 same arguments apply here and it would be interesting if we could find who's still
21 interested in that and who might talk to us. I think we could dig back in an older
22 literature and get people for that.

23 DR. SHAPIRO: Okay, well I'll take that as something that we'll turn our
24 attention to right away. As with Alex, I feel some pressure of time on this one myself,
25 and I think it's a timely issue so we should really get started.

26 MR. CAPRON: Could I ask for clarification on one point, Mr. Chairman?
27 I don't understand quite where we stand in responding to this staff memo. The staff has
28 recommended the five reports that are set forth under B as the priority. My own sense of
29 priority would include a slightly different ranking. Are we going to collectively come to a
30 consensus on this at this or some other meeting?

31 DR. SHAPIRO: I think the answer to that is yes. It's not the whole list, at
32 least with those we think we want to address quickly. That was our purpose of my
33 bringing up this latter topic. And so if you or anyone else has ideas about how you would

1 rank these and/or insert other ones, now's a perfectly appropriate time for that.

2 MR. CAPRON: I'm also not quite clear in my head what the
3 eventual—not only direct staffing strength but ability to have for three or six months on
4 staff—four part-time consultants, so I don't really know what person-power is going to
5 be available for this. There's the additional question of whether we would begin any
6 studies that we do not anticipate could be finished by October of 1999. What is the
7 possibility that either we or some other group would be able to continue the work? In
8 other words, do we aim for having everything done by the Summer of 1999 and voted on
9 it finally in October? Or do we say this is going to be rolling process, with reports in
10 various conditions, and if we're demonstrating our value we might expect that the
11 Commission will be authorized beyond 1999? The President certainly anticipated last
12 June a five-year lifetime for the Commission so that it would be available to respond to
13 the Sunset Provisions in the cloning statute.

14 DR. SHAPIRO: My view of that is that we should take the latter
15 strategy—that this is a rolling effort. We don't need to aim for the completion of
16 everything by some magic date in 1999 or any other date. And if we're as lively as we
17 ought to be, no matter what date we pick, we're going to have unfinished business in
18 front of us. So on the one hand, I think of it as a rolling process and we'll generate
19 reports as we can. On the other hand, I do want to make sure that we have sufficient
20 concentration to staff these orders and to get a certain number of reports out between
21 now and then—perhaps four or so that we might want to complete by then, given the
22 work that we already have under way plus that that we'll take on. So it is a kind of
23 rolling process with the presumption, however, that we're going to focus enough to get
24 some of these reports done and out in that period. Obviously, the ones that we're
25 discussing at tomorrow's meeting will be done. I hope we can take on this one. I think
26 that could get done by that time, and the Institutional Review Boards strike me as an
27 important issue that we can still discuss. That will be another option. But there are others
28 that won't get done and other efforts that won't get done. Bette?

29 MS. KRAMER: Harold, do we...are we obliged to give a high priority to
30 those issues that were specifically mentioned in the samples?

31 DR. SHAPIRO: Well I think we are, although there's one of those issues
32 that is so broad that we couldn't possibly sort of respond to it in any kind of complete
33 way. The genetic information item in there is so broad and includes so many things that I
34 wouldn't have any sense of completion just by doing some aspect of it. But I think we
35 are obliged to take on important aspects of those.

36 MS. LEVINSON: I thought you were going to mention the first one, not

1 genetic information, but the protection of human subjects. Because several of these
2 reports relate to that. It's an ongoing issue. But you might also want to think about these
3 as not individual, self-contained studies. Think about ways to tie them together to
4 address the adequacy of human subject protections.

5 DR. SHAPIRO: I think that's a good point. I think one of the issues in
6 front of us—and we'll probably have to pick up some of this discussion later because we
7 have a guest and I don't want to keep her waiting longer than necessary—is how we do
8 package the various ongoing efforts, let alone those that we'll take up, in ways that are
9 really effective. So we're going to be discussing the OPRR issue later. In what kind of
10 framework should that be packaged with other kinds of things that are very closely
11 related to that? So that's an issue we still have to address. I don't know, Eric, how you
12 feel about that.

13 DR. MESLIN: I think it is entirely appropriate given that there is some
14 ongoing research that the Commission is deliberating about: both the federal agency
15 survey that is soon to be completed, and the IRB study that is being considered here
16 based on what Jim Childress is discussing. We've been talking about the federal
17 oversight of human subjects in this country, and it seems that there are a couple of very
18 neat and logical ways of packaging those so that we can both fulfill the mandate of the
19 Commission in being able to respond to the requests for commenting on the adequacy of
20 the system, and also address what are some very pressing matters. One can easily see
21 two or three of these things being linked in one report. The only other point to raise is
22 that we specifically wrote the suggestion about genetics in an ambiguous way, and that
23 was purposeful for at least one important reason. And that there has been an awful lot of
24 work under way, both at NIH and HHS, on various aspects of genetics subjects. In your
25 briefing books, you have seen materials released by the Vice President at the James
26 Watson lecture he gave at the NAS a few weeks ago. And I'm aware, as I'm sure David
27 Cox is, that the National Human-Genome Research Institute has a longstanding interest
28 in many of these subjects. Bill Robb has indicated to us, although he's not here today,
29 that in his capacity at chairing an interagency committee, which was constructed
30 following the report of the Task Force on Genetic Testing, that there is a considerable
31 amount of interest within HHS about many of these matters. So the suggestion that staff
32 is raising is whether we ought not to consult very carefully with those who are already
33 well ahead and to elicit from them what NBAC's contribution to this discussion might
34 be.

35 DR. CASSELL: On the genetic issue?

36 DR. MESLIN: On the genetic issue.

1 DR. SHAPIRO: Other comments right now? If not, we can return to this
2 subject as time allows. I'd like to turn to our guest, Eric.

3 DR. CASSELL: I myself would move the Institutional Review Board up
4 under as the second topic, and that also will allow us to sort of shake out a little bit what
5 we mean by the genetic issue.

6 DR. COX: Harold, I really second that. I think that for all the things that
7 we talk about in essentially almost all of our reports, we schlep everything off onto
8 Institutional Review Boards. In fact I think that's not just our group but that has been
9 the tendency for recommendations with respect to ethical issues. I, for one, think it's
10 going to make it very difficult for people who are members of the Institutional Review
11 Boards unless we revamp that soon, or at least consider it.

12 DR. SHAPIRO: Let's not end the discussion here, but we'll leave it for a
13 moment. There are three issues on this list that I'd like to spend some time with the staff
14 working on before our next meeting, which is only weeks from now. One is the
15 ethical/legal issues regarding research abroad; the Institutional Review Board that Dave
16 and others and just talked about, and Eric; and the *Belmont Report* revisited, which is a
17 different kind of thing. It's not the same kind of activity. We'll probably go about that in
18 a different way. But I want to give some careful thought to how we might sponsor
19 something that might really be a contribution to the world of scholarship in that
20 particular area. It's a good time to do it, and as someone mentioned we have the 20th
21 anniversary coming up shortly. I don't know when, exactly.

22 DR. MESLIN: April 1999.

23 DR. COX: Harold, can I just make one point about that? I am also
24 extremely keen on that *Belmont Report* revisited as I said at the last meeting, and I think
25 that some of the words that the staff used in this really capture my own feeling quite
26 well—to think of it now in the context of access rather than just the context of
27 protection.

28 DR. SHAPIRO: Right.

29 MR. HOLTZMAN: And that's exactly the context that I'm particularly
30 interested in.

31 DR. CASSELL: That's an issue that just came up at our very first
32 meeting. And I think maybe Eric raised it and that is obviously a very important issue
33 very much on people's minds. Steve?

1 MR. HOLTZMAN: Again, this is about education and maybe reaching
2 out to the public ... national policy is being decided today, or whenever, but not on the
3 basis of scholarly position.

4 DR. SHAPIRO: There have been some times when ideas moved the
5 world. This might be just one of them.

6 MR. HOLTZMAN: ... ideas to move the world is because the world has
7 access to those ideas.

8 DR. SHAPIRO: Oh that's not arguable. The issue of...I mean it's an
9 important issue you raise, I don't know what we can or should do in that respect but
10 we'll certainly give that some thought, whether I think in my own mind that it is an
11 appropriate time and appropriate for us to sponsor something that is quite scholarly in
12 this area. We don't need to put that aside as one for the other. And we ought to think
13 through how we can mobilize ourselves. It's the least of something that might have the
14 effect of the topic. Well I am going to insist that we end; Alta, you'll have to hold your
15 comments until later. I apologize for having to end, but I do want to turn to our guest,
16 whom I didn't quite introduce, just mentioned before: Elyn Saks, who's over here on my
17 left, from the University of Southern California is here to talk to us on capacity
18 assessment instruments. Welcome, and thank you for coming.

19 PROFESSOR SAKS: Oh, thank you very much. I'm very pleased that the
20 Commission has invited me to talk about a topic that's interested me for a long time. The
21 one bit of it that I'm going to talk about today—namely, assessing the sort of premier
22 treatment competency from an available lot—is very much a work in progress.

23 The issue I'm going to discuss today, assessing the MacArthur Treatment
24 Competency instruments, is very much a work in progress. I need to do more reading,
25 more rereading, and more thinking but I wanted to tell you what I'm thinking about
26 today. It's a common place and it's block-letter law as well that decisions to undergo
27 treatment or participate in research must be voluntary and formed in competence. And
28 then the question becomes what do those terms mean. I'm going to talk about
29 competency and the premier instruments devised to answer that question are
30 MacArthur's Treatment Competency instruments, designed in particular by Drs. Tom
31 Grisso and Paul Applebaum. They're the foremost researchers. Their instruments
32 measure four things. Their Understanding Treatment Disclosure (UTD) instrument
33 measures whether the patient can understand general information about his
34 treatment—his illness in the treatment. The Perception of Disorders (POD) instrument
35 measures whether he appreciates what illness he has and treatment prognosis with and
36 without treatment; in other words, as applied to general information about his particular

1 situation. The Thinking Rationally about Treatment (TRAT) measure measures
2 fundamental reasoning ability. And a submeasure of the TRAT measures whether a
3 patient can evidence a choice. These instruments, the researchers say, measure capacity
4 as opposed to legal competency—in other words, capacities that are relevant to what we
5 might define as legal competency. They also propose something called the MacCAT-T,
6 which is a streamlined version of the research instruments that requires some clinical
7 judgment and allows for a competency finding.

8 What I'm going to do today in my talk is talk about the normative
9 dimensions that we need to think about when we're talking about designing a
10 competency instrument, and how MacArthur does on that count. I'm going to assess the
11 different measures and talk about importing these treatment competency instruments to
12 the research context, and then conclude.

13 The normative issues. As is usual in the case of bioethics, the key conflict
14 is between autonomy and paternalism, and many people think we draw the line between
15 autonomy and paternalism interests by saying that we allow competent, and only
16 competent, people to decide. But that just pushes back the question because how we
17 define competency is going to really itself draw the line. Obviously requiring much in the
18 way of ability is going to favor paternalistic interests and vice versa. It's also not widely
19 appreciated, I think, and not by the MacArthur research designers, that the
20 autonomy/paternalism question replicates itself when we ask how to define competency.
21 And that freedom includes not only freedom to decide what to choose to do—whether to
22 be treated or participate in research—but also within broad limits how to decide. So
23 more specificity is saving the values at stake: we want to protect the vulnerable. And that
24 translates into requiring needed abilities to make a decision, at least at a high level of
25 generality. Second, we want to protect people's rights to be unconventional, and that
26 translates allowing people some scope in the methods that they use to decide, and to
27 decide on what to believe. And third, we want to take into account the widespread mild
28 irrationality that psychiatrists, psychologists, and psychoanalysts have long discussed.
29 This is important because we either must declare many more incompetent or we must not
30 declare incompetent the floridly ill who are exhibiting these same mild deficiencies.

31 In practical terms, what does this all mean? It means we've got to justify
32 the ability to the chosen, we have to justify the skill level of the tasks prescribed and
33 measured. For instance, on the UTD, what's the reading level when information is
34 disclosed? And then we must justify the level of performance required on each task. And
35 all of those balances, all of those line-drawn problems are going to require balancing
36 autonomy versus paternalism.

37 I think the MacArthur researchers fall down a little bit on the normative

1 dimensions, and they acknowledge that. In fact, they say they are not answering the
2 normative questions at all. In fact, they smuggle some normative judgments in. For
3 instance, even by selecting instruments that they select and abilities that they measure,
4 they're making the normative judgment that those abilities that measure up to and down
5 from certain levels are important for treatment competency. You could also devise an
6 instrument that measures facility at learning foreign languages, but nobody would
7 propose that as an instrument that was relevant to treatment competency. So they are
8 making normative judgments and they're not really justifying them.

9 And then there are other judgments that they explicitly leave open and
10 need to be justified, such as where to draw the line. They suggest where impairment is on
11 their capacity instruments but not what level of impairment should translate into
12 incompetency. Any adequate competency standard must struggle with these issues, and
13 the MacArthur instruments are at least an incomplete effort to respond to the need for
14 instruments.

15 Now I'm going to look at the instruments themselves—first of all, to
16 evaluate the classificatory scheme itself. I think the big problem is that four measures are
17 incomplete. They incompletely cover the field in the sense that the Understanding
18 Treatment Disclosure information I read as requiring comprehension but not necessarily
19 belief of some general information, whereas the Perception of Disorders instrument
20 requires belief of that information as applied to one specific situation.

21 What this means is that you're not testing for forming adequate beliefs
22 about the general information or understanding the specific information. The general
23 specific distinction is beside the point; I think it's sort of a red herring. What you should
24 really distinguish between is understanding and the sense of comprehension: you
25 understand my view that it's 2:30 versus understanding of the sense of belief you
26 understand that it's 2:30. So that's kind of an incompleteness in their classificatory
27 scheme.

28 Are the abilities that they describe necessary for treatment competency? I
29 think they all are and maybe more are. To go through this quickly, comprehension seems
30 important because you have to comprehend in order to assess evidence and form beliefs.
31 Forming beliefs is important because decisions are made on the basis of desires and
32 beliefs, so you must adequately capture the world and how you're interests are going to
33 be affected. Reasoning is important. You need to be able to put the information together.
34 If you can't put it together—if someone is reasoning, "If I want to do P I must do Q, I
35 want to do P therefore I'll not Q," we would say that the person's decision to not Q is
36 probably not competent. Evidencing a choice, you know that there we have a decision,
37 whether it's a threshold issue that triggers a competency issue or is necessary for

1 competency itself. It may not be necessary for competency itself. Someone who can't
2 communicate may very well go through the reasoning processes that we would require
3 for him or her to make a competent decision. But it's probably not important to decide
4 that because you have to have someone evidencing a choice to decide whether to honor
5 the choice.

6 Now let's look at the specific abilities—and maybe more abilities are
7 required, by the way, than these four. Decisions, I said, are made on the basis of beliefs
8 and desires. Maybe you need to be in touch with your true desires. Maybe you really
9 have to be yourself so you're making authentic choices. Maybe you need to not be
10 subject to volitional impairment. There are other things that we need to require. I think
11 there are probably problems with these ideas but they at least need to be thought about.

12 The specific instruments. The Understanding Treatment Disclosures
13 instrument, or the UTD, appears to suffer from minor problems that could be easily
14 corrected. First, it does not give the patient credit for reciting information about his
15 illness and about the treatment, even if it may be correct, if it hasn't been given to him in
16 the disclosure. One theory is that we want patients to understand what they've been told.
17 Another theory is maybe they have better information about themselves than what
18 they've been told, and they do understand that information. And maybe all we really
19 require is information at a high level of generality; for example, that mental illness is an
20 illness that affects mental symptoms and there are treatments for them and there are not
21 horrendous risks, but there are some risks, rather than what the particular risks are. At
22 the very least, the UTD, I think, does need to warn people being evaluated that when
23 they give information that's extra-disclosure information, they're only really being asked
24 to tell what they've just been told. We don't want to mark people down for that.

25 Second, the UTD may measure things that aren't necessary to
26 understanding. It measures being able to attend and process, which clearly are but also
27 being able to retain for quite a bit of time, so that may be a problem. Conversely, it may
28 measure only retention and not understanding. Presumably, a very clever parrot could
29 repeat back information that it was given, or somebody who has a perfect auditory
30 memory but has no comprehension of a language could repeat back information and not
31 really understand it. So these are problems with the UTD but I think with some work the
32 instrument could be quite a good instrument and it does measure something very
33 important.

34 Let's go on to the Thinking Rationally about Treatment measure, the
35 TRAT. This measure, I think, may require evidence of abilities that aren't at all necessary
36 in a given case. It measures things like transitive reasoning ability and weighing
37 consequences and measuring, comparing alternatives. But imagine a situation where a

1 patient so disfavored one risk of a particular treatment that that was enough for him to
2 decide that he wanted the other one. And he trusted that the doctor wasn't going to give
3 him something that was really horrendously dangerous. That person may not need to
4 evidence all those reasoning abilities.

5 Second, it may underestimate the existence of these reasoning operations
6 by the way they are tested. Basically they give a vignette and then ask the patient how he
7 decided. He may have met or done a lot of the measures, but just not say that he did
8 them. So maybe he should be asked, "Did you think of other consequences?" although
9 maybe that's too leading and sort of leaves to psychometricians the task of revising the
10 instrument in light of this concern.

11 Third, there's a submeasure on the TRAT that measures expressing a
12 choice, and I think it doesn't make sense to mark patients down if they only evidence a
13 firm choice on a second inquiry. Can't people take a little bit of time to make up their
14 minds? So I think that's a problematic measure that could be revised easily as well. The
15 Perceptions of Disorder instrument includes two subparts: the nonacknowledgment of
16 disorder (NOD) subpart and the nonacknowledgment of treatment potential subpart. I
17 think the POD is a deeply flawed instrument and needs to be really rethought. The POD
18 measures patients' beliefs about their condition and its treatment. But requiring certain
19 beliefs is a tricky business because many beliefs are controversial and they're not
20 obviously false. Requiring such beliefs, then, is not obviously necessary to competency;
21 that is, it doesn't serve our "protecting the vulnerable" concerns. Indeed, the patient with
22 such a belief, as against the majority view, who turns out to be right is in a sense super-
23 competent. Also given that many beliefs are controversial, it's part of patients' freedom
24 within broad limits to decide what's true no less than what's good. That's our autonomy
25 concern. And finally, many people suffer from mild distortions and that raises our
26 concern about discriminating against the mentally ill.

27 In my view, it's a very hard question where you draw the line, but I think
28 the POD draws it at the wrong place. The first subtest on the NOD requires a patient to
29 believe the diagnosis his doctor gives him, making the doctor the final authority on truth.
30 Why ever do we then get second opinions? His doctor, of course, may be wrong. What if
31 the patient believes a former doctor's diagnosis? What if he admits he's ill but disagrees
32 with the particular diagnosis?

33 The second test on the NOD requires patients to rate the severity of their
34 illness as given on the brief psychiatric rating scale. But if the question is how severely ill
35 patients feel, they may know that better than anyone else. And if the issue is their
36 location on a common metric of severity, how are we to expect patients to know that
37 common metric? They're not in a position to make comparative judgments about their

1 own illness compared to other patients' illness. The NOD also requires patients to admit
2 symptoms they have been displaying. To the extent that these are grossly demonstrable
3 symptoms and don't require a good deal of interpretation, and to the extent that they
4 don't just duplicate the illness question, I think this subtest makes sense. It's a patent
5 distortion of reality to deny that you're evidencing grossly demonstrable symptoms like
6 frenetically pacing or not sleeping. The NOD requires patients essentially to agree with
7 their doctors about their prognosis with and without treatment in general and medication
8 in particular. Once again, the general data may be fairly indisputable; for instance, the
9 odds of doing a certain way with or without treatment. But it's perfectly plausible for
10 patients, for instance, to expect to be in the bottom ten percent, say, that doesn't respond
11 to the treatment. That may be pessimistic, but a lot of people are pessimistic and a lot of
12 people are unduly optimistic, too. So I don't think that's a gross distortion of reality. It
13 will be clear that there's a range in the kinds of beliefs you can require when you're
14 trying to judge competency. At one far end is the POD, which basically requires patients
15 to believe whatever their doctors believe about them. At the other far end is a standard
16 that would say that you had only not believed things that are impossible. I think that goes
17 a little bit too far: you can believe things that are completely implausible given the
18 evidence, but not impossible and maybe you should be incompetent then.

19 In the middle there's a range of standards. You could require patients to
20 believe what most doctors would believe about them, or what most people would
21 believe. Or, since these are kind of majoritarian referrals-on, you could talk about skills
22 themselves involved, like you can't believe beliefs that are based on no evidence or that
23 are patently false or that are delusional. Anyway, these are some of the possibilities, but I
24 think the POD makes the wrong choice.

25 I like a kind of patently false belief standard because I think it adequately
26 protects autonomy concerns and meets other values at issue. And I think on such a
27 standard—and this is controversial—denial of mental illness would rarely count as a
28 sufficient distortion of reality to imagine your own competency. I hasten to add that I
29 have no doubts whatsoever about the reality of mental illness and the severe suffering it
30 causes. That's not the issue at all. I still think denial generally should not make one
31 incompetent.

32 First, patients may simply be unwilling to admit something that's very
33 stigmatizing. They may be frankly dissimulating. Second, even if they're in denial, denial
34 is common; it's fairly understandable, and it's often an adaptive defense. Third, there are
35 no incontrovertible physical means of establishing a mental illness diagnosis except for
36 some organic disorders. It's as if we were living in the time of no EEGs when you
37 couldn't really tell if someone suffered from epilepsy or hysterical seizures. Someone
38 who looks as if they suffer from a psychotic disorder may really suffer from a factitious

1 disorder or whatever. By the way, this is true of many physical illnesses too. Fourth,
2 there's widespread skepticism and misunderstanding about mental illness in society.
3 Much of this is a failure to understand—it's unenlightened—but to the extent that it's
4 common we run into problems again around discriminating against the mentally ill.

5 Fifth, patients, since in my view must believe they are suffering from
6 obvious symptoms, arguably have enough reason to take medication that they're told is
7 likely to ameliorate their symptoms, as if they admitted that they were ill. Perhaps we
8 should require them to admit that they have a condition that looks like, say, X or Y
9 mental illness and that with this condition they are believed by doctors to be as
10 antecedently likely to benefit from treatment as people who really have it and so forth.
11 But to actually make them say they have the mental illness, I'm not sure that's necessary.
12 And it may be a difficult thing for them to do. So I think the POD should be revised.

13 At the very least, it should set a number of different levels of beliefs that
14 should be required, and then let individual evaluators make their own normative
15 judgments. Alternatively, if it's agreed that the line that they draw is the wrong line, then
16 maybe some kind of intermediate standard should be adopted.

17 The MacCAT-T is the treatment instrument. It suffers from many similar
18 problems as the other instruments. It allows clinical judgment to play a role; it's a more
19 streamlined version; it's more tailored to the individual patient. But without going into
20 details, I'm going to suggest that it suffers from a lot of the same problems as the other
21 instruments.

22 Now I'd like to talk about importing the instruments to the research
23 context. In this context you may require that patients demonstrate additional abilities
24 than the ones we discussed; in particular, the ability to withstand pressure to accede to
25 their doctor's request. Transference is very powerful in all doctor/patient relationships,
26 but in the ordinary doctor/patient relationship there is a coincidence of interest in what
27 the doctor is recommending and what the patient's acceding to so we need to be less
28 concerned, arguably. Second, you need to revise the instruments to accommodate the
29 research situation. For instance, in the UTD, one needs to include the most important
30 information—such as that the treatment is experimental or that it is a nontherapeutic
31 experimental measure, and that the doctor has an interest in doing the research as
32 well—and make sure that patients understand that. Third, there are additional normative
33 inquiries that are raised by this context.

34 First of all, there is a value of increasing scientific understanding that
35 needs to be factored in when we decide how we measure competency. Second, the old
36 question of whether we should have a variable competency standard reappears here. It's

1 arguable that since patients making decisions in the research context aren't making such
2 obviously good choices as when they accede to their treater's treatment choices, we
3 should require a higher level of ability. There are arguments pro and con there and I
4 think a kind of compromised solution makes sense, although I don't think there's time to
5 go into that.

6 So to conclude, there are questions around what the NBAC should
7 recommend to IRBs, and I think that's a really difficult issue because the best instrument
8 around has quite a few flaws and it doesn't make a lot of the normative judgments that
9 you need to make in order to use the instruments. I think there's a real danger that
10 people are simply going to say, "This is the level that they marked for impairments so
11 that's the level I'm going to use," without thinking about it. On the other hand, it's the
12 best instrument we have around. Maybe clinical evaluation should be possible. I think
13 that in the research context, particularly with vulnerable subjects, you should assess for
14 competency if there's any reason to think that it's not there. But how you should assess
15 is a difficult question. An easy recommendation is that more research should be done.
16 We need more research on how maybe some of the criticisms I and others have made of
17 these instruments could be accommodated by revising the instruments. We need research
18 into what level of belief should be required, and finally, we need much more research
19 into the normative questions. Thank you.

20 DR. SHAPIRO: Thank you very much. You managed to give us a lot of
21 information, and a lot to think about in a very short period of time.

22 PROFESSOR SAKS: I know, I talk fast.

23 DR. SHAPIRO: I appreciate it, and I thank you very much. It was helpful
24 to me, and thank you very much for distributing the outline to help me get along as you
25 were talking, so thank you very much. Let me turn to questions. Jim and Eric?

26 DR. CHILDRESS: Thank you very much. This was very helpful. A
27 couple of things for clarification. Did I understand you to say you believe these are the
28 best instruments available?

29 PROFESSOR SAKS: So far as I know, yes.

30 DR. CHILDRESS: And in your overall discussion, are you putting them
31 in a larger context, that is, are you also looking at some of the invaluable questions that
32 are lurking behind the alternatives as you're thinking about this in your larger context?

33 PROFESSOR SAKS: You mean in terms of looking at other

1 DR. CHILDRESS: Not necessarily in the same detail because you've
2 already ... one reason you focus on these is that you think they are the best, but are you
3 doing a bit of

4 PROFESSOR SAKS: I had not really looked in detail at any of the other
5 instruments. If indeed there really are some that have been studied and tested, so far as I
6 know, there may be individual evaluators who have their own kind of instrument. But
7 this is sort of...this is where the action's at right now.

8 DR. CHILDRESS: Thanks.

9 DR. SHAPIRO: Eric?

10 DR. CASSELL: One of the issues we have to face is that there isn't really
11 a good instrument, but this is the only instrument that we recommend to IRBs, for
12 example. But it's not really good. It's the only boat we have. It happens to have a big
13 hole in the bottom, but would you please just row faster? And I have a prejudice against
14 that kind of a recommendation. I think we're able to say that this is an issue that should
15 be a high priority research issue; not just more research is necessary. Some research is
16 necessary because I have sick people who can meet every one of these criteria but cannot
17 decenter. And because they cannot decenter, they cannot make a consent....

18 DR. SHAPIRO: Excuse me, I didn't understand what you ...

19 DR. CASSELL: "Decenter" means to take the position of another. They
20 can only see things from their own position. You can actually show that with a child's
21 A-B-C-D block. You show them all four faces, all rotated around like that; then you go
22 back to the A and you say "What's on the other side?" and they can't do it. And it isn't
23 because they don't remember it, it's because they cannot take the position of somebody
24 on the other side of the block. There are just issues about all of this that are very
25 important because it may turn out, and in fact I think it does, that people cannot
26 demonstrate capacity like this alone. These all presume an isolated, using your word,
27 autonomous person out there making a decision and whether you judge it to be a
28 capacitative decision or not. And that may be the basic problem. So I would like us not
29 to come out for an inadequate instrument at all.

30 DR. SHAPIRO: Thank you. Alex, then Alta.

31 MR. CAPRON: I'm trying to think about what Professor Saks said in
32 light of where we were in this process, and I want to know whether my sense is correct.
33 We can obviously call, and probably will end up like every good Commission calling for

1 more research on any number of different topics. But in the present context, we are
2 stepping into a stream that has been flowing for many years and into which the National
3 Commission for the Protection of Human Subjects placed a rock. And unlike the other
4 rocks that it placed there, it did not become a stepping stone toward the adoption by
5 HHS and eventually the whole federal government of standards for research in a
6 particular area. Now their stepping stone was a little bit different. It was the mentally
7 institutionalized, but it's many of the same issues. And one of the things we talked about
8 last time, and we had to deal with in the report, is whether there are separate categories
9 among those who have some incapacity, or who have...where there's lack of clarity
10 about the mental capacity if they are institutionalized. The question that we will have to
11 address is whether when we put forward a report, our expectation is that out of that
12 report, the federal regulators could draw a set of recommendations that would say, "In
13 addition to the usual standards that apply for research on anyone else, here are special
14 steps that have to be taken." And part of my expectation has been that where the
15 treatment involves treatment for mental illness, one of those steps would be the
16 assessment of the capacity for the person to make decisions for him or herself. I think
17 Eric is quite right and he's reminded of this in other contexts, that it isn't only the
18 mentally ill but it is anyone facing an illness for whom a research intervention is being
19 offered as a possible means of addressing that illness in some fashion—connected in
20 some fashion to that illness, either with a so-called therapeutic intent or even without
21 that, but in that context. We have to be worried about the ability of the person to do
22 what the model bioethics said they should be doing, of making a judgment of whether
23 this makes sense for them now.

24 Obviously, if we are going to give guidance to IRBs outside the scope of
25 the regulations, part of that guidance could be what they should expect investigators to
26 do. And I think Professor Saks' eventual paper for us could very useful as a document
27 for IRBs to read in the interim between the time—if there is any time, if it doesn't take
28 forever for there to be regulations on the subject—the time that the regulations come
29 into effect and the time that all the additional research which we would love to see being
30 done on instruments like this, is completed enough to have revisions in the instruments.
31 And I think we're going to be faced, therefore, with a couple of choices. One choice
32 would be whether we, after having the full paper and deliberating about it, want to say,
33 "Actually, the instrument should only be used if," and then address qualifications that we
34 would expect IRBs to insist upon. Or, whether we are going to say simply that the
35 instruments should be used with the following thoughts in mind, but be very unspecific
36 about that. In light of that, I would like—and this is not a staged question, this is not like
37 one of those questions on the floor of the House—Elyn and I have not had a chance to
38 talk about this question—I would like to have your further reflection on a couple of the
39 points that you raised. And I, actually I guess they're really one point, it's just something
40 that you brought out about the point. The basic question, it seems to me, is whether this

1 instrument, which was developed for use mostly in treatment settings ought to lead one
2 to say whatever gradations—and I'm like everybody else, not entirely clear about what
3 kind of scoring this yields, and Trish Backlar has described the instrument to us before
4 and we talked a little bit about it, but we probably need to know more before we say
5 much more. But, whether, as you were suggesting at the end, one would expect it were a
6 higher score, I guess, on this because the assumption that whatever's being done is being
7 done for the benefit of the patient, cannot be made in the context that we're most
8 concerned about, which is nontherapeutic research that may involve more than minimal
9 risk. That's the area that concerns us the most. And if so, how in particular a couple of
10 the points that you raised play into this. You talked about the authenticity point, and you
11 made a passing reference to questions about volition. And the authenticity point is
12 obviously of great importance because when we're dealing, as we are, at least with the
13 original impetus for this, our subjects who at the present moment may or may not truly
14 reflect their true selves—and that's in a way the underlying question—are they able to do
15 that now? And so it seems to me that if you think these instruments don't adequately
16 attend to authenticity, then they are missing a dimension that seems centrally important
17 here. And I don't quite know how to evaluate that because if a person has a mental
18 illness which is not by any surgical or organic means fully curable, in a way that authentic
19 person has a set of values that involves being a person with that illness. And this is
20 something that other people in the disability community have reminded us very strongly
21 of; that it would be wrong for us to look at this and say we understand the standards that
22 ought to be used as if you didn't have paraplegia or something. I mean you do—that is
23 the authentic; you have to decide in terms of that. But I also think that the volition
24 question is very much at the heart of what we've been concerned about. So I'm bothered
25 also by the sense that the measurement doesn't get into volition. So this is a very long-
26 winded wind-up to the question: Could you tell us anything more about that now, and to
27 the extent that you can't fully now, would you think that your eventual paper will delve
28 into those particular points? Because I think that would be particularly helpful to us in
29 addressing what are central issues. Thank you.

30 PROFESSOR SAKS: Well, Alex, I think you raised a lot of interesting
31 questions. Unfortunately my paper's only supposed to be about 20 or 30 pages; I'm up
32 to page 45 now so I don't know how much I'm going to be able to get into those things.
33 But you raised a number of points. One, should you require a higher level in the research
34 context in which you don't have the added protection of the doctor acting solely for the
35 patient's benefit, and I think that's arguable. Maybe not...maybe it's a sort of risk
36 variable, not because you think you should vary the level of competency if a patient's
37 making a possibly bad choice but because there's a chance that the evaluator, since—I'm
38 not saying evaluators are malicious or anything, but they have unconscious reasons for
39 wanting something to happen—evaluators may be likelier to find competency when it's
40 not there. There may be those additional reasons that have a variable competency

1 standard in this context.

2 As to the authenticity question, I think it's a fascinating question, and I
3 think sort of noncognitive, both authenticity and volition are important things to think
4 about in terms of competency. The authenticity question is really, really hard, right to the
5 very reasons you bring up. You know you give the person the medication and afterwards
6 she's back to herself and says thank you. You know, you could reverse the experiment.
7 You have a doctor who doesn't believe in medication, takes a manic patient off his
8 medication and he's kind of reluctant to get off of it, then he gets off of it and he feels
9 great and he thanks the doctor. So it can't be just the later self, and do we prefer—we
10 want to say we prefer—healthier selves, well I kind of do too. But maybe that's just
11 importing the value judgment. These instruments do not speak to authenticity or volition.
12 And the volition problem is important too. I mean I think those are really difficult
13 questions. I don't know that I could get to them in this paper; maybe in another paper. I
14 don't know if other people have thoughts about them.

15 MR. CAPRON: Well I guess then what you would end up doing is
16 flagging the fact.

17 PROFESSOR SAKS: I would flag them, yes.

18 MR. CAPRON: The instrument doesn't and then we would be faced with
19 whether we have any means of suggesting. I mean we aren't engaged in an academic
20 exercise here. In the end, we have got to take input from all the different sources we're
21 getting input and say either because of the total inadequacies of instruments and
22 measurements and the history of abuses and so forth, the regulations should say, "Don't
23 do research of this sort with these people." Or we should say that the research may go
24 forward ...the regulations ought to embody the following additional protections. And it
25 comes down to something fairly practical, but it has to be clear enough that an IRB that
26 doesn't sit around and get to hear Elyn Saks give her paper, and may not even all of
27 them ever go to our appendix and read the paper, can do a decent job just looking at the
28 regulation, knowing whether or not they've added the suitable protections. And it would
29 be lovely if you had come in here and said the MacCarthy instrument is so perfect and
30 you just use it and just insist everybody use it. But you're not saying that, so you've
31 complicated our lives.

32 DR. SHAPIRO: We'll hold you responsible for that altered interest.

33 MS. CHARO: Thank you. I heard you making some criticisms that
34 focused on seemingly extraneous information being collected by the instrument. And
35 then in other points it appeared that there was an absence of information gathering that

1 might be pertinent, this past discussion being one example. And it struck me, unless I
2 missed it, that there's also an absence of any measurement of emotionally-appropriate
3 reactions to information, so that there's some measure that people are appalled by things
4 that they should be appalled by, and attracted to things they should be attracted to. It
5 would be very helpful to understand from you exactly what the list is of gaps, because
6 extraneous information seems to me to be less problematic than gaps.

7 PROFESSOR SAKS: Why is that?

8 MS. CHARO: Because if we unduly screen people out but not to the
9 point that there are no human subjects available, we've not hindered the research
10 endeavor and a few people that might have been eligible just don't become research
11 subjects, big deal. But if there are people who shouldn't be enrolled that do get enrolled,
12 that is more of a matter of concern. And since we are potentially in a situation in which
13 we say that anybody whose ability to make decisions is in question, and certain mental
14 illnesses will be presumptive evidence that their decisionmaking ability is in question,
15 we're at the point of saying for people where there's this question raised, it may be
16 necessary to administer an instrument. I'd like to understand from your presentation
17 exactly how far away we are from being able to say that such an instrument exists. So
18 what would be the list of gaps that need to be filled so that we know exactly how
19 realistic it is to build this kind of requirement into a regulatory framework?

20 PROFESSOR SAKS: Well, I think what you'd need to do is ... if you're
21 not worried about the false positives, people being found incompetent who aren't
22 incompetent...

23 MS. CHARO: It's not great and it has a stigmatizing possibility that is of
24 concern but it's of a different order of concern than inappropriate enrollment.

25 PROFESSOR SAKS: Right. What are the gaps, what needs to be done?
26 Well, the central gap is addressing the normative question. As one example, in my third
27 sort of normative issue I said that a lot of people are mildly irrational, and Dr. Cassell
28 was saying that a lot of his patients, even if they're not psychiatric patients, can't
29 decenter, aren't in a good position to decide. And people may be subject to transference
30 or misweighing, misunderstanding probabilities, or whatever, overvaluing the vivid
31 memory. One normative question that I haven't really stressed is do you want a standard
32 that finds many, many more people, incompetent? Mildly irrationally people too, and that
33 again depends on how you balance autonomy versus paternalism. So the value questions
34 are important questions because I think you can't recommend that the MacArthur
35 instruments be used without somebody, whether it be you or the individual researchers
36 or the IRBs or the MacArthur researchers, deciding where the line should be drawn. The

1 things that the instruments leave out are the kinds of things Alex talked about, capacities
2 that aren't included, all the noncognitive capacities like knowing your true needs and
3 values, being true to yourself, not being subject to irresistible impulses or other volitional
4 impairments. Maybe not being overwhelmed by really profound emotions that disable
5 you from choosing—maybe those would interfere with other abilities like ability to
6 understand or ability to exercise your true preference. But all of those things are not
7 measured at all by this instrument. And so I think those are sort of normative questions.
8 They're capacities that are not looked at. I think it is a problem, possibly a problem—we
9 might be concerned about false positives here, too. Some people who might want to
10 contribute to research think they'll ultimately benefit.

11 MS. CHARO: So should my take-home message be that up until now
12 there has never been a defensible way to assess competency?

13 PROFESSOR SAKS: No, not at all. People assess for diseases all the
14 time without having reliable and valid instruments; they do the best they can and maybe
15 we should have a clinical evaluation. Or maybe people should use the MacArthur
16 instruments with some modifications and flag the level they're going to use and give a
17 few sentences or a paragraph or a page about why they think the line should be drawn
18 here. Or you all should do it. I don't think the answer is, since there's not a great
19 instrument around to say, "Well, let's just not assess."

20 MS. CHARO: No. That's exactly what I'm trying to get at, and I'm
21 going to conclude with this, because I appreciate that an instrument can be incapable of
22 handling the hard, borderline cases. I understand that there can be a definitional problem.
23 You know what day is, you know what night is, but dusk poses a problem. What I'm
24 trying to figure out is whether this is a question of whether the instrument can now sort
25 dusk out into day and night or whether the problem is we can't tell day from night.
26 Right? Because that to me is a crucial thing. Because if the only issue is that it doesn't
27 handle the hard cases, you can then set a policy in which there is a presumption. In hard
28 cases, if there's any doubt at all, you do enroll, you don't enroll, and you can just make a
29 pragmatic decision based upon your preferences about protecting access to research or
30 protecting people from abuse. But if a problem is bigger than that and you really can't
31 tell, it seems to me...

32 PROFESSOR SAKS: It depends on what you mean by hard cases. Do
33 you mean the few cases who come up who are questionable and nobody really knows
34 what the answer is, or do you mean some of the value questions that come up over and
35 over and over again that are just not answered by this instrument, or may be answered
36 the wrong way? I'm not sure what you mean by hard cases.

1 MS. CHARO: That would almost lead you to ... wouldn't part of the
2 answer be we don't know day from night if we were really judging what day and night
3 is? We don't know day from night with this instrument. It isn't just the borderline.

4 MR. CAPRON: Could I be permitted just a quick intervention?

5 DR. SHAPIRO: Yes, then Trish has been waiting patiently to speak. But
6 just quickly.

7 MR. CAPRON: The quick one is, Alta, I'm not sure that the result of
8 being found incompetent on this instrument would be you wouldn't be in research. The
9 crucial question is...

10 MS. CHARO: But we're on the verge of making recommendations where
11 under some circumstances, if you can't decide for yourself, you can't be enrolled.

12 MR. CAPRON: For certain research. But for other research, it shifts over
13 to families, and that is not an uncontroversial move. If a person feels that he ought to be
14 making the choice and somebody runs an instrument on him and says you can't make the
15 choice, X is going to make the choice for you because this is not highly risky research or
16 whatever....

17 DR. SHAPIRO: Trish, I apologize for taking a long time to get back to
18 you.

19 MS. BACKLAR: I really appreciate very much you're coming, Professor
20 Saks, and giving us such a detailed analysis, and I really look forward to reading your
21 paper. There are two suggestions I want to make. When we get Professor Saks' paper, it
22 might be very interesting to ask Dr. Grisso and Dr. Applebaum to write a small response
23 because you are talking about things which I think will be of great interest to them, and
24 I'm sure that they may have some agreement with you. One of my concerns about the
25 MacArthur Competence Assessment tool is that it may be manipulating consent, which is
26 really in a sense part of what you were talking about. The other issue, though, where I
27 come out differently from you, is that I think that the easy cases are the clear cases of
28 serious mental disorder. The difficult cases will be in that twilight zone where it's very
29 difficult to tell if somebody actually does have capacity or if they don't. I think it would
30 be exceedingly difficult to get this absolutely precisely answered as we wish it. And
31 that's why we're building and developing protections and safeguards so that when we
32 get that particular group of people we're sure we've got something in place. We know
33 certain cases are clearly the way they represent themselves.

1 DR. SHAPIRO: Thank you. We'll take two more questions right now,
2 then ask Dr. Saks anything she'd like to add, then we're going to break. Eric?

3 DR. CASSELL: Well, my colleagues had a right to put this instrument
4 out there; even as you say it's flawed according to rules, it's going to be used. Here is a
5 recent paper in the *New England Journal* about tests for dementia. Four well-accepted
6 standards for dementia vary by ten-fold. Ten-fold in the number of people classified as
7 demented. And that would seem to be a much simpler thing, so we may have to come
8 out and say there is no. In the absence of a test that has reliability, what then is to be
9 done?

10 DR. SHAPIRO: Trish, special privileges.

11 MS. BACKLAR: I think one really has to look at this and understand the
12 tests. The test was really very oriented towards people with schizophrenia. Then
13 everything that you see here, and when you read Berg and Applebaum's paper on
14 research issues, this all makes sense if you're looking at people with schizophrenia. The
15 rest of it, that's where it goes into the shadows.

16 PROFESSOR SAKS: I mean I don't know that I agree with you about
17 people with schizophrenia.

18 MS. BACKLAR: Another time.... You don't have to make another talk.

19 PROFESSOR SAKS: It's voluntary. I would just add one bit of research
20 that was done on the instruments, which was quite interesting. They compared
21 schizophrenics and people with angina and people with depression to normal controls.
22 They found that schizophrenics only scored in the impaired range on each of the tests 25
23 percent of the time, omitting the evidence in the choice test. If you combined them, it
24 was 50 percent, and the three tests didn't track each other. The POD, which is the one I
25 find most objectionable, was not really well correlated with the other two, and the other
26 two were well correlated with each other, which may say something about it. They say
27 since they all measure different things we should use all of them, but that's one of those
28 normative judgments.

29 MS. BACKLAR: They did an aggregate in which it came out half full or
30 half empty.

31 PROFESSOR SAKS: Right. Which is sort of interesting that only 50
32 percent if you aggregate them are incompetent.... I'd want to test them a few months
33 later in the community. I think we suppose that people with mental illnesses are

1 incompetent much more often than they are. Thank you very much for having me.

2 DR. SHAPIRO: Thank you very much, and thank you very much for your
3 work. It's very stimulating and we look forward to your paper. We had scheduled a
4 break at 2:45. We are, of course, well beyond that and into a period where we had
5 scheduled for public comment. Now I made a mistake before when I indicated the
6 number of people that were making comments. Most of those who will be speaking to us
7 will be here tomorrow as opposed to this afternoon. We do have someone here this
8 afternoon, though, from the Patient Rights Network, Mr. Bob Aller, if I've pronounced
9 the name correctly. And my proposal to the Commission would be that we allow Mr.
10 Aller to address us right now and then we'd take a break subsequently so we don't have
11 to keep him waiting. Mr. Aller, I very much appreciate your being here, and we're ready.
12 The normal rules of the Commission are five minutes. Thank you, and thank you very
13 much for coming.

14 MR. ALLER: We just had a few questions for the Commission. Dr. Shure
15 is here from NIMH, and a few years ago I wrote to him and said, "Could you send us a
16 sample of an informed consent that's proper for medication withdrawal study?" And the
17 reply at that time was—and the reply currently, of course—is that NIMH doesn't keep
18 informed consents. At that time I wasn't sufficiently sophisticated to say, "Well, what
19 about your intramural research?" It was basically, "We don't have copies of the
20 extramural research." But out of curiosity a couple of years ago, we did a Public
21 Records Act request to one of the local hospitals that does a great deal of research, or
22 they receive about \$70 million a year. We asked for all of their consents across the
23 spectrum, about 60 of them, and particularly everything in psychiatry was deficient.
24 Now, of course, we wrote to OPRR and sent them on to OPRR. But the deficiencies
25 were things like if anything happens it's your problem—exculpatory language. Failure to
26 provide alternative treatments. They were rather material issues that had been somehow
27 not properly conveyed. And so a lot of us who are looking at the problem have said,
28 "Well, we kind of suspect that it's possible there is widespread noncompliance with the
29 current regulations." Now the answer to all of these...there are a lot of academic issues
30 and questions, and people are thoughtfully commenting on them, but is the Commission,
31 and what is the extent of the Commission's acquisition of current consents on either
32 symptom-provoking, nontherapeutic research, or other kinds of research that's
33 conducted with those who are decisionally impaired? And we would like to know what
34 the Commission is doing about it because it's easy to acquire all of the NIMH
35 consents—that's a simple request—but it gets much more difficult when the individual
36 institutions are addressed. And they have been often difficult in response to public
37 records requests. They have kind of stalled and we've had difficulties. But what is the
38 Commission's take on this matter?

1 DR. SHAPIRO: Let me turn to our staff to respond to that question.
2 Eric?

3 DR. MESLIN: This issue has come up before and I'm pleased to tell you
4 what the status of it is. Several Commission meetings ago it was put to us that that very
5 problem is worth investigating. And staff, over the last month and a half, have been
6 putting together a formal research report which will identify as broad a range of studies
7 with respect to various designs, types of conditions, and various pharmacologic agents
8 so that we can be better informed about what the published research is and therefore to
9 find out what the actual protocols are in the consent documents that have been used. We
10 had hoped that by this meeting we would have a sufficient analysis of that literature
11 available for the Commission's deliberations. As it turns out, it's taking us a bit longer to
12 gather those data but we are hopeful that we will be able to present a full staff summary
13 of both those types of research and an analysis of the protocols and consent forms by the
14 next meeting.

15 MR. ALLER: So you're acquiring protocols and consent forms after the
16 papers are reviewed?

17 DR. MESLIN: Yes.

18 MR. ALLER: Is there a ... what kind of number?

19 DR. MESLIN: We've got a number of different search strategies and
20 depending on which model one uses, there are anywhere from 60 to 350 different types
21 of papers that we think fall under this general net. The good news about the way we
22 proceeded is that we are trying to capture what the range of research is rather than
23 identifying what we believe to be especially problematic alone and then zeroing in on
24 particular papers. We'd like to be able to see what the world looks like and this has
25 allowed us to capture—and I've sort of got some staff notes—about 330 papers at this
26 point. And we hope that we can acquire as many of those protocols as possible. I would
27 rather we don't...

28 MR. ALLER; And the informed consents...?

29 DR. MESLIN: And the consent documents. They go hand-in-hand
30 because an analysis of the consent forms alone is incomplete. And analysis of the
31 protocols alone is incomplete. And because it's a staged approach, one can only go
32 through published papers, at least that's the way we feel it's best and most appropriate.
33 It will take us a little bit of time but we're putting this as a very high priority.

1 DR. SHAPIRO: Well we think that will be a very enlightening question
2 that can be answered, particularly because there are suspicions that there may be
3 widespread noncompliance and perhaps there is a great deal of compliance. But we think
4 answering those questions has a lot to do with formulations of new policies.

5 MR. ALLER: Thank you very much. It's very much appreciated.

6 DR. SHAPIRO: Well, Dr. Aller, thank you very much for coming. We
7 very much appreciate your taking the time to be here with us today. Let's try to take a
8 break for about 10 minutes.

9 BREAK: 3:23 p.m.

10 DR. SHAPIRO: We have a couple of agenda items left this afternoon.
11 And one has to do with the issue of changing regulations, the processes that are involved
12 in changing regulations, as we might very well be in that situation. And I'm going to turn
13 to Rachel Levinson in a moment to take up that subject, and then we'll get to the federal
14 oversight of research. Rachel?

15 MS. LEVINSON: Okay, I'm going to try and get through this as quickly
16 as we can. Can everybody hear? I'm going to tell you about the mechanics of the
17 rulemaking process because that's what we're really talking about doing. It's no different
18 to change a rule than to make a new rule, even when you're talking about changing the
19 common rules. So I'll talk about how federal agencies make rules, regulations. The
20 rulemaking process is defined in the Administrative Procedure Act that was signed into
21 law by President Truman in 1946. It has a purpose relating to rulemaking, which is to
22 give the public advance notice of what the government is thinking about doing, and to
23 gather some language and to run it by those people particularly who would be affected
24 by such a rule.

25 The way this happens is that the agency that is effecting the rule will
26 publish a notice of proposed rulemaking in the *Federal Register* for comment. That is
27 not a document that people ordinarily read in everyday life. What the agency should do,
28 and often does, is to take that publication and send it around to the affected parties,
29 maybe the chemical industry if it has to do with regulating chemicals. Or sending it to
30 professional societies or industry advocacy groups, whatever group might particularly be
31 affected or interested in the rule. They have a minimum of a 30-day comment period. It
32 can be extended and often is for a rule that's particularly complex. We encourage up to
33 at least 60 days, not 30 days, as long a period as possible, assuming that there isn't any
34 particular reason to rush it. And all of the comments that are received in response to this
35 publication become part of a public docket that's available for review by anyone. You

1 have to provide a reading room or some space where someone can come in and read
2 those documents. The comments that are received must be considered and given weight
3 in the development of the final rule, which will contain a discussion of the comments. So
4 that if certain comments were taken, then that's explained. If comments were not taken,
5 that also must be explained as to why the agency decided that they should not
6 incorporate those comments into the final document. Then there is a final rule that will
7 be published and it should go into effect at least 30 days after publication, again to
8 ensure that the public isn't blindsided by a rule. So this process is necessary in order to
9 make sure that there is ample time for the public to comment and to give feedback to the
10 agency that's putting a rule into effect.

11 The rule itself may be done in order to interpret, implement, or define
12 either a law that's been passed that tells that agency what they should be doing, or a
13 policy, a major policy change that the agency is going to put into effect. And it defines
14 for the public, in advance, what they are going to do.

15 There are possibilities for an interim final rule that will go into effect even
16 before the comment period, but that only happens in rare instances—ones that probably
17 would not affect NBAC unless there is one that has to do with a public health
18 emergency. And that's probably the only instance that would affect NBAC.

19 The President issued an Executive Order that instructs executive agencies
20 to the extent permitted by law to take regulatory action only if the potential benefits to
21 society for the regulation outweigh the potential costs to society. So there is a general
22 attitude that you don't regulate unnecessarily. And this is also part of the current reg
23 reform—regulatory reform—effort to cut back on regulations, to put them in plain
24 English, to try and make them understandable, to try and make them sensible, and to
25 make sure that we try and cut back on the regulatory burden to the extent possible. So
26 where a rule might affect several different groups, we want to make sure that there's
27 only one rule and not several rules that are trying to accomplish the same feat that would
28 be applied to the same community, thereby having a layered burden.

29 The common rule adds a level of complexity that Joan Porter described, I
30 think, in great, if not excruciating, detail. And I would encourage you to go back and
31 look at that. That didn't start out to be a rule; it started out to be a model policy,
32 implementing the recommendation from the President's Commission and I'll read it one
33 more time because I think it's very useful: "The President should, through appropriate
34 action, require that all federal departments and agencies adopt as a common core the
35 regulations governing research with human subjects issued by the Department of Health
36 and Human Services, as periodically amended or revised, while permitting additions
37 needed by any department or agency that are not inconsistent with these core

1 provisions.” So what that anticipated is that there would be a need for customization, if
2 you will, by individual agencies depending on their statutory authorities or depending on
3 the communities that they service, that would require that they have some form of
4 individualization.

5 OMB didn’t like that because they felt that there had to be uniformity
6 across the government and that that is a central tenet in developing a common rule. And
7 if it can’t be done that way, then it doesn’t...basically can’t be a common rule. And they
8 said there must be no departures. And that added to the complexity of trying to get the
9 language worked out in every single individual section of the common rule. And it took a
10 long time to iron that out.

11 When you tinker with a common rule, then, you have to understand that it
12 can’t be at such a great or fine level of detail that it would cross or conflict with existing
13 policies in each of those agencies. So you’re almost forced to deal with the level of
14 general principles. And that may or may not be satisfactory to accomplishing whatever
15 you’re desired ends are.

16 OMB, the Office of Management and Budget, will be involved in
17 reviewing all proposed rules and negotiating with the agency sponsors. And they are
18 often the convening body in negotiating between agencies who have policies that are
19 dealing with the same subject. And the National Science Foundation and the National
20 Institutes of Health, for example, both wanted to put out policies dealing with scientific
21 misconduct, and OMB had them sit down over and over again to try and make sure that
22 they used exactly the same words. Because both agencies fund the same researchers, and
23 there is great justification in having them use exactly the same policies so you don’t have
24 to have researchers who are funded by both agencies filling out two different sets of
25 forms. So I’ll remind you again that it took ten years to adopt only Subpart A of the old
26 HEW regulations.

27 There are several different options for initiating the process of revisiting
28 the common rule. And the choice of the method should be based on the substance of the
29 desired result. That’s the take-home message. Don’t start with what the rules are and
30 what the process is for changing the rules. Start with what you want to accomplish and
31 work backward and then we’ll figure it out; we’ve got plenty of people, administrative
32 attorneys within the departments or outside, who will help you figure out the best way to
33 get to where you want to go. But that’s really the place to start: what do you want to
34 accomplish?

35 Informally, you could start with dealing directly with the agencies. They
36 have a great deal of latitude within the common rule or within their statutory authorities

1 to change their policies. You may not want to revisit the common rule; it may not be
2 something that's appropriate. You can talk to the Interagency Subcommittee on Human
3 Subjects; that's one way to get started, to get ideas, to think about sort of a reality
4 check, how could you implement a change. But the membership of that group is limited
5 to those agencies that are signatory to the common rule. Also, these people often have a
6 low level of authority. Joan Porter pointed out that while these people may be the ones
7 who are most committed within the agency to seeing these changes take place, they often
8 have a difficult time in bumping it up to the appropriate level to get it done. But there are
9 ways to help with that through, for example, the National Science and Technology
10 Council process.

11 Number two. You have in your charter a forcing clause. We bled over
12 getting that forcing clause in there, which turns out now to be standard language in a lot
13 of charters. But at the time it was very difficult to get it included, and I'll read it to you
14 just so you have it in mind: "Reports by the National Bioethics Advisory Commission on
15 specific issues shall be submitted to the National Science and Technology Council
16 chaired by the President and then to the appropriate committees of Congress," etc., etc.
17 "The Commission may specifically identify the federal department agency or other entity
18 to which particular recommendations are directed, and request a response from the
19 federal department agency or other entity within 180 days of publication of such
20 recommendation." Then you put reports in the *Federal Register* and on the web, and
21 these reports may specifically list the department agency or entity to which any
22 recommendations are directed, and the date by which such responses are expected. This
23 could be very powerful. You may or may not want to use that. Again, it depends on
24 what it is that you're trying to accomplish.

25 A third option is recommending executive action through the President,
26 through an Executive Order or a Presidential Directive, or other ways. Just a statement,
27 but that is available also. An example is the review of classified research, classified
28 human subject research, that was carried per the recommendations of the Advisory
29 Committee on Human Radiation Experiments. The President gave those agencies
30 conducting human subject research a year to do a survey and to report back, and to
31 change the common rule having to do with classified research involving human subjects.
32 So they are told absolutely by the President to get this done. And they're going to get it
33 done.

34 So that's another option, and those are three at least obvious ones in a
35 kind of range of formality. And I'm sure we'll come back to this when you have
36 recommendations and you want to think about the best way to get them implemented.
37 These are just sort of an introduction. I don't think you need to focus on the mechanics
38 of the process at all, but just think about what you want to get done and we'll figure out

1 with help the best way to get it accomplished.

2 DR. SHAPIRO: Thank you very much. This really is a very helpful
3 outline of some of the possibilities, excuse me, for us. Are there any questions for
4 Rachel?

5 DR. COX: What happens then to the process?

6 MS. LEVINSON: The law is the starting point from which the agencies
7 then develop the rules that implement the law. The law doesn't have, or rarely has, any
8 specifics that tell you how to do it. The agencies then have to work and develop a rule
9 through this process.

10 DR. COX: Exactly. But if a law exists it means people have to do it,
11 right?

12 MS. LEVINSON: Yes.

13 DR. COX: Thank you.

14 DR. SHAPIRO: Any other questions? Okay, thank you very much. Let's
15 go on to our next topic, which is Federal Oversight and Research Involving Human
16 Subjects. Alta?

17 MS. CHARO: In many ways, this is kind of a holding pattern right now
18 as we await further information from the Gonzales contract, from the McKay study,
19 from the OIG study, etc. But it's a good opportunity to tie what Rachel was just saying
20 and what's been going on in the decisionally-impaired people to something which I hope
21 you had a chance to read, as well as to listen to, a couple of months ago. And that is the
22 way in which the structures that are used for the protection of human subjects in the
23 United States affect what seem to be two intersecting goals that have been identified by
24 this Commission. One of those goals is to ensure the appropriate protection of those who
25 are currently covered by existing regulations and that is the purpose of the federal agency
26 survey: looking at the effectiveness of the federal agencies at accomplishing just the tasks
27 that they have taken on themselves up until now. And the second goal, which was
28 expressed in the resolution that was passed last year, is the expansion of some minimum
29 core protections to all people—regardless of the source of funding that is behind the
30 research in which they are being enrolled. Now these two things are not the same. The
31 expansion of protections to something that is universal throughout the United States
32 might be the expansion of some minimum level of protection in which what you got as a
33 guarantee might depend upon the source of funding. Just as the common rule now

1 commits a variety of agencies to a core level of protection at the level of things like
2 informed consent, but does not commit all agencies to certain special kinds of
3 protections aimed at specific populations that are identified as being particularly
4 vulnerable to exploitation. One can imagine a system in which you have universal
5 protection to the extent of informed consent, but that particular kinds of implementation
6 strategies, through IRBs for example, or special protections such as the ones we're
7 considering for people with decisional impairments wouldn't necessarily apply unless the
8 funding source was from a particular place like a particular agency.

9 Now the recommendations that we got from Fletcher and McCarthy and
10 that have been analyzed for us by Rob Tanner and the rest of the staff, along with the
11 Glenn bill, focus on some of the problems that we can identify ahead of time in trying to
12 translate these goals however we decide upon them into some kind of action. And just by
13 way of a quick reminder for you, Fletcher and McCarthy in their presentations identified
14 certain kinds of structural issues that will dog us. One is the location of the office that's
15 in charge of protection of human subjects. The suspicion has been that absent an office,
16 that is, sufficiently high up in the government with some degree of authority over
17 agencies and departments, it's going to be very difficult on a regular basis to ever have
18 steady improvement in a quality protection of human subjects. Concrete example: When
19 we get to the discussion of Marino's paper and the recommendations, there are going to
20 be recommendations for change that if we wanted to incorporate into regulation, would
21 first require that there be some degree of departmental enthusiasm and sponsorship at
22 HHS, which in turn requires that the heads of many, many different agencies that could
23 be affected by these regulatory changes were equally enthusiastic about the Secretary
24 pushing for such a change. We can anticipate at the pragmatic level but this would be
25 difficult to accomplish.

26 Second, even if the Secretary of HHS were interested in this kind of
27 improvement and had either overruled or persuaded or been supported by her various
28 agency heads, she would not have had the authority under any kind of current structure
29 to impose this kind of view upon other departments that might have the same issue, but
30 instead were left with persuasion. So one of the key questions had been location. An
31 independent kind of agency that sits outside any particular department in theory has that
32 kind of jurisdictional power over all departments but suffers from being all by itself out
33 there—not necessarily with strong congressional sponsors—without a large portfolio
34 that gives it leverage with various congressional oversight committees on appropriations
35 committees—and so, therefore, may be rather vulnerable.

36 It would be easier, structurally, to try and move human subjects'
37 protection at least higher up in HHS so that one could get around some of the difficulty
38 of the negotiations among agency heads in order to get a common message going up to the

1 Secretary, and begin to work right within the Office of the Secretary on a common
2 policy within HHS. But of course that does leave us with the problem of HHS not
3 having any authority over the departments.

4 In addition, there is the question of accountability and enforcement, and
5 again you've been given a review of the different ways that Fletcher and McCarthy
6 proposed this might be handled and how the Glenn bill would handle it. There is an
7 opportunity here for us to keep in mind, I'm not sure when the discussion would actually
8 take place, the kind of intersection between accountability and enforcement and the
9 current ways in which OPRR operates. For example, by way of reminder, OPRR now
10 has an extremely voluminous kind of assurance document that it tends to negotiate with
11 individual institutions, which goes into excruciating detail about how it is that they plan
12 to regularly review and protect human subjects. And for institutions that don't regularly
13 do this kind of work, it's quite typical that they're not going to have this complicated,
14 negotiated, multiple project assurance but instead they'll have single project assurances;
15 and occasionally OPRR itself is in the business actually of reviewing protocols,
16 something for which it doesn't actually have a lot of personnel.

17 The expansion of human subjects protection into non-federally-funded,
18 non-multiple project assurance institutions, non-FDA investigational drug and device
19 settings means that the question of administerability of any of these kinds of mechanisms
20 for accountability and enforcement is crucial. And whether one wants to continue with
21 the current assurance mechanisms or move to something more like the registration type
22 of mechanisms that were being proposed with more streamlined kinds of guarantees and
23 even some consideration about the acceptability of either regional governmental level or
24 privatized IRBs offering up some opportunity for review for people at institutions that
25 rarely do research are all part and parcel of this collection of items. Again, if you think
26 about the kinds of recommendations that might emerge from the Marino paper in which
27 there is the possibility of asking for competency assessments, consent monitors,
28 standardization of the people who are presumed to be capable of acting as surrogates for
29 those who are incapable of speaking for themselves temporarily, one has to keep in mind
30 the workability of those recommendations against the backdrop of who exactly is going
31 to be in charge of implementing these things, who's in charge in Washington of making
32 sure that these implementation plans are adequate and are followed through, and who's
33 in charge of cracking down if these things are not done properly according to new rules.

34 And so if this looked complicated before, it's even more complicated
35 now. I hope that I've made it worse for you. Eric, I'm going to leave to you the
36 description of what you're hoping to get out of the discussion because I know that with
37 very little time allocated today, the goal was not for everybody to decide here and now
38 which set of structures they want to vote on.

1 DR. MESLIN: think that's a fair summary. First, I want to just echo your
2 gratitude to Rob Tanner, who is sitting at the back, who put in an awful lot of work on
3 this analysis. This was requested by the Commission at its previous meeting, and we
4 were able, with both Rob and Melissa Goldstein's excellent help, to put together this
5 side-by-side for you. It really is meant to be a permanent part of the Commission's
6 record of deliberations so that we do not need to continue reminding ourselves of what's
7 gone on before.

8 There are two points that I think are worth reminding the group. The first
9 is that it's entirely appropriate, as Alta as indicated, that if the Commission decides that a
10 somewhat more comprehensive report that encompasses the federal agencies survey,
11 encompasses IRBs, and encompasses the appropriate administrative structure for federal
12 oversight is the way that you want to go, then this is a first step to understanding what
13 the basic facts are for any recommendations that you wish to carry forward.

14 The second point is that we still have an awful lot of information that can
15 be brought in. We are anxiously awaiting, we believe it will be within the next ten days,
16 the commissioned paper by C.K. Gonzales which is, if you will, the third leg of the three
17 legs that we've commissioned that will provide background on aspects of privately
18 funded research. It was staff's suggestion in the accompanying memo that you might also
19 want to consider commissioning a paper from an administrative law person or someone
20 who has the kind of skills that Rachel was referring to in her description of the nuts and
21 bolts and the details, because this is, as I think the Commission has agreed to describe it
22 at its previous meeting, not a discussion simply about the location of the current Office
23 for Protection from Research Risks, but consistent with the Commission's mandate, a far
24 more unique opportunity to talk about what is the appropriate structure, not just for now
25 but for 15 to 20 years from now. So the reason for raising it is to keep it on the agenda.
26 It will become a regular theme at future meetings, and we want the Commission to ask
27 staff for further input and to recommend to us what else you would like to know in order
28 to keep this item relevant and current for you.

29 DR. SHAPIRO: David?

30 DR. COX: There's something I'd be really interested in knowing. In the
31 history of the Congress of the United States, has there ever been a situation where the
32 Congress felt strongly enough about an issue that they protected a free-standing agency
33 with the kind of ability to go and look across different agencies, as we might be
34 suggesting here?

35 MS. LEVINSON: One example they gave would be Office of
36 Government Ethics, and that gives you the flavor of how it can be kind of faddish. They

1 can be interested in something for a while and then it can go away. And that's the
2 problem with their free-standing office that I think both of the presenters intimated
3 before, and one reason why having it within another existing structure is beneficial to a
4 certain extent.

5 DR. COX: But there has ... but thanks, because I asked for one example
6 and you gave it. But I mean that's that kind of situation, right, where...

7 MS. LEVINSON: I can give you one more.

8 MR. CAPRON: I don't think it's possible to answer that question in a
9 way that's really useful for us in the abstract, and I think Alta hinted at one point. There
10 are certainly a lot of, and have been more in the past—several of them have been closed
11 down—free-standing governmental agencies that at various time have stepped on
12 important people's toes and have been under threat. When they are protected, it's often,
13 as Alta suggested, because they have enough breadth in their work that there are
14 congressmen who have ongoing interest in their survival for sometimes parochial
15 reasons. An agency that mostly exists to protect human subjects might find one or more
16 knights-in-shining-armor who share that concern. It might also find that to the extent
17 that it is interfering with the headlong rush of scientific research at a major research
18 institution in somebody's state that that senator or representative hears volubly about
19 what a nuisance it is to comply with regulations. I frankly am not at all convinced,
20 however, that having it in a department provides that much additional insulation, for the
21 simple reason that the people who often have broader interests are also themselves
22 vulnerable to those broader interests of their department, not being dragged down by
23 what they, themselves, may regard as a peripheral enterprise. And ironically, I would be
24 most comfortable thinking of this agency, if it were to be lodged in the department, being
25 put in the Treasury or some other place that doesn't conduct research. The whole
26 problem here is that, I mean there are two problems that we're trying to address. One is
27 the ability of the present structure to actually operate well on a government-wide basis.
28 And the other is that the lead agency is at two or three levels down from the top of the
29 department which sponsors most of the research and the sense that it is, itself, not able to
30 operate independently might be increased, might be helped, by putting it at the right hand
31 of the head of the department instead of under the table of the person conducting or
32 sponsoring most of the research, perhaps. But it might not. I mean it's not at all clear to
33 me that we solve the central problem of conflicts of priority. I don't even say conflicts of
34 interests, just conflicts of priorities, what comes first. And it is not to be critical of the
35 department that is sponsoring the research, it is just that as we found with the Atomic
36 Energy Commission, it had a dual agenda and I think we see a dual agenda here.

37 I would like to get a better sense than I now have because we had a

1 discussion of this with Drs. Fletcher and McCarthy when they first reported. We had a
2 discussion of this at the last meeting when I was asked to review it. We've had a
3 discussion that's begun by Alta now which she's reviewed. We have the charts. My sense
4 is that this is an integral part of our report on the federal agency response. Because while
5 we are not finished with that, and I am very desirous of having more input and feedback
6 from the federal agencies on their sense of how well; we have represented what they've
7 done well and haven't done well; I think there will be no question that there are certain
8 deficiencies that exist. Not the least of which is the absence of any database on how
9 much research and how many subjects there are in the federally-sponsored side, to say
10 nothing of the private site.

11 Knowing that, certainly one response to that set of problems will be the
12 response of saying we really need to change the structure. And so it seems to me that it's
13 logical that it should be an integral part of that report. And I just want to have some
14 sense from the staff side or from my fellow Commissioners that these two things are
15 proceeding so that they are likely to get done at the same time, that the part that Bill
16 Freedman has been working on the federal agencies and so forth—we've seen drafts of
17 that and that's moving along and we know where that is. This is still at a more
18 conceptual level. I mean we see what the problems are. At what point are we going to go
19 down this list and say these are the suggestions about locations, these are the suggestions
20 about function, these are the suggestions about design and so forth. We're not adopting
21 the McCarthy model or the Fletcher model or the Glenn model. We're making
22 recommendations and to the extent we say this is similar to or this one draws from, fine.
23 But we're going to have to have our own answers to that. When are we going to do
24 that? That's what I'm not clear about. Are we going to do some of that today? Are we
25 going to set aside hours to do it at a future meeting? Because I think we have to do that
26 for the staff to know what they should start writing about this. We have to give them
27 directions as to ... in the end we have a certain amount of evidence and a certain amount
28 of argumentation from different groups. What we need is our own version of those, of
29 that evidence and argumentation, that will lead to the kinds of conclusions which we
30 think are appropriate. We need to reach the conclusions and then fill in the evidence in
31 terms of writing it out. And that's going to take time.

32 One final point. I do agree with the staff's suggestion that it might be
33 useful to have someone with administrative law background look at and think about any
34 peculiar problems that would arise in one place or another in terms of the ability to
35 promulgate and enforce regulations from different postures. I think that could be helpful.

36 DR. CASSELL: What you're saying is that we have to come down and
37 make a decision on what we believe this, what this form is, what it's meant to do, and
38 where we believe it ought to be.

1 MR. CAPRON: Yes, exactly. Thank you for a briefer statement.

2 DR. SHAPIRO: I think that's right, and our current intention is in fact to
3 have those come out in the same report together, both the issues regarding OPRR,
4 however you want to discuss the slide. That issue and the project we've been involved in
5 for a long time now which Bill Deeman's been working on. And also likely, although I'm
6 not so sure, that the issue ...what we have to say for the IRBs in general might also be
7 part of such a report because that would give us a kind of look at the structure of this
8 whole thing. We'll have to see how it goes along. And I think in terms of the actual
9 discussion of when do we actually say we want it in Treasury or HHS or do we want it
10 in an independent agency or whatever else we're going to decide, I think that's going to
11 come up sometime in the next two meetings as we get a chance to put the material
12 together for staff.

13 DR. MESLIN: Just a quick update for Professor Capron where some of
14 these reports are, we expect the federal agency survey data to be completed by the end
15 of March and written up at that point and be available. That would mean it would not be
16 available at the March meeting, which is at the beginning of the month, but it would be at
17 the May meeting. And that could be very advantageous. If the two reports that are
18 currently under discussion and close to prime time are presented, and I'm just saying this
19 hypothetically, presented for the Commission's sign-off in its draft interim mode at the
20 next meeting, then my sense is that you all would recognize what the major issues were
21 that came out of those two reports that would inform the analysis of the Freeman data
22 and would further inform any analysis of the federal oversight issue. If all goes according
23 to what might be optimistically described as a unique plan, there could be a
24 comprehensive report that deals with all three of these by the summer, a working draft of
25 a report by the summer.

26 MR. CAPRON: I followed everything up to the last sentence or two.

27 DR. MESLIN: Not including the IRBs. I'm not even mentioning that.

28 MR. CAPRON: Well, that goes to an earlier point. Alta mentioned in
29 passing something with which I agree, indeed we discussed it a little last time, which is
30 that the ... we don't have to think of this as a report on OPRR. I mean we really ought to
31 think of it as a report on a means of protection, and OPRR and its equivalents are very
32 likely to be necessary in any sense in the departments as their local administrator of these
33 issues. Then the question comes up about the IRB, and as you may recall, at the last
34 meeting I tried to argue that the issues about adequacies and inadequacies of IRBs are
35 actually relevant in indicating that there's a problem there that needs to be addressed.
36 What not to hold up and ought not to be directly handled in a report dealing with the

1 location of the office, because whether it's OPRR and its equivalent agencies or a new
2 office or some combination, those IRB issues are going to have to be addressed. And so
3 it doesn't...the one doesn't turn on the other.

4 I also do not see any value, in fact I see ... if we're talking about the same
5 three reports—the tissue report, the impaired subjects report, and the federal agency
6 report—I don't see any value in putting the three of them together.

7 DR. MESLIN: No, no, no.

8 MR. CAPRON: So I misunderstood what you were saying.

9 DR. MESLIN: Yes, you misunderstood.

10 MR. CAPRON: Well, what were you saying then about linking the three
11 of these in a report?

12 DR. MESLIN: I'm sorry you misunderstood. By having them completed,
13 those reports would be on the table and serve as excellent case studies for the
14 Commission's deliberations about the broader issues of human subject protection. We
15 wanted to wait for the Freeman data to be complete before we said anything about the
16 location of OPRR. I didn't mean to lead you to believe that those would be linked.
17 Those are reports, stand-alone reports, issued on their own and deliberated about on
18 their own.

19 MR. CAPRON: Okay, I see.

20 DR. MESLIN: I'm sorry you misunderstood.

21 DR. SHAPIRO: Arturo?

22 DR. BRITO: I just had a brief question for Alta to see what her thoughts
23 were and Alex touched on a little bit about possible conflict of interest or conflict of
24 priorities. With placing this or having the location in the HHS, what do you think...is
25 there any way to actually avoid that and is there another location that you've thought
26 about that's still doesn't make it an independent agency?

27 MS. CHARO: Yes. This has come up before in some ways by way of
28 review. Alex has made the comparison to the old Atomic Energy Commission that was
29 simultaneously charged with the promotion of research and deployment of nuclear
30 technologies, and at the same time regulation of them for the purpose of insuring safety.

1 And over time that proved to be unwieldy and eventually we had a separation of function
2 into DOE and NRC. Similarly, the INS has been coming under very similar kinds of
3 scrutiny right now in its role of being both the kind of intake and outtake agency with
4 regard to foreign nationals. There is no way to completely overcome this kind of
5 problem. If you locate an office, for example, at the level of the Secretary of HHS there
6 will be a variety of agencies that are trying to promote research for whom many of the
7 regulations, although recognized as valuable and essential to ethical research,
8 nonetheless create paperwork barriers to quickly accomplishing some of their goals and
9 this will bring pressure on the Secretary to balance those agencies' goals for promotion
10 of research against the commitment to a kind of uniform enforcement. And we've seen
11 some of the debates on this topic about research needs and human subjects protection in
12 very recent days, such as the question about emergency settings. And both wanting very
13 much to promote new ways to treat injuries like brain traumas at accident sites, and at
14 the same time to protect people against having been made into experimental subjects in
15 inappropriate ways.

16 Alex's suggestion of putting something at Treasury reminds me of a
17 conversation I had actually with Gary Ellis, because one of my first instincts was we put
18 it in Justice Department because it really is a matter of civil rights, that people not be
19 exploited. And then the hint of possible problems with Justice's own research agendas
20 made it seem that that was not necessarily going to be the perfect solution, although at
21 first blush it seemed like a great solution. I've also suggested in conversation—I suspect
22 other people have as well, half facetiously and half seriously—looking at OMB because
23 OMB already has its fingers all over the place. It's too entrenched to be killed by
24 Congress. Everybody's scared of it. And so if you put enforcement research ethics and
25 got their commitment to this, it could be a devilishly strong place. On the other hand, I
26 don't think there's anybody in government that trusts those people. I mean government
27 people feel about OMB the way citizens feel about the IRS. I mean they're a necessary
28 evil in our life. Rachel says no, but when I worked in government I never knew anybody
29 that liked OMB. So we just have differing views on a cranky, terrible problem. Finally,
30 there is a genuine question about jurisdiction here because to the extent that one wants
31 to extend—this is how I'm starting, by the way—by saying do you want to extend
32 human subject protections to everybody or do you want to strengthen for those who are
33 currently protected? And you want to extend human subject protection to encompass
34 those people in currently uncovered settings; for example, privately sponsored research
35 that doesn't involve investigational drugs and devices. People at state psychiatric
36 hospitals would be another example of an uncovered institution. You've got to question
37 about the authority of any particular part of the federal government to exercise that kind
38 of jurisdiction, right? If there's no federal money flowing so that it's a condition of
39 spending, if it is not pursuant to the FDA's own authorizing statute which sets out rules
40 for investigational drugs, and if it's not because it's part of the federal agency's own

1 activity, the question is on what basis are you regulating. But that becomes a kind of
2 uncomfortable fit for an office that's located entirely within a single department whose
3 mission is spelled out in its own enabling statutes and may not extend to gross levels of
4 regulation of the private sector. So if your goal is to extend protection to all the people
5 in the U.S., you do have the beginnings of some arguments in favor of a stand-alone
6 agency whose enabling statutes really get to that kind of thing but leaves you with all the
7 problems that have been identified already about political support for that agency over
8 the long run.

9 DR. BRITO: The conflict of interest of the apparent—or what would
10 appear sometimes to be a conflict of interest—with a lot of the agencies in Washington,
11 since it is the same group of people or it appears to be the same group of people within
12 and out.... So is there a place for, if we decide to recommend an independent agency as
13 opposed to having it as part of HHS, is there a place to have a place outside of
14 Washington and still be national? Is that too far-fetched to...?

15 MS. CHARO: Well you could put them at the missile sites that aren't
16 being used anymore out West, but I don't know that geography is really going to be the
17 key here. I think the key in the pressure to make ... in some ways it always comes down
18 to the funding issue because you've got agency directors that want to fund certain kinds
19 of research. And if they're running into problems in getting their grants-making
20 operations under way.

21 DR. SHAPIRO: It seems to me that as we begin to think seriously about
22 this, our discussion here tends to focus on the location issue. It's the easiest one to
23 describe and problems with the existing location are pretty obvious. And then there are
24 these other complications all of you have heard. And it seems to me that that may not be
25 independent of the other, one of the other characteristics, that is the jurisdiction issue.
26 Which I think is a burden of your comment, Alta, if I understood it correctly, that these
27 things in fact may be related to each other. We ask ourselves, just a thought experiment,
28 supposing we want to put aside for the moment extending the protection beyond the
29 federal government tether. What decisions would we make? What would seem to us to
30 be the most logical issue or the preferred way to deal with location and the other issues
31 that are coming up? That might actually be a useful exercise.

32 MS. CHARO: One of the things that would be helpful in the clarification
33 of goals, because I completely agree with Rachel, you start with what you want to come
34 out with, and figure out if it is not going to be, for example, immediately extension of
35 human subject protection, even within the federal government, is it an extension of the
36 common rule to all federal agencies which doesn't yet exist, I mean? Is it to get the
37 entire federal government to sign on, even though a lot of places don't do a lot of

1 research just for the sake of consistency. Or is it to deepen the quality of the protections
2 for the agency who are already members...adhering to the common rule or is to extend
3 the subparts for those people who have only got Subpart A. It would be a good starting
4 point to figuring out what level of office would be most appropriate, how many sign-offs
5 you'd need, how many people would likely not sign off.

6 DR. SHAPIRO: You know I think it's important that we have this
7 discussion before we start honing in on exactly where its location ought to be.

8 DR. CAPRON: If you think that the impediment to extending federal
9 jurisdiction over privately-sponsored research are substantial, and independent of the
10 question of the objections of particularly departments to having to be accountable to
11 either another department or a new federal agency, you might still say if the evidence is
12 eventually there, that you have a well-operating federal system that has avoided problems
13 and the research, that kind of research is better than it once was because of this agency,
14 and some indication that privately-sponsored research continues to have problems, at
15 that point what would it be like to extend? And you could design in, you might adopt a
16 method not because you intend to recommend today or believe that today you have
17 enough evidence to say we have a crying national need to regulate privately-sponsored
18 or state-sponsored research. But to say we're not going to make two changes inside of a
19 decade; you're not going to move it to the Office of the Secretary of X, and five or ten
20 years later set up a separate agency barring the most incredible crisis of the world, you
21 might say we're going to design it in a way that would allow the addition of another
22 function at a future date when the evidence is strong enough to justify that.

23 DR. SHAPIRO: That's my own advice is to learn how we might
24 approach it in a useful way. I think it makes the subject less complicated and I'd like to
25 solve an easier problem first. It's as simple as that. And if that's very easy to solve, we
26 can then ask ourselves the question whether at this time we are prepared to go for more.
27 Do we feel we know enough and have enough good ideas?

28 MS. CHARO: No. I would like not to see us back away from that but
29 there is the question of how one gets there. You can suggest that it ought to be
30 recognized that everybody should be protected, but leave to state common law, state
31 legislation, individual institutions the way in which to do it, or you can also...or you
32 could say we're now in a position to start recommending federal legislation that will
33 reach these people. They are separate questions.

34 MR. CAPRON: And we could also say that we recommend that we
35 recognize that additional evidence may be needed. Part of it, if Congress were to do this,
36 it would be based on findings. I mean part of the reason...this would certainly be

1 challenged. If someone were doing totally privately-sponsored research at an institution
2 that doesn't even get any other funds, you don't have the argument that came up around
3 funding of colleges where they were getting money for one activity and the question was
4 could you then control their discrimination on the basis of religion or sex, when funds
5 weren't used for that fashion. And the basic answer of the court was couldn't, actually.
6 But it would require finding that we have bad abuses and a reason for saying that having
7 federal jurisdiction would prevent those abuses from occurring. My own sense would be,
8 if we were...if we were called to testify before Congress right now, we don't have full
9 evidence. We have anecdotal evidence, we have certain examples of the problems. But
10 we also do not have the ability to say that there is in place a federal mechanism which,
11 when faced with comparable problems in federal research, solves them and avoids them
12 occurring. And so it's harder to make out either side of the argument, the need or the
13 solution. It might, therefore, make sense for us to say we are in principle, we believe as a
14 matter of protection of every person in the United States, that it shouldn't matter in that
15 protection whether the research is sponsored by a private entity or the federal
16 government. You should at least have informed consent and prior IRB review. We could
17 say that, and we have said that already. But we might say that while we recommend that
18 the agency be capable of taking that step, that we believe further evidence needs to be
19 gathered on both of the two points that I just described in order to have the kind of
20 legislation that would stand up to challenges that might be mounted against it. And I
21 would just as soon see us address it in those terms. Now if between now and time we
22 write the report that evidence is strong enough, maybe the fact that we don't have in
23 place the perfect federal mechanism yet becomes a reason for thinking, well, the
24 mechanism that we're recommending we believe would solve the identified problems and
25 would be a mechanism capable of supervising private research in a way that actually does
26 avoid the kinds of problems that we're now enumerating in our report, that are sufficient
27 to justify either legislative findings or the act of Congress. When it is up for passage
28 people in the private sector coming forward and saying we don't believe there are
29 grounds for you to assert your jurisdiction. There aren't the kinds of problems that
30 would justify federal intervention. And then post-passage, also, if it were passed,
31 someone coming in and saying this legislation exceeds federal authority. There's not a
32 sufficient nexus of federal concern. Now, under civil rights legislation there was, and I
33 don't follow this well enough, maybe Alta does know, at one time the notion that a
34 bottle of ketchup was being delivered to a motel in Atlanta was enough for the federal
35 government to say you cannot discriminate against someone sitting at that lunch counter
36 or checking into that motel. You know, that was enough. It was some interstate traffic
37 and it's hard to believe that anybody conducts research without getting pipettes and
38 reagents and books and so forth in interstate commerce. So if it's that kind of a
39 challenge, but frankly that kind of a challenge is obviously harder to mount if you also
40 say "and there's a screaming need for this." When left to their own devices, the states
41 have not regulated this adequately and private parties are exposing research subjects to

1 unjustifiable risks. I mean the court is not unmoved by such arguments. It was obviously
2 the fact of racial discrimination at an absolute level that led to the upholding of those
3 civil rights statutes—not just a bottle of ketchup going through interstate commerce.
4 And so I wouldn't want to see a statute recommended when we could not ourselves say
5 to a committee of Congress here is the bill of particulars that would support your
6 legislation. I think we need to have that, as well as some assurance that we're
7 recommending a mechanism that will work.

8 DR. SHAPIRO: Alta?

9 MS. CHARO: I'd like to bring this back a little bit closer to something
10 concrete for this group of people. As we go through the recommendations from the draft
11 report on people with decisional impairments we have a opportunity to make
12 recommendations about regulatory changes. Now, I think the value of that exercise for
13 this discussion is going to be in having people realize how futile most of our work is
14 going to be because of the extremely remote possibility that any regulatory changes that
15 you might want could actually be implemented because of the current placement that
16 those regulatory changes would be proposed and the number of sign-offs, coupled with
17 the enormous number of people who wouldn't be affected by those regulator changes
18 because they exist in uncovered institutions like state mental hospitals and are not being
19 treated with experimental drugs. They're being treated...they're in research protocols
20 that involve previously uninvestigated uses of already approved drugs, very
21 commonplace in this field. Or the withdrawal of approved drugs. I think it's important
22 for us to keep that in mind, not because it's an exercise in getting depressed, I mean, we
23 can do that on a regular basis anyway. It's because I think that will help to concretize
24 exactly what people want to focus on. Unlike Alex, I've tussled with him across the table
25 a number of times and the issue would be evidence of abuse because there would be no
26 way to cumulate that evidence absent a regulatory mechanism that forces an accounting.
27 And if you're going to require the evidence in order to create the regulatory mechanism
28 to get the accounting to create the evidence, we have an impossible paradox here. But I
29 do agree with him completely that any effort to go beyond a simple resolution that there
30 ought to be universal, at least minimal, protections is going to be impossible to
31 implement until we have some experience with a workable system in an area where it's
32 easier to implement than that is where we've already got jurisdiction, like the federally-
33 sponsored research. On that score, I agree with him completely.

34 Until we solve the problem of how you get everybody to do what they're
35 supposed to do already if they're already under an obligation to do it, which is the IRB
36 report about the ability of a decentralized local IRB-based system that's governed by
37 multiple assurances and minimal oversight in education from OPRR, until you tackle that
38 and tackle the question of uniformity of regulation among federal agencies and change

1 regulation at the federal level, you don't have any kind of system to build on as you try
2 to expand that into the private sector. It is worth, though, keeping in mind as we talk
3 about these location issues the possibility that you might want to eventually extend it so
4 that whatever you're recommending in terms of structures within the federal government
5 be done either with the eye toward having a new and different structure someday when
6 you're ready to tackle the private sector, or the creation of a structure today for the
7 federal government that's flexible enough to handle the private sector. Again, the
8 jurisdiction under the commerce clause I don't think is really all that problematically
9 investigated for the cloning report, but the enabling statutes of individual departments
10 are problematic because they don't really have the reach of some of these and need some
11 attention. So it's that kind of staging that's really kind of part of the discussion here, is
12 the order of events.

13 DR. SHAPIRO: I think the issue of staging is a critical strategic issue in
14 all of these concerns, and I think that we're more easily going to be able to develop
15 useful ideas if we allow ourselves that freedom of saying, you know, approach this
16 problem instead of stage it. And we can learn as we go. We don't have to know it all
17 right now, we can learn as we go. At least speaking for myself, I find that extremely
18 helpful. It came up in the cloning issue when we were trying to decide whether we
19 wanted to recommend legislation right away or we wanted to try something else first and
20 then go to legislation. Well we decided a certain way there, but even going through the
21 discussion of staging as opposed to just trying to get to the final institutions, I think, can
22 be very helpful and it can develop interesting and helpful strategies on which we can
23 agree a good deal faster. That's my own sense of it.

24 MR. HOLTZMAN: ...think about an alternative view which has issues
25 like this; sometimes bigger things are easier to accomplish than little things.

26 DR. SHAPIRO: We'll remember that, too. As they say, you, too, have a
27 point. Okay, let's go on to the final agenda topic we have for this afternoon, which is the
28 material in Tab F of your book. It was an analysis of the various statements that have
29 been made on the tissue samples issue. The staff has produced a comparison of this in a
30 tabular form. Let me first turn to Eric to see what he'd like to say, and then I'd like to
31 turn to Tom and see what his reaction is.

32 DR. MESLIN: Thanks very much. In the voluminous Tab F, there are 11
33 items, three of which really relate to this afternoon's discussion. The first is a memo to
34 me from one of our staff, Shawn Simon, who did a very thorough job of providing what
35 was intended to be at the request of the Commission from last meeting a mirror put up to
36 your face which allowed you to reflect on both where other professional associations...

1 DR. CASSELL: ...put up to your face to see if you're still breathing.

2 DR. MESLIN: I'm trying to figure out what, if you hold the mirror up to
3 my face what's on the other side of that mirror. It's that block problem ... two-sided
4 mirror. It's hard to come back after that. Following the memo is the side-by-side which
5 both shows a number of organizational perspectives and NBAC's positioning based on
6 where we think you think you are. The purpose of presenting that to you is to confirm
7 that that's where you might be and to alert you to both some consistencies and some
8 inconsistencies in the way that your views have been expressed so far.

9 A second item, or third item if you count those as two, follows about four
10 items later and it is a memo to me from Melissa Goldstein. And Melissa has provided a
11 very helpful summary, again based on your request, where the current federal regulations
12 sit with respect to some of the proposals that you are currently debating. And that's a
13 five-part analysis. I don't think I need to say much more than that since it was merely a
14 way to get us started in the discussion today which will obviously continue tomorrow,
15 and maybe Tom Murray would like to either add some comments or lead the discussion
16 a bit more fully.

17 DR. SHAPIRO: Well I think it is very hard to look at this topic without
18 taking on the real issues that lie behind this, and whether we like the various categories
19 that have been proposed and whether it's identifiable or not identifiable, all those various
20 issues. So perhaps, and I don't want to do that today because we don't have enough
21 time to give some thoughtful consideration of that, but maybe we could begin by asking
22 whether there are any questions and information from members of the Commission. Is it
23 clear what's here, do you understand, do you don't understand it? Steve?

24 MR. HOLTZMAN: It may or may not be substantive. I wanted some
25 clarification about Melissa's memo because I'm not sure I understood it or how it was
26 consistent with Shawn's memo. And even trying to understand the conclusions that she
27 says are the letter of the language, cohere with what she then says under B. Is
28 anyone...did anyone else feel a tension?

29 DR. MESLIN: Part A and B?

30 MR. HOLTZMAN: Part A and B. I mean A seems...says basically draws
31 a conclusion on what the statute says. Then B offers interim to alternative interpretation
32 of what the statute says. Is that fair, Eric?

33 DR. MESLIN: Yes. Just to put this into context, the genesis for the
34 memo was two-fold. One, there was a considerable amount of discussion at previous

1 meetings about whether or not the proposed framework that Dr. Emanuel had been
2 sharing with us did or did not fully include or was covered by the current regs. And at a
3 previous meeting, I believe Zeke stood up and indicated certain numbers of his boxes
4 were or were not covered by the regs. And Gary Ellis, who was present at the time, was
5 concerned about whether that interpretation was correct. So in order to provide a bit of
6 clarity, it was suggested to us by some of the Commissioners that an attempt to put that
7 issue into some context would be of use. Melissa then produced a document which
8 identified five items, which had been proposed in the boxes, existing versus proposed
9 items of identifiable tissues, and you can see the rest of the memo. And it was her effort
10 to provide an interpretation of the regs with respect to those five items that is before
11 you.

12 MR. HOLTZMAN: Right. So under subsection A she draws and
13 interpretation about what is meant by identified, let's put it that way. And then under B,
14 which is the same issue, she offers an alternative interpretation.

15 MS. CHARO: I think when I read it, I got to tell you, I felt like she was a
16 very well-trained, Yale-trained lawyer who was struggling to find any possible way to
17 make what had been the current discussion at NBAC consistent with existing regs. And
18 she came up with the best possible, stretched, taffy-thin interpretation that I personally
19 would never want to rely upon as the basis for our recommendations because I think the
20 struggle she goes through just shows what we'd have to go through if we were going to
21 do this.

22 MR. HOLTZMAN: To me this is all very simple actually. In terms of
23 what's really at stake here is this sentence that if the information is recorded by the
24 investigation in such a manner the subjects could not be identified directly or through
25 identifiers linked to the subject. You either take that to mean that the "cannot" is a
26 statement of logical possibility and therefore it's anonymous or it's not. And if it's not
27 anonymous, then it fails. Or, we put the emphasis on with respect to the investigator's
28 epistemic state

29 MS. CHARO: And the facts break. The fact is it does not say that it's
30 okay to use, da-da-da-da-da. If the investigator can't identify the source of the tissue, it's
31 that it's the source of the tissue cannot be identified by anybody.

32 MR. HOLTZMAN: I'm sorry.

33 MS. CHARO: That's the bottom line.

34 MR. HOLTZMAN: You're saying that's what it says.

1 MS. CHARO: That's right. If there are links, if there are links that exist...

2 MR. HOLTZMAN: Okay, no, actually, the ...

3 MS. CHARO: Then the person can be identified.

4 MR. HOLTZMAN: ... the question is which of those two things it says.

5 MS. CHARO: Right. What I'm suggesting is that as a fellow lawyer,
6 when I read her memo and she attempted to somehow interpret these words so that they
7 only apply from the subjective point of view from the investigator, I was impressed by
8 the extreme creativity and the need to have gone to a school as good as Yale to come up
9 with an argument that was even tolerable for that interpretation. I was ... I was quite
10 persuaded by how hard it was for her to do this.

11 MR. HOLTZMAN: So in other words...

12 MS. CHARO: That we shouldn't try to do this ourselves.

13 MR. HOLTZMAN: ... but you found that what she did in section A was
14 just the plain language interpretation of this, whereas in B she was doing a stretch.

15 MS. CHARO: Correct.

16 MR. HOLTZMAN: Okay.

17 MR. CAPRON: That was my interpretation. I would like for the record
18 to say that I believe a Columbia-trained lawyer would be able...

19 DR. SHAPIRO: To do even better, right?

20 MR. CAPRON: ... besides agreeing with Alta's sense when I read this, I
21 want to suggest something about NBAC's posture here. I would find it ironic for us to
22 be working on the one hand on reports that aim to ensure protection of human subjects,
23 and on the other to reach a conclusion which says that either a existing protection ought
24 to be removed or ought to be read in this strange fashion. It seems to me it puts the
25 omission in an extraordinarily uncomfortable posture if in one of our earlier
26 reports—given the fact the cloning report is already out there, probably our second
27 report—we say well although past Commissions have said this and that and that has led
28 the federal government to adopt a common rule which says this, that ought to be out the
29 window when it comes to tissue samples. Or that can be read in such a way as it would

1 still allow. The other thing is I wanted to know, although we're not really discussing
2 fully the substance of it, my impression, looking through the report, the very useful
3 charting that is in the staff document, is that other than situations in which the particular
4 group making the recommendations doesn't make the distinction at all, and just applied
5 the same rules to all categories, almost all of them in some fashion treated differently the
6 anonymous versus the encrypted or coded. And so it really does make very stark how,
7 compared to the LC group and HHS thinks in terms of the existing regulations, we
8 would look very, very different just in our way of describing the world by going with the
9 standards that are here. Now I understand the argument was well you start off by saying
10 that there are these "categories" but you say you don't want to apply different rules to
11 them so you might as well treat them all as one category. But even that step of saying
12 we're going to end up describing them all as one category will look very different. It
13 doesn't mean it's wrong, it's just that we should be very clear that we are departing from
14 the way that almost everybody has looked at this.

15 DR. SHAPIRO: Steve.

16 MR. HOLTZMAN: I think it's very important for our terminology to be
17 accessible and be explained against the backdrop. If we want to define certain categories
18 in terms of the policies we use, we should make that very clear. Just for the record, and
19 Zeke is unfortunately not here, some of us... Some of us who are neither Columbia nor
20 Yale nor wherever-trained lawyers, okay, or lawyers at all, but feel we have some sense
21 of plain-speaking language, actually read this entirely differently than you do without any
22 twisting of logic whatsoever. Because I find important the phrase, "recorded by the
23 investigator," okay. And maybe we...and therefore the notion, or what I wanted to say is
24 that when I was first exposed to this subject, I found it a real twist of the logic—the
25 notion that it was based on the nature of the sample as opposed to how it was being
26 used. Because it goes to the logic of what you're trying to protect, which is the subject.
27 And if in the nature of the study, you can...it's in the nature of the study that they cannot
28 be identified, that they would be protected.

29 DR. SHAPIRO: Okay, Tom, then Alta, then David.

30 DR. MURRAY: There's a distinction, one distinction which I think is
31 important that I would like...that I believe is a good one to make. And that is between
32 whether or not the tissue is effectively anonymous in its use by the investigator versus
33 whether the tissue in its original state, say, held in the collection somewhere, is
34 anonymous. And we've opted for the former and I think that is ...that's the right thing to
35 do and I will be happy to talk about that more tomorrow.

36 Now, that still leads to a series of distinctions about what makes tissue

1 anonymous in its use in research. And there I think we've got several different
2 distinctions and I will also offer some of them. And I think I just don't want to confuse
3 the first distinction with a series of other things having to do with whether or not there's
4 a coding scheme that will allow someone to reidentify the tissue, whether it comes with
5 lots of additional demographic information versus no demographics. Those are other
6 kinds of distinctions that we do need to focus on because I think there was merit in the
7 criticism last time that we were not careful enough in making those distinctions. So I
8 think we do need to make those. But I would...I'm going to propose tomorrow that the
9 first one is a useful one for it.

10 DR. SHAPIRO: Alta.

11 MS. CHARO: I'd like to make a suggestion about the vocabulary being
12 used. The word anonymous is being used in different ways by different people. For
13 example, in Melissa's memo she uses the word anonymous to mean unidentifiable by any
14 possible means. She does not use the word anonymous to mean coded so that it's
15 impossible for anybody without a code-breaker to know about whom the tissue is...from
16 whom the tissue is brought. And yet in our own..in the Subcommittee's own work, the
17 word anonymous seems to be used for coded samples in many situations. And so I'd like
18 to suggest an abandonment of the word anonymous because it is prone to so many
19 differing and perfectly natural interpretations. Just for the sake of making sure we all
20 know what we're saying when we say it. And to suggest no matter what rules eventually
21 emerge, and whether or not they're the same for any of these different categories, that
22 we stick to "unidentifiable," meaning there's no way anybody outside of an admission
23 team could track back the tissue to the donor. Unidentifiable, period, end of story, no
24 links at all, coded for those things that are linked, and identified for those that come with
25 a name. Tom has already...I'm open to suggestions but something that's truly clear so
26 that at least when we continue to talk we all know what we're saying.

27 DR. MURRAY: I actually like the idea of talking and saying
28 nonidentifiable or unidentifiable rather than anonymous. I am perfectly happy with that. I
29 think...maybe should I wait...no I'll say it very quickly. I'm sure we'll talk more about it
30 tomorrow. In Shawn's memo, he talks about the standards the Secretary offered,
31 reasonable, a standard of reasonableness. They reasonably—I don't have the precise
32 language here—be regarded as nonidentifiable. I think, I don't think we want a standard
33 of divine unidentifiability. I think we want a standard of reasonable unidentifiability.

34 MS. CHARO: But if you go back to the history of that, what we're
35 talking about there really is about the *N* in various of your boxes. I mean if you've got
36 certain kinds of demographic data, does it yield the ability to know who it came from
37 right ... so it was not by implication. If you've got it coded and you've got a big enough

1 firewall, it renders it unidentifiable. That was not the intent behind that notion. It was
2 that demographic data does not render something identifiable. It can still be considered
3 unidentifiable so long as the N is large enough that you don't know who it's from. And
4 that's very different from coded data.

5 DR. SHAPIRO: David?

6 DR. COX: I'd like to step back for a second and ask a broader question.
7 What are we really talking about? What's our goal? And I think Pat Barr at our last
8 NBAC meeting did this quite eloquently. Because it's not really whether one should look
9 at the definition of what's anonymous or identifiable or any of that, but what is it...why
10 are we considering this issue? And we're considering it, in my view, to figure out how to
11 in one hand use stored tissue samples to advance research, and on the other hand
12 protecting subjects' rights in the process of doing that. And so I think that one of the
13 reasons why this discussion continues to focus on this statement about what's identifiable
14 or what's not identifiable, is really sort of obfuscating what the real issue is, which is are
15 things okay the way they are now or is it going to require a change in the way we're
16 doing business? I can't answer that question unless I step back and say, what is it we're
17 trying to achieve, what's going to be the practical structure in which we're going to
18 achieve it? So talking about it in context of firewalls that don't exist is very difficult for
19 me. Talking about it in the context of structures that may exist right now, that allow
20 research to be ongoing and then say do they afford the appropriate human subjects
21 protections, I find a much more useful endeavor. So that's what I'm going to try and do
22 tomorrow. And not really have a discussion about is there a way to sort of fit this into
23 the present regs or not. I mean I don't find that useful. I see why it's one way of looking
24 at the problem, but I don't find it nearly as useful as saying what is it we're trying to
25 accomplish and is things that we have in place right now sufficient to allow that to take
26 place.

27 DR. SHAPIRO: David, I'd like to ask a question which really came from
28 an issue which you raised last time and as also, we don't have time to resolve today, but
29 we can get back to it tomorrow. You may remember that you raised—I believe it was
30 you that raised the issue—that you looked at all the interesting research that's been
31 going on, that it really required extensive access to the medical records in order to make
32 some sense out of it, in order to carry the projects forward in most cases. And indeed if
33 you look at Dr. Korn's paper, his examples have that characteristic. Many of these cases
34 required detailed knowledge of the medical record of 70 or 80 subjects or whatever it
35 was in order to carry forward. Now to the extent that that's correct, you always need a
36 lot of information but nameless, Social Security number aside, so it's not name and
37 address, but it's substantial medical information or substantial information content. I'm
38 trying to figure out in my own mind whether that per se will make this identifiable and

1 whether one is really faced with that sort of irreducible problem. That you need enough
2 information or you don't. Given what you think about...and it's really a question of what
3 the scientific agenda looks like in this area.

4 DR. COX: So Harold, I'll give you my answer to that. That's exactly
5 where I'm coming from personally, because I think that if the scientific research is going
6 to lead to something that's useful, which to me is a therapy, then to think about that
7 you're just going to not need...not every single piece of research that's being done is
8 going to need the detailed medical records. But ultimately a structure that allows that to
9 happen and focuses primarily on that end of it instead of what the traditional end has
10 been which is that you just do it where you don't need the medical record. I think that's
11 what's different here. And the... and so I don't believe that the structure that we're
12 looking at right now and that we've used for the past hundred years is going to serve us
13 well in the next hundred years.

14 MS. CHARO: Harold, a lot of the information you need really does not
15 identify people, you know, 36-year old female with following condition and following
16 history, right.

17 DR. SHAPIRO: I'm just asking a question. I don't have a view of it.

18 MS. CHARO: Right, but the...as long as the cell slide is large enough that
19 is doesn't reduce it to two people in the country, you know, on this particular
20 Chippewah reservation in Wisconsin, you're not going to have this problem. But the
21 trick that exists is when what you want to do then is move forward and continue
22 tracking, not the person but their medical records.

23 DR. SHAPIRO: That's what scientists want to do, you know.

24 MS. CHARO: Right. That's exactly...in some ways this is a very
25 temporary problem because for all the people that are already dead the entire medical
26 record is accessible already. So you can get their entire life history with the disease. For
27 the people whose tissues are just being collected now, you can in fact create a
28 prospective consent process that allows for going back into the medical record and
29 extracting information. So it's only for people who've got existing tissue or currently
30 alive, part of their prior medical history...their medical history prior to the tissue
31 collection is accessible and what you want is only their current and future medical status.
32 It's a transient problem in some ways that is creating all this enormous....

33 DR. COX: I think I really disagree with that, Alta. I don't think it's
34 transient. And Harold, you said it in a very nice way in this other issue in terms of

1 staging. Now maybe this is not a good analogy but that's the way I'm using it, because I
2 think that one of the ways that much of this research is done is first you go and you look
3 at a very large sample of people, and then you would say I want to look at a subset of
4 those people in more detail. And then you look at even a more subset of those people.
5 Now certainly the conclusions that you come to ultimately you'd like to go out and apply
6 it to a very broad-based number of people. But the process by which the research is done
7 is that getting a sample and then learning more about that sample and learning even more
8 about the subsample of that. The, I think that that's the process. And given that being the
9 process, to set it up so that everything is well, you don't really need to know that much
10 about a particular group of people, in fact the process says just the opposite, that what
11 you want to do is learn more and more and more. Now it depends on what the stage
12 you're at is, because if people always stay at one stage and they're just at that general
13 stage, they never need to learn more. But what are we trying to accomplish? We're
14 trying to accomplish more detailed information and more specific clinical trials to come
15 up with therapies than I think that you do get more and more detailed information. So
16 it's the staging where you have broad numbers of people and then more specific, and
17 then you get more specific.

18 DR. SHAPIRO: In that environment I think Alta's right. A lot depends
19 on whether the material you need as you go ahead in the process you describe is the
20 prospectively collected or whether it requires going back to stored tissue. All right, we
21 will get our chance to exercise a good deal of this tomorrow again. So...let's not...

22 MR. HOLTZMAN: It's not a transient problem.

23 DR. SHAPIRO: Oh that's not. I understand that.

24 MR. HOLTZMAN: We're going to continue to have the issue of people
25 giving tissues in the surgical context simply or under generalized consent because you
26 can't envision all of the future studies you will want to do and you will want to have a
27 system to continue this epidemiological information, it can be more and more detailed
28 but it won't necessarily be sufficient to identify the individual.

29 MS. CHARO: Wisconsin is currently writing up a surgical consent form
30 that will allow people to release for an enormous variety of currently unforeseeable uses.
31 So I do think it's possible to have for prospective collection a solution for this problem.

32 MR. HOLTZMAN: And therefore those samples will have to be
33 maintained in a fashion such that they are not unidentifiable, using nomenclature.

34 MS. CHARO: You mean, in other words, coded.

1 MR. HOLTZMAN: Sure.

2 DR. SHAPIRO: The issue for me, Alta, there is I'm sure that those kinds
3 of consent forms can be structured. Now I haven't looked at...

4 MS. CHARO: Whether or not they're legitimate.

5 DR. SHAPIRO: ... but whether they have..what the ethical content of that
6 kind of thing is as exactly the issue that we're going to have to struggle with.

7 MR. CAPRON: But isn't part of the issue here whether the consent
8 should basically be a little bit clearer notification that such research is out there, do we
9 have your permission to get back to you about this, or to use your—one choice, which is
10 what the cancer people suggested we look at—or to use this tissue without your further
11 consent provided that we do it only with coding so that we won't have your name on the
12 sample. I mean that choice could be put to somebody in a way...which in effect says
13 before you really get involved in research, we'll come back to you with the specific
14 project and we'll get your consent. But what we're asking for now is whether you want
15 to have this tissue that's available for that, just be alerted that this is going on. And that
16 would be a huge change because all the studies that we've seen indicate that most people
17 don't even know that their tissues are saved and used for research.

18 DR. COX: Yes. But, Alex, the process ... what you just described is the
19 way the process of research is going to be done. And you said the bottom line: it's a
20 huge change from what we're doing right now in terms of how the people that are giving
21 the samples are involved in the process.

22 MR. CAPRON: But we're...I think what, frankly, what I sense the
23 tension in this room is when I was talking about the Secretary of HHS. There is a
24 conflict of priorities here. And we can derive any conclusions we want. It's appropriate
25 that we be a body that represents the spectrum of views but there is that conflict of
26 priorities and we're going to be pressed to come up with the most reasonable balance of
27 those priorities.

28 DR. SHAPIRO: With that we are four minutes past our adjournment
29 time. And it's the first time we've allowed us to go past adjournment. So thank everyone
30 very much. Eric, what time do we reassemble tomorrow morning?

31 DR. MESLIN: Tomorrow morning we're at 8:00 a.m. And we're in the
32 Wilshire Room, which is just around the corner, same floor, just out the back of the
33 doors here. It's the entire Wilshire. You get three chairs a person. We'll see you at 8:00

1 tomorrow morning. Thank you very much.

2 ADJOURNMENT, DAY 1: 5:34 p.m.